Katholieke Universiteit Leuven
Group Biomedical Sciences
Faculty of Medicine
Department of Public Health
Centre for Biomedical Ethics and Law

Symptom Prevalence and Symptom Treatment in Patients Staying at Residential Palliative Care Units. What is the Role of Palliative Sedation?

Patricia CLAESSENS

Doctoral thesis in Biomedical Sciences

Leuven,19.11.2012

Katholieke Universiteit Leuven
Group Biomedical Sciences
Department of Public Health
Centre for Biomedical Ethics and Law

Symptom Prevalence and Symptom Treatment in Patients Staying at Residential Palliative Care Units. What is the Role of Palliative Sedation?

Patricia CLAESSENS

Jury:

Promoter: Prof. Dr. Paul Schotsmans
Co-promoter: Prof. Dr. Bert Broeckaert & Prof. Dr. Johan Menten
Chair: Prof. Dr. Kris Dierickx
Secretary: Prof. Dr. Koen Milisen
Jurymembers: Prof. Dr. Bernadette Dierckx de Casterlé, Prof. Dr. Bart Van Den Eynden, Prof. Dr. Sam Ahmedzai, Prof. Dr. Kris Vissers, Prof. Dr. Martin Hiele

Leuven, 19.11.2012

Doctoral thesis in Biomedical Sciences

aan Victor en Margot

et je veux te voir voler
libre dans le ciel
toucher les étoiles
savoir que tu es belle
je ne peux que t'apprendre
m'apprendre à te lâcher
aimer c'est aussi un peu ça

(Axelle Red)

Aan Christophe

Sail away with me
What will be, will be

(David Gray)

DANKWOORD

Het behalen van dit doctoraat is voor mij het einde van een lange rit geweest. Een rit waarbij ik veel mensen heb mogen ontmoeten en vooral waarbij ik door ontelbaar veel mensen ben bijgestaan. Zonder elk van deze personen had ik hier vandaag niet gestaan. Nu rest mij het meest belangrijke van al mijn taken vandaag, namelijk het bedanken van deze personen die het verschil gemaakt hebben op deze lange weg.

Mijn oprechte dank gaat uit naar mijn promotor Prof. Dr. Paul Schotsmans en mijn co-promotoren Prof. Dr. Bert Broeckaert en Prof. Dr. Johan Menten. Bedankt voor jullie begeleiding, kritische commentaren en opbouwende feedback, maar vooral bedankt voor jullie aanhoudend geloof in dit doctoraat. Zoals ik had beloofd, jullie hebben wel iets langer moeten wachten dan ik initieel dacht, presenteer ik jullie vandaag ‘mijn doctoraat’.

Dank wil ik uitspreken aan alle leden van de examencommissie, die vanuit hun kritische zin, dit werk hebben aangestuurd en mee vorm hebben gegeven.

Het FWO en andere sponsoren, verdienen een woord van dank. Zonder hun financiële steun was dit onderzoek onmogelijk geweest.

Er zijn heel wat mensen actief betrokken geweest bij het uitvoeren van dit onderzoek – aan alle betrokken instellingen, de hulpverleners en niet in het minst de patiënten mijn oprechte dank om mij iedere keer weer te woord te staan en ontelbare keren de vragenlijsten in te vullen! Jullie hebben mee ‘een steen verlegd in de rivier’. Liesbeth, bedankt voor de hulp bij het verzamelen van de gegevens van de eerste pilootstudie! Als masterstudent was het niet altijd even gemakkelijk om aan dit project mee te werken. Je hebt schitterend werk geleverd. Kristel, ook jij van harte bedankt. Gedurende een jaar hebben wij samen de voorbereiding van de dataverzameling en de opleiding van de verpleegkundigen uitgewerkt.

De leden van de werkgroep research van de Federatie Palliatieve Zorg, bedankt voor jullie feedback doorheen het proces.

Bernard Bruggeman, Luc De Visschere en Hans De Clerck wil ik bedanken voor hun geloof in en ondersteuning bij dit project.

Aan de Arteveldehogeschool – Prof. Veeckman bedankt omdat je mij de ruimte hebt gegeven, binnen mijn job, om dit project tot een goed einde te brengen. Pascal, oprechte dank omdat je aan mij dacht toen je centen ter beschikking had en om er voor te zorgen dat ik 'in quarantaine' aan deze eindsprint kon werken! Claire, bedankt om mij even vrij te laten! Aan elk van jullie, de last is van mijn schouders en ik ben klaar om er voor te gaan!

Aan alle collega's van de Arteveldehogeschool, bedankt voor jullie interesse, jullie steun en vooral de geanimeerde ontspannende gesprekken! Een speciaal woordje van dank aan Patrick, alias 'voâdere', weet je nog wat ik dacht toen ik als 'groentje' op Artevelde aankwam, …, laat het duidelijk zijn, …, het tegendeel is bewezen! Bedankt omdat je er altijd was!

Mijn ouders, bedankt om me te laten zijn wie ik ben, en om ervoor te zorgen dat ik geworden ben wie ik nu ben! Zonder jullie aflatende steun stond ik hier vandaag niet! Patrick, Mady, Marilyn, Maria en alle andere familie en vrienden, jullie zorgden voor ontspanning, logistieke ondersteuning, kortom alles wat je nodig hebt om aan het einde van een doctoraat te geraken.

Christophe, Victor en Margot, jullie zijn de drijfveer in mijn leven! Bollie, bedankt voor het geloof, de steun, de bemoedigingen als het even moeilijk ging. Ik ben er nu, …, de rugzak valt af, …, 'sail away with me, what will be will be, …(D. Gray).

21st of October 2012

Patricia Claessens

TABLE OF CONTENTS

CHAPTER 1: GENERAL INTRODUCTION

When I use a word, "Humpty Dumpty said in a rather scornful tone,
"It means just what I chose it to mean – neither more nor less."
"The question is," said Alice,
"Whether you can make words mean different things."

Lewis Caroll,
Alice's adventures in Wonderland

PROBLEM STATEMENT

In taking care of the terminally ill patients, who are subject to a multiplicity of symptoms (Hermann & Looney, 2001), palliative care experts are often confronted with symptoms that are difficult to treat. Although with the necessary skills most of these symptoms can be controlled quite well, a number of symptoms, though treated, are not sufficiently relieved (Rousseau, 2004; Lo & Rubenfeld, 2005; Hasselaar et al., 2007; Jansen, 2010). These not adequately manageable symptoms are called *refractory symptoms* and can be distinguished from difficult symptoms because they cannot be adequately treated without compromising the patient's consciousness (Menten, 2003; Salacz & Weismann, 2005; Vissers et al., 2007; Juth et al., 2010; Olsen et al., 2010).

Palliative sedation holds a prominent place as one of the options of last resort when patients are confronted with refractory suffering (Quill et al., 1997; Quill et al., 2000; Quill et al., 2009; Cherny et al., 2009; Juth et al., 2010; Olsen et al., 2010) and as such is increasingly implemented in different palliative care programs all over the world (Boyle, 2004; Howland, 2005; Cunningham, 2008; Anquinet et al., 2011).

Although palliative sedation is an important and necessary therapy for some patients at the end of life, it is linked with potential adverse outcomes and risks – such as loss of the ability to feel, think and interact, distress among families, a life-shortening effect etc. (Cherny et al., 2009). For these reasons palliative sedation remains a much debated and controversial issue within and outside the palliative care (Billings & Block, 1996; Craig, 2002; Taylor, 2003; Tännsjö, 2004; Cooney, 2005; Howland, 2005; Vissers et al., 2007; Cassell & Rich, 2010; Jansen, 2010; Olsen et al., 2010). and raises relevant ethical questions which cannot be neglected. Many of these ethical questions remain unanswered due to inconsistencies and a lack of clarity in published –often retrospective studies- on this topic (Ventafridda et al., 1990; Fainsinger et al., 1991; Stone et al., 1997; Chater et al., 1998; Fainsinger et al., 1998a; Fainsinger et al., 1998b; Peruselli et al., 1999; Morita et al., 1999; Fainsinger et al., 2000 a,b; Menten, 2003; Hasselaar et al., 2008).

To prevent the care of terminally ill patients being undermined by an abusive, injudicious or unskilled use of sedation (Cherny et al., 2009), there is an urgent need for more clear and rigorous information based on clinical research data concerning the practice of palliative sedation. All the more because care for patients with life threatening illnesses will become more frequent in the ageing population due to an increase of cancer diagnoses and non-malignant progressively deteriorating incurable disorders (e.g. dementia, liver or kidney insufficiency, respiratory or cardiac failure…)

(Cannaerts et al., 2004). Systematic and methodologically correct research – in this case prospective, longitudinal studies - in which the use of palliative sedation is evaluated in relation to symptom prevalence and symptom treatment, level of consciousness and food and fluid intake can clarify this picture . By using sound frameworks, it will become clear when, why and how clinicians use sedation for patients suffering a terminal malignant or non-malignant disease.

AIMS OF THE STUDY

This research project aims to describe the characteristics of patients who are being sedated for refractory symptoms in Flemish palliative care units (PCU's) from the time of admission until the day of death. Following research questions will be answered:

1. What is the profile of patients who are being sedated for refractory symptoms in palliative care units in terms of demographics, functional status, level of consciousness and food and fluid intake and this from the day of admission until the day of death?

2. How many palliative care patients, residing in a PCU, ultimately receive palliative sedation?

3. Which type of sedation is used (intermittent or continuous, deep or mild) and why?

4. What is the profile of patients receiving palliative sedation residing in a PCU in terms of symptom prevalence and symptom distress?

5. What is the severity, the frequency and level of distress of refractory symptoms that give rise to a discussion of sedation as therapeutic option?

6. Does the patient receive food and/or fluid during sedation? How does this relate to food and fluid intake during the period before sedation and is this different from non-sedated patients?

7. How does the level of consciousness evolve during the PCU-admission in sedated and non-sedated patients?

CONCEPTUAL BACKGROUND

To be able to give meaning to the results of this study it is important to make clear what is meant by 'palliative sedation'. Although different attempts have been made to conceptualize palliative sedation (also called terminal or controlled sedation or palliative sedation therapy) (deGraeff et al., 2007; Vissers et al., 2007; Hasselaar et al., 2007), there is still a lot of indistinctness and disagreement concerning terminology and even more with regard to the definition of palliative sedation (Cooney, 2005; Hasselaar et al., 2007; Broeckaert, 2008; Rietjens et al., 2008; Hauser & Walsh, 2009; Cassell & Rich, 2010).

TERMINAL SEDATION VERSUS PALLIATIVE SEDATION

During the past years several different terms were used in literature for the practice of palliative sedation. One of the terms – that has become widespread – is 'terminal sedation' (Ventafridda et al., 1990; Enck, 1991; Greene & Davis, 1991). Progressively this term became subject of debates and several authors disagreed to use this term (Broeckaert, 2000; Broeckaert 2002; Broeckaert & Nuñez-Olarte, 2002; Broeckaert, 2008; Krakauer, 2000; Cowan & Palmer, 2002; Jackson, 2002; deGraeff & Dean, 2007; Koh et al., 2009; Van Delden, 2007; Cassell & Rich, 2010) Two major points of concern are stated. 'Terminal sedation' is a very vague term and has a negative connotation (Broeckaert, 2000; Broeckaert, 2002; Broeckaert & Nuñez-Olarte, 2002; Broeckaert, 2008). It might insinuate that sedation 'terminates a patients' life' (Broeckaert, 2000; Broeckaert, 2002; Broeckaert & Nuñez-Olarte, 2002; Broeckaert, 2008). This term ignores that sedative doses are given in relation to the intensity of the suffering (principle of proportionality) and as such are not always maintained until death. Moreover this term might blur the line between euthanasia and palliative sedation (Broeckaert, 2002; Broeckaert & Nuñez-Olarte, 2002) and is most used by those who oppose to palliative sedation because they believe it is a form of 'slow euthanasia' (Van Delden, 2007).

Since the growing dissatisfaction about the term 'terminal sedation', a variety of other terms have been and are being proposed. One is 'controlled sedation' (Cherny & Portenoy, 1994; Vermylen & Schotsmans, 2000). Others are 'sedation for intractable distress in the dying' (Krakauer, 2000; Chater et al., 1998), 'sedation in the imminently dying (Carver & Foley, 2000; Janssen & Sulmasy, 2002; Wein, 2000), 'total pharmacological sedation' (Peruselli et al., 1999), and 'sedation' (Ventafridda, 1990; Stone et al., 1997; Fainsinger et al., 2000a,b; Chiu et al., 2001; Fondras, 1996;

Kohara et al., 2005; Müller-Bush et al., 2003). Unfortunately, all of these terms have one or more shortcomings (Broeckaert, 2002) and are therefore not fully convincing.

In 2000 Broeckaert introduces the term 'palliative sedation' (Broeckaert, 2000; Broeckaert, 2002; Broeckaert & Nunez-Olarte, 2002) a term which several other authors and organizations share by now (Juth et al. 2010; de Graeff et al. 2007; Lo & Rubenfeld 2005; Menten 2003; Keizer & Swart 2005; Morita 2004 a,b; Morita et al. 2004 a,b; Porta Sales 2002; Rousseau 2000; Cherny et al., 2009) and which possesses a number of benefits. In contrast with 'terminal sedation', 'palliative sedation' refers to the use of sedation in a palliative care setting. It encompasses the intention of reducing the impact of symptoms in order to limit the amount of suffering a palliative patient is confronted with (Broeckaert, 2002; Broeckaert & Nunez-Olarte, 2002). This term allows to differentiate between the various forms of sedation that exist within palliative care (deep vs mild – intermittent vs continuous) (Broeckaert, 2002; Rietjens, 2009). For these reasons we will use the term 'palliative sedation' to describe the practice of sedation for the management of refractory symptoms at the end of life.

DEFINING PALLIATIVE SEDATION

In line with the evolution described above, a lot of different definitions have been proposed in the literature for sedation in palliative care, some being rather broad, but the majority being very strict and narrow (Claessens et al., 2008).

Although narrow descriptions are in a lot of ways correct, they often just describe a specific part of the practice of palliative sedation or one specific form of palliative sedation. For the purposes of research, these narrow definitions can be very relevant because they allow to delimit the focus of the research. For use in clinical practice, however, these narrow definitions, pose several problems. Regardless of the conceptual indistinctness they bring about, it is impossible to get a clear insight in the practice of sedation when this is based on very restricted definitions.

In order to be able to define palliative sedation in a way that it entails all possible theoretical options of the practice and to make sure that each palliative patient who might need palliative sedation receives it, we need a broad definition based on the core elements of the clinical practice. An accurate description of palliative sedation is crucial to distinguish palliative sedation from euthanasia and to answer some of the ethical issues that might arise when dealing with this aspect of palliative care (Broeckaert & Nunez-Olarte, 2002).

Taken into account the aim of this research, we believe that the definition that Broeckaert developed in 2000 is the most appropriate definition to be used for this study. Broeckaert (2002) defines palliative sedation as:

> *"The intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms (Broeckaert, 2002)."*

This means that palliative sedation is an intentional medical treatment, based on the notion of adequacy and proportionality and thus entails all forms of sedation (deep-mild, intermittent-continuous), for refractory symptoms in patients with a limited life expectancy (Broeckaert & Nunez-Olarte, 2002; Hauser & Walsh, 2009; deGraeff & Dean, 2007; Kirk et al., 2010).

By using this definition we will be able to capture all possible cases of palliative sedation that occur and give a clear description of the variety of the clinical practice as it occurs nowadays on specialised palliative care units in Flanders.

OUTLINE OF THIS DISSERTATION

This dissertation presents the results on the above-mentioned research questions. **Chapter 2** provides a review on the body of literature that is available on the topic of palliative sedation. Research literature is included and an overview is given on prevalence figures, indications for sedation, survival, link with food and fluid intake, decision making processes and attitudes of physicians. **Chapter 3** addresses the results of a validation study of a modified version of the Edmonton Symptom Assessment Scale. This scale was used to measure the symptom distress and symptom experience. **Chapter 4** describes the characteristics of patients, from the time of admission until the day of death, who were being sedated at some time for refractory symptoms in palliative care units. **Chapter 5** focuses on the evolution of the oral and artificial food and fluid intake of the patients. A description is given of the effect of initiating palliative sedation on the oral and/or artificial food and fluid intake of terminally ill patients. **Chapter 6** reports in detail on the evolution of the level of consciousness of patients residing in palliative care units from admission until their day of death. In doing so, we specifically want to find out what the impact is of palliative sedation/use of sedatives on the level of consciousness of terminally ill patients. In **chapter 7** we elaborate on the role of the nurse in coming to a decision on palliative sedation, carrying out palliative sedation and caring further for the patient and his family. In doing so, the focus is on the multi-disciplinary character of the decision-making process and how the

emotional burden of the several care providers can be diminished. This dissertation closes with a discussion of the most important findings and summarizes the implications for future research and clinical practice.

CHAPTER 2: LITERATURE REVIEW

Published: Palliative Sedation: a Review of the Research Literature. Journal of Pain and Symptom Management, 2008, 36, 310-333.

ABSTRACT

The overall aim of this paper is to systematically review the following important aspects of palliative sedation: prevalence, indications, survival, medication, food and fluid intake, decision making, attitudes of physicians, family experiences, and efficacy and safety. A thorough search of different databases was conducted for pertinent research articles published from 1966 to June 2007. The following keywords were used: end of life, sedation, terminal sedation, palliative sedation, refractory symptoms, and palliative care. Language of the articles was limited to English, French, German, and Dutch. Papers reporting solely on the sedatives used in palliative care, without explicitly reporting the prevalence or intensity of sedation, and papers not reporting on primary research (such as reviews or theoretical articles) were excluded. Methodological quality was assessed according to the criteria of Hawker et al. (2002). The search yielded 130 articles, 33.8% of which were peer-reviewed empirical research studies. Thirty-three research papers and one thesis were included in this systematic review. This review reveals that there still are many inconsistencies with regard to the prevalence, the effect of sedation, food and fluid intake, the possible life-shortening effect, and the decision-making process. Further research to clarify all of this should be based on multicenter, prospective, longitudinal, and international studies that use a uniform definition of palliative sedation, and valid and reliable instruments. Only through such research will it be possible to resolve some of the important ethical issues related to palliative sedation.

PROBLEM STATEMENT

Patients suffering from a terminal illness, with or without a malignancy, are often confronted with several symptoms during the last phase of their lives (Georges et al., 2005; Hermann & Looney, 2001). In the majority of cases these symptoms can be controlled successfully (Vainio et al., 1996; Zech et al., 1995; Ahmedzai, 1997). However, in some patients symptoms remain uncontrollable (Lo & Rubenfeld, 2005; NEC, 2006). These refractory symptoms may be physical or psycho-existential (Cherny & Portenoy, 1994; Müller-Bush et al., 2003; Menten, 2003). Refractory symptoms differ from difficult or 'difficult-to-treat' symptoms, because despite multiple efforts of clinical experts they cannot be adequately treated without compromising the consciousness of the patient (Cherny & Portenoy, 1994; Menten, 2003). They have a major negative effect on patient functioning and well-being (Menten, 2003; Coyle et al., 1994; Cherny et al., 2009), often increase as the patient approaches the end of life (Ventafridda et al., 1990); and interfere with a peaceful dying process. Palliative sedation has been placed in the foreground as one of the options of last resort when patients are confronted with refractory suffering (Quill et al., 1997, 2000; Cherny, 2006). As such, palliative sedation is increasingly implemented by palliative care programs (Howland, 2005; Boyle, 2004).

For more than 20 years now, palliative sedation has been a much debated and controversial issue within and outside the field of palliative care. Some authors have described it as a form of slow euthanasia, an alternative for euthanasia, or mercy killing in disguise (Howland, 2005; Billings & Block, 1996; Craig, 2002; Taylor, 2003; Simon et al., 2007). According to these authors, palliative sedation is highly problematic and is associated with many important ethical questions. Despite a very extended theoretical discussion in the medical literature, most of these questions remain unanswered due to the lack of conceptual clarity, clear definitions, and guidelines, and the huge number of contradictions in the international empirical literature on the subject (Rousseau, 2003; Claessens et al., 2003).

In this paper we systematically review the published research literature on palliative sedation. Since we introduced the term 'palliative sedation' in 2000, to overcome the drawbacks of other terms, we chose to use this term in this article to label the practice of sedation in palliative care (Broeckaert, 2002; Broeckaert & Nuñez-Olarte, 2002). In this review, we give an overview of the available results published in the medical literature with regard to the practice of palliative sedation. These results are critically reviewed in relation to the methodologies used to obtain them and the limitations confronted

when doing research in a palliative care population. Suggestions for further research are also advanced.

METHODOLOGY

SELECTION AND DESCRIPTION OF INCLUDED STUDIES

To retrieve the most relevant literature on palliative sedation, we conducted a thorough search of the following databases for pertinent research articles published from 1966 to June 2007: Pubmed, Cancerlit, Cinahl, Cochrane, Libis (books), and Invert (Dutch articles). The following keywords were used in different combinations: end-of-life, sedation, terminal sedation, palliative sedation, refractory symptoms, and palliative care. The search yielded a total of 134 relevant articles, 35.8% of which were peer-reviewed empirical research studies and 23.13% of which were peer-reviewed theoretical articles (Table 1). We limited the language of the articles to English, French, German, and Dutch. Papers reporting solely on the sedatives used in palliative care, without explicitly reporting the prevalence or intensity of sedation, and papers not reporting on primary research (such as reviews or theoretical articles) were excluded for the purpose of our review. The methodological quality of the articles was assessed according to the criteria of Hawker et al. (2002) (Table 2). Each part of the study was appraised as good, fair, poor, very poor. Total scores could vary between 9 and 36 were 9 = very poor, 18 = poor, 27 = fair, 36 = good.

Table 1:

Study type of the articles

Study type	N	%
Empirical study – peer reviewed	48	**35.82**
Theoretical paper – peer reviewed	31	**23.13**
Research paper – non-peer reviewed	0	**0**
Theoretical paper – non-peer reviewed	4	**2.99**
Professional document	0	**0**
Case study	14	**10.44**
Dissertation	1	**0.75**
Comment/editorial/letter	25	**18.66**
Review	9	**6.72**
Other	2	**1.49**
Total	**134**	**100**

Bold faced numbers represent the relative frequency, the percentage of the amount of articles versus the total amount of articles

Based on the above-mentioned inclusion criteria, 36 research papers and one doctoral dissertation were included (Table 3 & 4). Of these 37, 19 described 14 separate retrospective studies (Table 3), eight (Rietjens et al., 2004, 2005, 2006; Miccinesi et al., 2006; Chater et al., 1998; Morita, 2004b,c; Van der Heide et al., 2007) of which were based on the reports of physicians. Eighteen of the 37 papers described prospective studies (Table 4).

The majority of the papers focused on a description of the practice of palliative sedation (prevalence, medication used, survival, decision making). Two papers, however, reported on the family's experience with palliative sedation (Morita et al., 2004a; Morita et al., 2004d), six papers gave an overview of the attitudes of physicians towards palliative sedation (Simon et al., 2007; Morita et al., 2002a; Morita et al., 2002b; Müller-Bush et al., 2004; Kaldjian et al., 2004; Blondeau et al., 2005), one paper evaluated the efficacy and safety of palliative sedation (Morita et al., 2005a), one paper evaluated the attitudes of the lay public on palliative sedation (Morita et al., 2002b), one paper compared the attitudes of the physicians with that of the lay public (Morita et al., 2003) and one paper compared palliative sedation with euthanasia (Rietjens et al., 2006) (Table 3,4).*Table 2*

Methodological Appraisal According to Criteria of Hawker et al., 2002

	Good	Fair	Poor	Very Poor	Comment
Abstract and title					
Introduction and aims					
Method and data					
Sampling					
Data analysis					
Ethics and bias					
Findings					
Transferability/generalizability					
Implications and usefulness					

Table 3
Overview of Retrospective Studies

Author(s) Year of publication	Purpose	Sample	Results
Rietjens et al., 2004 Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands **Rietjens et al. 2005** The practice of terminal sedation in the Netherlands **Rietjens et al. 2006** Terminal sedation and euthanasia	To describe the practice of terminal sedation in the Netherlands Comparison of cases of euthanasia and terminal sedation based on their clinical characteristics	Quantitative, retrospective, face to face interviews based on structured questionnaire with regard to cases of sedation in past year, Netherlands N = 410 physicians (51% clinical specialists, 30% general practitioners & 19% nursing home physicians), 51% men, face-to face interviews using structured questionnaire, based on case of last patient that received terminal sedation *Terminal sedation = the administration of drugs to keep the patient in deep sedation or coma, until death, without giving artificial nutrition or hydration.*	**Prevalence**: 52% of physicians ever practiced terminal sedation Terminal sedation was used in 10% of all deaths during 2000-2001. **Patient characteristics (n = 211):** 78% ≥ 65 year, 54% patients with cancer, 47% male **Indications:** 51% pain, 38% agitation, 38% dyspnea, 11% anxiety **Decision-making PS:** 59% physician discusses with patient, 93% with family, 79% discussed with other caregivers, 17% not discussed with other caregivers **Medication:** 21% benzodiazepines, 35% combination of benzodiazepines and morphine and 4% benzodiazepines in combination with other drug **Intention with regard to PS:**36% without intention to hasten death, 47% partly intention to hasten death, 3% explicit intention to hasten death **Survival:** 40% physicians believed that life was shortened by 24 hours or less, 27% believed by more than one week **Comparison PS and euthanasia:** PS was mainly done in hospital, euthanasia at home, pat. receiving PS were older (p<.001); less pat. with PS had cancer (54%), patients with PS suffered more anxiety (p<.001), confusion (p<.001), depression (p = .06), bedsores (p = .002), loss of appetite (p = .003), unclear consciousness (p< .001), inactive (p = .001), sedated patients more pain and dyspnea and more often very ill.

Table 3
Continued

Stone et al., 1997 A comparison of the use of sedatives in a hospital support team and in a hospice	Determine the frequency, indications and doses of sedative drugs used in a hospital support team and in a hospice inpatient unit, determine how long patients survived after being sedated	Quantitative, retrospective, chart review Hospital support team and hospice inpatient unit, Great Britain, n = 61 patients, medical, nursing and drug charts reviewed, Sedative drugs = benzodiazepines, phenothiazines, butyrophenones, phenobarbitone, used for symptom control or sedation Sedation = the prescription of sedative drugs where reducing the level of consciousness was part of a treatment strategy with the aim of relieving distress	**Prevalence**: 43% sedatives for symptom control, 26% sedatives for sedation, 12% sedatives for both **Patient Characteristics**: mean age 69.5, mean survival of 19 days after admission **Indications for PS**: 60% agitated delirium, 27% mental anguish, 20% pain, 20% dyspnea, 3% other **Medication**: 80% midazolam - MDD = 22mg, 33% methotrimeprazine – MDD = 64mg, 37% haloperidol – MDD = 5mg **Survival**: no differences between sedated and non-sedated patients
Morita et al., 1996 Sedation for symptom control in Japan: the importance of intermittent use and communication with family members	Report the present circumstances surrounding the use of sedation for symptom control in Japan	Quantitative, retrospective, chart review, Hospice, Japan N = 143 patients, 53% male, mean age 62.4, average period of stay = 57.7 Sedation = medical procedure to palliate patients' symptoms by intentionally making their consciousness unclear. It included an increase in morphine dose resulting in secondary somnolence, and the use of sedative drugs.	**Prevalence**: 48.3% sedated, 90% of these patients death was expected within days **Indications**: 49% dyspnea, 39% pain, 38% general malaise, 23% agitation, 10% nausea, 48% suffered more than one symptom. **Survival**: sedated patients survival after sedation = average 3.9 days **Use of sedation**: intermittent = 44%, intermittent to continuous = 27%; continuous = 14%, intermittent with death after single use = 15% **Decision-making**: Patient and family fully informed 7%, family fully informed and patients partly 45%, neither family nor patients informed 4% **Medication**: 55% midazolam, 55% morphine, 33% haloperidol, 15% diazepam, 13% scopolamine, 6% bromazepam, 4% chlorpromazine, 4% barbiturates

Table 3
Continued

Fainsinger et al., 2000b A multicenter international study of sedation for uncontrolled symptoms in terminally ill patients	To improve previous reports by data collection that would enable better characterization of the prevalence of this problem, and by utilizing a multicenter international group, to provide a broader understanding of the circumstances leading to the decision to use sedation in terminally ill patients	Quantitative, retrospective, data collection form completed on the day of death or as close to that date as possible, 4 hospices, Israël (n = 100), Cape town (n = 93) and Durban (n = 94), Spain (n = 100) Median age = 63 year, 48% male *Sedation = to decrease the patient to an unresponsive condition*	**Prevalence**: Israël = 15%, Durban = 29%, Cape Town = 36%, Madrid 22% **Indications**: mainly delirium and dyspnea, **Length of sedation**: range 1-6 days **Medication**: 80% midazolam
Fainsinger et al., 1998 Sedation for uncontrolled symptoms in a South African Hospice	Develop understanding of end-of-life problems and there management and help develop improved patient management	Quantitative, retrospective, chart review, Hospice, Canada, n = 76, 46% male *No definition*	**Prevalence:** 30% sedated patients, **Patient characteristics:** mean age 60 years, duration of stay = 8 days **Indications:** mainly delirium and dyspnea **Use of sedation:** 61% continuous subcutaneous infusion of midazolam, 30% intermittent doses of benzodiazepines, 9% chlorpromazine & lorazepam. **Medication:** Mean dose midazolam = 29 mg
Fainsinger et al., 1991 Symptom control during the last week of life on a palliative care unit	To assess the prevalence and severity of different symptoms in patients admitted to our palliative care unit and the need to administer treatment resulting in sedation during the last week of life	Quantitative, retrospective, chart review, N = 100, 41% male, mean age = 62, mean duration of stay = 40	**Prevalence:** 16% sedated **Indications:** 6% pain, 39% delirium

Table 3
Continued

Miccinesi et al., 2006 Continuous deep sedation: physicians' experiences in sic European studies	To estimate the frequency and characteristics of continuous deep sedation in six European countries	Quantitative, retrospective, questionnaire about medical decision making Random sample (stratified) of death certificates of people ≥ 1 year in 6 European countries Response rate: Belgium = 59%, Denmark = 62%, Italy = 44%, The Netherlands = 75%, Sweden = 61%, Switzerland = 67% Sedation: Continuous deep sedation (CDS) with or without artificial nutrition or hydration (ANH)	**Prevalence CDS**: Belgium = 8,2%, Italy = 8,5%, Denmark = 2,5%, Sweden = 3,2%, Switzerland = 4,2%; CDS with ANH: 0.9-5,5%; CDS without ANH: 1,6-3,7% **Patient characteristics**: mainly cancer patients, more frequent in hospitals, less frequent patient ≥ 80 years, probability of receiving sedation increases by 17% for males, 15% for cancer patients, 91% if between 65-79 years, 134% if ≤ 65 years, 63% dying in hospital
Kohara et al., 2005 Sedation for terminally ill patients with cancer with uncontrollable physical distress	Investigating the influence on consciousness of sedative drugs on the consciousness of the patient	Quantitative, retrospective, chart review, patients admitted to palliative care unit, Japan, n = 124 *Sedation = a medical procedure to palliate patient symptoms refractory to standard treatment by intentionally dimming consciousness*	**Prevalence:** 51% sedation **Patient characteristics:** mean duration of stay = 29 days, median age = 64, 67% male, low PPS-score before sedation **Indications:** 63% dyspnea, 40% general malaise/restlessness, 25% pain, 21% agitation, 6% nausea and vomiting, 54% > 1 one symptom **Survival:** sedated patients died after 3.4 days **Medication:** 98% midazolam, MDD during last 4 days ranges 26.0 – 32.5 mg **Use of sedation:** 69% continuous sedation, 30% intermittent of which 80% evolved to continuous

Table 3
Continued

Muller-Busch et al., 2003 Sedation in palliative care – a critical analysis of 7 years' experience	Provide a critical analysis of seven years' experience with the application of sedation in the final phase of life	Quantitative, retrospective, chart review, patients who died on PCU, Germany, n = 548 Sedation during last 48 hours	**Prevalence**: 14,6% sedated patients in last 48 hours Patient characteristics: sedated patients significantly younger **Indications**: tendency to shift to more psychological distress **Survival**: mean survival after sedation = 2,6 days **Decision-making**: ↑in request for sedation by patients over time **Medication**: slowly increasing doses of midazolam **Use of sedation**: 60% continuous sedation, 40% intermittent **Nutrition and hydration**: 33.8% no oral intake, all patients receive infusions
Chater et al., 1998 Sedation for intractable distress in the dying – a survey of experts	Better understand the use of deliberate sedation to treat intractable symptoms in the dying	Quantitative, retrospective, self-developed questionnaire Palliative care experts from different countries, n = 61, response rate = 87% *Terminal sedation = the intention of deliberately inducing and maintaining deep sleep, but not deliberately causing death in very specific circumstances:* *1. for the relief of one or more intractable symptoms when all other interventions have failed and the patient is perceived to be close to death, or* *2. for the relief of profound anguish (possibly spiritual) that is not amenable to spiritual, psychological, or other interventions, and is perceived to be close to death.*	**Prevalence:** 77% reported using PS in last 12 months, **Indications:** 20% pain, 14% anguish, 12% respiratory distress, 12% agitation, delirium **Medication:** 37% one drug, 30% 2 drugs, 28% 3 drugs, mainly midazolam **Decision making:** 50% patients major involvement, 27% of patients, minor involvement, 22% no involvement. 96% families major involvement, 27% minor involvement, 4% no involvement **Succes of sedation:** successful in 90%

Table 3
Continued

Morita et al., 2004a Concerns of family members of patients receiving palliative sedation therapy	To gather vivid family descriptions about their experiences in palliative sedation therapy	Quantitative, prospective, cross-sectional, multicenter survey and content analysis 48 statements, bereaved family of patients receiving palliative sedation, median age = 57, 64% female, 55% spouse, 25% child	69% patients considerably or very distressed before sedation, 88% reduction of symptom frequency, 55% patients explicit wish for sedation, others could not express wishes, 89% of families received a clear explanation about sedation, 79% prior discussion about end-of-life treatment between pat. and family, 78% family expresses some level of satisfaction with sedation, 77% evaluated time of start as appropriate, 25% of family expressed high levels of distress, 50% concerns about not being able to communicate with pat., 33% perceived the decision-making as a burden, 85% believed that sedation was dignified,
Morita et al., 2004d Family experience with palliative sedation therapy for terminally ill cancer patients	To clarify the family experience during palliative sedation therapy, including their satisfaction and distress levels, and the determinants of family dissatisfaction and high-level distress		
Morita, 2004b Differences in physician-reported practice in palliative sedation therapy **Morita 2004c** Palliative sedation to relieve psycho-existential suffering of terminally ill cancer patients	To clarify the physician-reported practices and the factors influencing sedation rates To clarify the prevalence and characteristics of patients receiving sedation for relief from psycho-existential suffering	Quantitative, retrospective, questionnaire regarding use of PS in past year Palliative care physicians, Japan, response rate = 80%, *Continuous deep sedation (CDS) is the continuous use of sedative medications to relieve intolerable and refractory distress by achieving almost or complete unconsciousness until death.*	**Prevalence:** CDS for physical symptoms: < 10% in 44% of institutions, between 10 – 50% in 53%, > 50% in 6,2% of institutions, CDS for psycho-existential symptoms: 64% institutions nonexistent, 32% institutions 0,5 – 5%, 3,6% institutions > 10%. 1% of total population deceased patients psycho-existential problems **Indications:** > 80% pain and dyspnea in patients with limited survival = strong indication and psycho-existential suffering exceptional indication **Decision making process:** 75% consent from patient, family & nurses; large variation in consent by multiple physicians, 49% of institutions physicians greater role than nurses, 15% nurses greater role and 36% equivalent role. 100% of competent patients, 100% of family, 98% of nurses **Survival:** predicted survival ≤ 3 weeks in 94% **Opinions of physicians on sedation:** ≥ 70% sedation does not damage patients' or families trust, sedation not criticized by colleagues, sedation has no legal problems, distress not adequately palliated without sedation, patients have right to choose sedation.

Table 3
Continued

Van der Heide et al., 2007 End-of Life practices in the Netherlands under the Euthanasia act.	To assess the effects of the 2002 Dutch law and changes in end-of-life care. To assess the reporting rates for euthanasia and PAS and physicians' reasons for non-reporting	Based on death-certificates, stratified sample of death cases, n = 6860 (response rate 77.8%), mailed questionnaire statistical analysis based on weighting procedure, statistical significance p <0.05.	**Prevalence:** 8.2% continuous deep sedation; in 7.1% in conjunction with decision that possibly hastened death (e.g. withholding hydration or nutrition; 1.1% sedation without conjunction of other decisions. Sedation in conjunction with other decisions most often used in patients aged 64 years or younger, in men and in patients with cancer.
Sykes and Thorns, 2001 Sedative use in the last week of life and the implications for end-of-life decision making	This study aimed to determine how sedation doses change at the end of life and how often the doctrine of double effect might be relevant	Quantitative, retrospective study based on chart reviews. n ¼ 237 hospice inpatient unit, 54% female mean age of 69.7 Four groups of patients: little or no sedation, significant levels of sedation for all seven days, significant amounts of sedatives during last 48 hours and those undergoing a marked increase of sedative drugs during last 48 hours *Sedation = significant sedation based on a judgment of the dose threshold for each drug*	**Prevalence**: 48% of patients' sedative drugs were used in doses above the sedative threshold. 52% received no sedation during last week of life. 13% received sedation for at least seven days and 56% received sedation during last 48 hours **Use of sedation**: 56% of sedated patients received it during last 24 hours, 54% received intermittent sedation between 48 hours and seven days **Effect of sedation**: Number of peaceful deaths similar in all groups Survival: No difference in survival between patients that received no sedation in last week of life and those that received sedation during last 48 hours. Patients receiving sedation during there last week of life had a significantly longer survival than the other two groups (P < 0.001) **Medication**: mainly midazolam, median dose of 50 mg/24 hours
Vitetta et al., 2005, Sedation and analgesia-prescribing patterns in terminally ill patients at the end of life	This study attempted to identify overall prescribing factors and variation in the use of sedation and analgesia in an inpatient hospice setting at the end of life	Retrospective case review, n = 102 Special attention to sedation and analgesia in the last week of life	68% of patients received regular sedation, two out of three of patients started regular sedation on admission or within seven days No difference in survival between patient that did receive regular sedation and those that did not Mean duration of admission: 26 days Sedation doses increased modestly toward end of life but were not associated with reduction in survival

Table 4
Overview of Prospective Studies

Author(s) Year of publication, Title	Purpose	Methodology	Results
Menten, 2003 Palliative sedation for refractory symptoms in terminal palliative cancer patients: procedure and results in University Hospitals Leuven	Analyze the indication, procedure and efficacy of palliative sedation for refractory symptoms in terminal palliative cancer patients in the University Hospitals of Leuven	Quantitative, prospective N = 26 palliative, terminal cancer patients, 38% PST, 62% PCU, fully conscious and requested palliative sedation *Palliative sedation = those situations where the terminal palliative patient and his physician intend to obtain a deep sleep. Sedation is done without hastening or causing death, just to relieve suffering from one or more intractable symptoms, when all other interventions have failed and the patient is perceived to be close to death.*	**Prevalence:** 1,33% sedated of PST and 3.13% sedated of PCU **Medication:** midazolam in all patients, start with low doses and titrated up based on medical history of patient, individual patient experience and intensity of refractory symptoms(s) **Indications:** mainly physical suffering in PST group, mainly psychological suffering in PCU group **Effect of sedation:** 48 hours after sedation full control of refractory symptoms in 92% of cases. **Use of sedation:** 34% intermittent sedation, 3 patients evolved to permanent sedation, 61% continuous deep sedation from start **Survival:** median duration of 4 days for permanent sedation, median of 5 days for intermittent
Ventafridda et al., 1990 Symptom Prevalence and control during cancer patients' last days of life	To document how long before death symptoms appear that patients term unendurable and that are controllable only with sedation-induced sleep, allowing the patient to respond to external stimuli only if provoked	Quantitative, prospective N = 120 terminal cancer patients, entered home care program, Italy, 61% male, median age 65.5 years *Sedation = when symptoms could not be relieved opioids or strong tranquilizers were increased until symptoms were under control and maintained until death*	**Prevalence:** 52,5% CDS **Indications:** 41% dyspnea, 39% pain, 14% delirium, 6% vomiting **Decision-making:** patient gave consent **Survival:** no difference in survival between sedated and non-sedated group

Table 4
Continued

Chiu et al., 2001 Sedation for refractory symptoms of terminal cancer patients in Taiwan	To investigate the frequency of sedation in terminal cancer patients, its relationship with intractable symptoms, understand the ethical acceptability and satisfaction of symptom control among patients, family and health care workers	Quantitative, prospective, daily assessment on assessment form N = 251, 54% men, 51% > 65 years, 31% survival < 7 days, 39,5% between 7 – 30 days *Sedation = medical procedure to palliate patients' symptoms by intentionally making their consciousness unclear.*	**Prevalence**: 27,9% **Indications**: 57% agitated delirium, 10% severe pain, 22,8% dyspnea, 7,2% insomnia **Medication:** 50% haloperidol, 24,3% midazolam, 12,9% Rapidly increasing doses of morphine Use of sedation: 52,9% intermittently, 37,1% continuously, 10% evolved from intermittent to continuous **Decision-making**: 42,9% consent from patient and family, 50% consent from family (mostly cognitive impairment of pat) **Effect of sedation**: 71,4% of medical staff satisfied with sedation, 90% of family thought it right to use sedation, 67% of family was satisfied **Survival**: no difference between sedated and non-sedated, median survival after sedation = 5 days,
Fainsinger et al., 2000(a) Sedation for delirium and other symptoms in terminally ill patients in Edmonton	To assess the prevalence of difficult symptoms requiring sedation at the end of life	Quantitative, prospective, self-developed data collection form N = 150, consecutive patients who died on acute care, tertiary unit and hospice unit Mean age respectively 71, 62 and 73 years, 60%, 68% and 46% male *Sedation = patients deliberately sedated by increasing doses to control delirium or observed to be reduced to a clearly unresponsive condition by pharmacological management*	**Prevalence:** 6% sedated for delirium in acute care, 10% in tertiary care and 2% in hospice care; 2% sedated for dyspnea in hospice care, overall prevalence of 7% **Survival:** range 1-5 days sedated

Table 4
Continued

Morita et al., 2005a Efficacy and safety of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan **Morita et al., 2005b** Ethical validity of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan	Explore efficacy and safety of palliative sedation therapy and identify factors contributing to inadequate symptom relief and complications To systematically investigate whether empirical evidence supports the ethical validity of sedation	Quantitative, prospective, structured questionnaire in yes/no format 21 palliative care units, Japan, inclusion of all adult patients who received CDS, n = 102, mean age = 63 years, 62% male, mean duration of stay = 42 days *CDS = the continuous use of sedative medications to relieve intolerable and refractory distress by achieving almost or complete unconsciousness until death.*	**Prevalence** CDS: 19% Indications: 44% fatigue, 41% dyspnea, 34% delirium, one pat. received sedation for psycho-existential suffering **Survival**: mean 2,6 days after sedation **Medication**: 76% midazolam, 34% Phenobarbital **AFOFL**: before sedation: 47% AH, 11% oral intake; after sedation: 31% of first group and 73% last group no AH and 69% of first group continued and 27% of last group started with AH. Reduction of hydration in 35% of patients due to fluid retention symptoms and/or patient wishes. **Decision-making**: 95% of competent patients stated suffering was intolerable, 67% pat. explicit wish for sedation, 29% family involved, 4% previously expressed wish pat. **Use of sedation**: 66% of sedated patients received intermittent or mild sedation before CDS **Efficacy and safety PS**: inadequate symptom relief in 17% of patients, agitation distress scale decreased significantly ($p<.001$), delirium remained serious in 4%. Explicit communication decreased from 40 to 7% after sedation and mean Communication capacity score ↓ significantly ($p<.001$). Respiratory rate did not decrease after sedation and serious complications reported in 22%. Possibility of shortening life: none = 67%, < 24 hours in 24%
Morita et al., 1999b Do Hospice physicians sedate patients intending to hasten death?	What is the condition of patients before they are sedated? Is life support care routinely withdrawn after sedation begins? Are there cases where physicians increase the dose of sedatives despite adequate symptom palliation? Are sedatives prescribed in an amount that will hasten death?	Quantitative, prospective, data collections sheet N = 71 sedated patients of one PCU, 55% male, mean age = 65 years, median length of stay = 28 days, Japan *Sedation = medical procedure to palliate patients' symptoms refractory to standard treatment by intentionally making their consciousness unclear.*	**Prevalence**: 45% **Survival**: median of 3 days after start sedation **Use of sedation**: intermittent = 61%, continuous = 39%, mild = 80%, deep = 20% **Indications**: 42% physical restlessness, 41% dyspnea, 13% pain, 1,4% nausea, 1,4% multifocal myoclonus, 1,4% psychological distress **AFOFL**: amount of fluids increased in 7%, maintained in 69% and decreased in 24% of patients **Medication**: 37% opioids, 31% midazolam, 31% haloperidol

Table 4
Continued

Morita et al., 1999a The decision-making process in sedation for symptom control in Japan	Describe the decision-making process of 87 sedated terminally ill cancer patients	Quantitative, prospective, structured data collection sheet N = 87 sedated terminally ill cancer patients of one PCU, Japan, 61% male, mean age = 63, median length of stay = 30 days,	**Prevalence**: 47% **Use of sedation**: 67% intermittent, 33% continuous, 41% mild, 49% deep **Indications:** 67% physical restlessness, 40% dyspnea, 18% pain, 6% nausea, 1% convulsion **Survival:** median of 3 days after sedation **Decision-making**: > 90% family members informed about risks and benefits
Cameron et al., 2004 Use of sedation to relieve refractory symptoms in dying patients	To document the use of sedation for refractory symptoms in patients admitted to an independent palliative care unit	Quantitative, prospective, N = 20 patients who received sedated drugs, South-Africa, mean age = 68 years, cancer, 36% male *Sedated patients = all patients receiving sedating drugs apart from sleeping tablets*	**Prevalence**: 20% **Indications**: 45% delirium, 25% nausea and vomiting, 15% convulsions, 10% dyspnea, 5% pain **Survival**: 3;8 days after start sedation **Medication:** mainly midazolam and haloperidol **AFOFL**: 20% received fluids during sedation, fluids were not started during sedation, always discussed with patients and families **Decision-making**: all patients and/or families fully informed
Peruselli et al., 1999 Home palliative care for terminal cancer patients: a survey on the final week of life	Describe the place, circumstances and 'quality' of death of patients admitted to home palliative care units, particularly focusing on symptom control and the patients' situation at death.	Quantitative, prospective, weekly assessment until death N = 401 randomly selected patients older than 18 and referred to PCU (home care) for management of terminal stage cancer, median age = 70 years, 57% male, 20% duration of care < 7 days and 71% between 7 and 90 days, *Total pharmacological sedation = the administration of drugs to obtain total loss of consciousness*	**Prevalence:** 25% sedated, high variation between centers

Table 4
Continued

Morita et al., 2002 Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: a nationwide survey	To clarify the frequency and practice of sedation therapy for terminally ill cancer patients and to identify physicians' attitudes toward sedation.	Sample of eligible physicians (oncologists and palliative care physicians) who met inclusion criteria, n = 697, response rate = 49.6%, mean age = 45; 92% male, 80% cancer setting, 13% hospice, PCU, self-developed questionnaire and 4 cases *Palliative sedation therapy = the use of sedative medication to relieve intolerable and refractory distress by the reduction of patient consciousness* *Distinction between mild-deep and intermittent-continuous*	**Prevalence**: mild sedation = 89%, intermittent-deep = 70%, continuous-deep = 66% for physical distress Mild = 64%, intermittent-deep = 46% and continuous-deep = 38% for psychological distress. **Opinions**: 83% agreed that patients had right to receive palliative sedation, 5.3% PS = unnecessary when conventional palliative therapy was performed, < 15% expressed concerns about losing patient trust, being criticized by colleges or by law, 19% concerns about less efforts made when PS becomes widespread, 19% PS does not sufficiently alleviate patient suffering, 37% PS often associated with risk of shortening patient life, 17% stated that PS is indistinguishable from other acts to hasten death, 48% regarded accurate determination of medical indications for PS as difficult **Attitudes**: when refractory physical and psychological distress, 14% of respondents chose continuous-deep sedation, when delirium and depression 35% chose psychiatric treatment without intentional sedation **Factors influencing physicians decision**: independent determinants for decision to choose for continuous-deep sedation were greater preference of symptomatic treatment ($p = .021$), higher levels of emotional exhaustion ($p = .014$), independent determinants of physicians preference not to choose for psychiatric treatment in cases of delirium and depression were less involvement in end-of-life care ($p < .01$) and greater age ($p < .01$).
Müller-Busch et al., 2004 Attitudes on euthanasia, physician-assisted suicide and terminal sedation – A survey of the members of the German Association for palliative medicine.	To evaluate the attitudes towards different end-of-life medical practices, such as euthanasia, physician assisted suicide and terminal sedation.	Quantitative survey, cross-sectional, Germany, n = 251 physicians, response rate = 61%, median age of 46 years, 70% male, median palliative experience = 7.8 years Definitions according to German literature and jurisprudence	Vast majority of physicians opposed to euthanasia 90.4%; 63.3% in favor of withdrawing life sustaining treatment in futile situations without consent of patient or relatives, 94% in favor of terminal sedation in cases of intolerable or hopeless suffering.

Table 4
Continued

Kaldjian et al., 2004 Internists' attitudes towards terminal sedation in end of life care	Determine the frequency of physician support for terminal sedation in end of life care, determine whether physicians who support terminal sedation also support physician assisted suicide and explore characteristics of physicians who support terminal sedation but not assisted suicide	Quantitative, prospective, cross-sectional, survey, USA, n = 677 physicians, response rate = 47%, mean age = 51 years, 80% men, 41% only internal medicine, 32% subspecialty, 27% Jewish, 24% catholic, 26% none, 17% non-Catholic, 65% cared for 1-25 terminal patients in past year. Terminal sedation = diminishing consciousness to halt the experience of pain if a terminally ill patient has intractable pain despite aggressive analgesia.	78% supported the use of terminal sedation, 23% did not agree with aggressive analgesia or PS, 47% agreed with PS but not with physician assisted suicide (PAS), 29%agreed with PS and PAS. When more experience with terminally ill people, more likely to agree with PS, three independent variables associated with agreeing with PS: caring for > 10 terminally ill patients in past year, Christian religious affiliation, monthly religious service attendance ($p<.05$)
Blondeau et al., 2005 Physicians' and pharmacists' attitudes toward the use of sedation at the end of life: influence of prognosis and type of suffering	To measure the effect of prognosis and the nature of suffering on the attitude towards sedation	Quantitative, prospective, four clinical situations/vignettes, Canada, 2*2 experimental design, physicians and pharmacists, nonrandom volunteer sampling technique, n = 124, response rate = 42%, 49% men, 80% physicians, 89.3% < 55 years old, Qualitative content analysis of comments Purposefully no definition supplied	**Attitude**: Attitude was favorable in situation of physical suffering, regardless of prognosis, with regard to existential suffering, attitude was unfavorable, only suffering variable had impact on attitude **Existential suffering**: if long-term prognosis favoring spiritual or psychological support, if short-term prognosis reference was made to interventions by psychologist, social worker, priest **Physical suffering**: high proportion held that sedation was indicated in case of intractable suffering, majorities main concern was the patients autonomy, need for free and informed consent

Table 4
Continued

Morita et al. (2003) and Morita et al. 2002(b) Similarity and difference among standard medical care, palliative sedation therapy and euthanasia: a multidimensional scaling analysis on physicians' and the general population's opinions	To examine the conceptual validity of the proposed criteria for palliative sedation therapy by investigating similarities and differences among standard medical care, the subcategories of palliative sedation therapy proposed, and medical acts to hasten death using a multidimensional scaling technique on actual survey data	Secondary analysis of 2 surveys based on Euclidean distance model of stimulus configuration of measures Survey 1: cf. Morita et al. 2002 Survey 2: convenience sample of Japanese people, n = 457. Participants had to answer 4-point likert-scale. Had to identify the degree to which they would want each treatment for severe physical or psychological distress refractory to optimal care. Options were: care without intentional sedation, mild sedation, intermittent deep sedation, continuous deep sedation and PAS/euthanasia Palliative sedation therapy = the use of sedative medication to relieve intolerable and refractory distress by the reduction of patient consciousness Distinction between mild-deep and intermittent-continuous	Continuous deep sedation was placed closer to mild and intermittent deep sedation in the physician responses, while it was mapped closer to PAS/euthanasia in the general population data.
Simon et al., 2007, Attitudes towards terminal sedation: an empirical survey among experts in the field of medical ethics	To find out how German-speaking medical ethics experts think about the term and the moral acceptance of terminal sedation	Prospective study based on questionnaires sent to medical ethics experts n = 281 (response rate of 59%)	Previous involvement: 92% knew the term terminal sedation, 32% had dealt with the topic in detail, 8% had never heard of the term Understanding of the term: 73% only speak of terminal sedation when sedation until death is intended; to 45% this meant complete elimination of consciousness, and to 55%, less deeper forms of sedation; persons with medical background preferred broader definition Alternative terms: 49% preferred palliative sedation, since it puts the focus on symptom control and reduction of the suffering Moral evaluation: 98% found terminal sedation morally acceptable. In cases of mental suffering alone, the acceptance was considerably lower Withdrawing food and fluid together with sedation was less acceptable than sedation alone

Table 4
Continued

Morita et al., 2001, Effects of high dose opioids and sedatives on survival in terminally ill cancer patients	Intention to compare the survival of sedated and non-sedated patients receiving inpatient palliative care, with clear definitions on sedative treatment and using multivariate analytic techniques to adjust for prognostic factors	Prospective study design, secondary analysis. Sample of consecutive patients admitted to a palliative care unit in Japan Assessment of patient characteristics, PPS, and clinical symptoms on admission and following six months Additional information about the use of sedatives and opioids was assessed by chart review for last 48 hours of life n = 209, 53% male, mean age of 67 years, average survival of 44 days	PPS less than 60% in 85% of patients Opioids prescribed in 82% of patients 60% of patients received some form of sedative in last 48 hours, such as haloperidol (43%), midazolam (23%), and hydroxyzine (15%) PPS, oral intake, edema, dyspnea at rest, and delirium independent prognostic value No significant differences in survival between groups

SAMPLES, SETTINGS AND DEFINITIONS USED - STUDIES ON THE PRACTICE OF PALLIATIVE SEDATION

The majority of the studies included in this systematic review discussed terminal cancer patients in palliative care units or hospices. Two studies reported on patients in a home care program (Ventafridda et al., 1990; Peruselli et al., 1999), and three studies reported on patients followed up by a palliative support team in acute care settings (Menten, 2003; Stone et al., 1997; Fainsinger et al., 2000a). Only one paper reported on patients in an acute care setting without the palliative support team being involved (Fainsinger et al., 2000a). All samples were quite similar with regard to the mean age and the ratio of men-to-women. Samples differed, however, in the mean duration of stay, with a minimum of 8 days and a maximum of 57.7 days. Almost all the studies provided descriptions or definitions of sedation. However, the terminology varied greatly (sedation, continuous deep sedation, total pharmacological sedation, palliative sedation, terminal sedation, controlled sedation [*authors' translation*]), as did the descriptions of sedation (Table 3, 4).

In studies in which physicians gathered information concerning palliative sedation (Rietjens et al., 2004, 2005, 2006; Miccinesi et al., 2006; Chater et al., 1998; Morita, 2004b,c; Van der Heide et al., 2007), physicians were asked to indicate how many patients were sedated in the past year. Additionally, they had to answer a structured questionnaire so that detailed information could be gathered. In two studies, the questionnaires were sent to palliative care experts all over the country (Morita, 2004b,c). One study sent the questionnaire to palliative care experts from different countries (Chater et al., 1998), and five studies sent their questionnaires to a random sample of physicians, selected by examination of death certificates (Rietjens et al., 2004, 2005, 2006; Miccinesi et al., 2006; Van der Heide et al., 2007). More information on sample size, response rates, countries, and methodology used can be found in Tables 3 & 4.

STUDIES EXPLORING ATTITUDES OF PHYSICIANS WITH REGARD TO PALLIATIVE SEDATION

In our literature search, we identified seven papers (Simon et al., 2007; Morita et al., 2002a, 2002b, 2003; Müller-Busch et al., 2004; Kaldjian et al., 2004; Blondeau et al., 2005) that reported on physicians' attitudes about palliative sedation. Three papers focused on the attitudes of oncologists and palliative care experts in Japan and compared these , in a secondary analysis , with the opinion of the lay public (Morita et al., 2002a, b, 2003). A fourth study examined the attitudes of internists in the

USA (Kaldjian et al., 2004), a fifth study assessed the attitudes of physicians and pharmacists in Canada (Blondeau et al., 2005), a sixth study surveyed the attitudes of all physician members of the German Association of Palliative Care (Müller-Busch et al., 2004) and a seventh study did a survey among medical ethics experts in Germany (Simon et al., 2007). The mean age of the respondents in these studies varied between 45 and 50 years. In four studies, the majority of the respondents were male, and data collection was based on self-developed questionnaires (Morita et al., 2002a; Müller-Busch et al., 2004; Kaldjian et al., 2004; Simon et al., 2007). In one study, the sample consisted of 49% male subjects and data collection was based on a critical appraisal of four clinical vignettes (Blondeau et al., 2005). Five of seven studies (Morita et al., 2002a,b, 2003; Müller-Busch et al., 2004; Kaldjian et al., 2004) defined palliative sedation, albeit in different ways. The sixth study purposefully omitted a formal definition to avoid bias and confusion (Blondeau et al., 2005), and the seventh study did not report on the definition in the paper (Simon et al., 2007). Three studies had relatively large samples (n = 697, 457 and 677, respectively) (Morita et al., 2002a,b; Kaldjian et al., 2004). Response rates were very similar but rather low in all studies (± 50%) (Tables 3, 4).

STUDIES EXPLORING FAMILY EXPERIENCES

We included two studies that discussed the experience families had when a family member underwent palliative sedation. Both studies (Morita et al., 2004a, d) were based on the same sample and study design. One of the studies gave an overview of the results (Morita et al., 2004d) and the other highlighted the concerns of family members of patients receiving palliative sedation (Morita et al., 2004a). In this cross-sectional multicentre survey, 185 family members of sedated patients answered a questionnaire. The mean age of family members was 57 years, 35% were male, and 55% were spouses (Morita et al., 2004d). The mean interval between patient time of death and return of the questionnaire was approximately two years.

RESULTS

PREVALENCE OF PALLIATIVE SEDATION

Our review revealed that the prevalence of palliative sedation varied considerably (Tables 3 & 4), especially in terms of setting, definition and methodology used. Most of the studies were carried out in palliative care units and/or hospices. The prevalence in these settings ranged between 1.33% (Menten, 2003) and 51% (Kohara et al., 2005). In two Italian studies (Ventafridda et al., 1990; Peruselli et al., 1999) performed in home care environments almost ten years apart, one study reported a prevalence of

52.5% and the other reported a prevalence of 25%. We also found a large difference in prevalence among hospital-based palliative support teams. Stone et al. (1997), for example, reported a prevalence of 26%, whereas Menten (2003) reported a prevalence of only 1.33%.

Prevalence of palliative sedation also varied across countries. Two studies reported palliative sedation prevalence as a proportion of all deaths in one of six European countries (Rietjens et al., 2004; Miccinesi et al., 2006). For the Netherlands (Rietjens et al., 2004; Van der Heide et al., 2007), Belgium and Italy ((Miccinesi et al., 2006)), the prevalence was 10%, 8.2%, and 8.5%, respectively. In Denmark and Sweden, a much lower prevalence of 2.5% and 3%, respectively, were reported (Miccinesi et al., 2006).

Forty-one percent of the studies distinguished between intermittent and continuous palliative sedation. Intermittent sedation was reported in 30–67% of cases, whereas continuous sedation was reported in 14–69% of cases. Morita et al. (1999b) reported that 51% of patients received mild sedation and 49% deep sedation. In a second study (Morita et al., 1999a), they reported that 80% of patients received mild sedation, whereas 20% received deep sedation. In several studies, intermittent sedation sometimes resulted in continuous sedation at the end of life (10%–27%) (Menten, 2003; Morita et al., 1996; Kohara et al., 2005; Chiu et al., 2001).

An interesting finding about the beliefs of the lay public and professionals was reported in the study of Morita et al. (2003). While examining the conceptual validity of the proposed criteria for palliative sedation, they ascertained that both physicians and the general population differentiate mild sedation and intermittent deep sedation from standard medical care. Moreover, they reported that physicians consider continuous deep sedation to be close in practice to mild and intermittent deep sedation. However, the general population considered it to be closer to euthanasia/physician-assisted suicide. These findings show that, although the majority of the definitions were limited to continuous deep sedation, Japanese physicians and citizens consider both mild and intermittent deep sedation as a therapy for refractory symptoms, and as such should be included in the definition of palliative sedation.

INDICATIONS FOR SEDATION

Sixty-eight percent of the reviewed studies listed only physical symptoms as the reason for sedating a patient (Tables 3, 4), the most important being delirium, dyspnea, and pain. Other physical symptoms listed were fatigue, agitation, physical restlessness, insomnia, and nausea and vomiting.

Twenty-seven percent of the studies mentioned psycho-existential suffering besides physical suffering as a reason for sedating a patient, even though this was only true for a minority of patients (Müller-Busch et al., 2003; Menten, 2003; Rietjens et al., 2004, 2005, 2006; Stone et al., 1997; Chater et al., 1998; Morita et al., 2005a,b, 1999a). Most frequently mentioned were anxiety, mental anguish, and psycho-existential suffering (without elaboration). In one study Morita (2004c) reported solely on the use of palliative sedation for psycho-existential problems. In this study, physicians indicated that patients received palliative sedation for feeling meaningless (61%), being a burden on others/dependency (48%), death anxiety (33%), wishing to control death (24%), isolation (22%), and economic burden (8.7%). Müller-Busch et al. (2003) and Menten (2003) report that palliative sedation was increasingly being administered to patients to treat psycho-existential refractory symptoms rather than physical symptoms.

SURVIVAL OF PATIENTS AFTER THE INITIATION OF PALLIATIVE SEDATION

Half of the reviewed studies reported on the survival of patients after palliative sedation (Table 3, 4). Based on retrospective reports from physicians, Rietjens et al. (2004, 2006) found that 38% of patients died within 24 hours, whereas 96% of patients died within one week. According to physicians' estimations, in 40% of patients, it was believed that palliative sedation shortened life by $\leq$ 24 hours, and in 27% of patients it was thought to have shortened life by more than one week. Morita (2004b,c) reported a survival time of less than three weeks in 94% of the patients receiving palliative sedation. Mean survival of patients after the onset of palliative sedation ranged from 1 to 6 days (Müller-Busch et al., 2003; Menten, 2003; Rietjens et al., 2004, 2006; Kohara et al., 2005; Chiu et al., 2001; Fainsinger et al., 2000a; Morita et al., 1999a,b, 2005a,b).

Other studies compared the survival of sedated and non-sedated patients (Ventafridda et al., 1990; Stone et al., 1997; Kohara et al., 2005; Chiu et al., 2001; Sykes & Thorns, 2003; Morita et al., 2001). In accordance with others papers, Vitetta et al. (2005) found no differences in survival time between sedated and non-sedated patients (Ventafridda et al., 1990; Stone et al., 1997; Kohara et al., 2005; Chiu et al., 2001; Sykes & Thorns, 2003; Morita et al., 2001).

MEDICATION AND ORAL OR ARTIFICIAL FOOD AND FLUID INTAKE

Thirty-two percent of the studies mentioned midazolam as the main drug used to induce palliative sedation (Müller-Busch et al., 2003; Menten, 2003; Stone et al., 1997; Morita et al., 1996; Fainsinger et al., 2000b; Fainsinger et al., 1998; Kohara et al., 2005; Chater et al., 1998; Morita et al., 2005a,b;

Cameron et al., 2004; Sykes & Thorns, 2003). Other drugs used either alone or in combination with midazolam were haloperidol, phenobarbital, and opioids. Twenty-four percent of the studies listed the mean daily dose of midazolam, which varied between 18.5 and 40 mg with a range of 1 – 450 mg/day (Menten, 2003; Stone et al., 1997; Fainsinger et al., 2000b; Fainsinger et al., 1998; Kohara et al., 2005; Chater et al., 1998; Morita et al., 2005b, 1999a; Cameron et al., 2004).

Only 8 of 37 papers provided information on artificial food and fluid intake in relation to palliative sedation. Again, figures varied significantly between studies. Miccinesi et al. (2006) and Menten (2003) reported that in 35-64% of cases, palliative sedation was performed without administering artificial fluids. Others describe the situation before and after palliative sedation (Morita et al., 1999a, 2005b; Cameron et al., 2004). When patients received artificial fluids before sedation, in 20%–69% of patients, fluid intake continued during sedation (Morita et al., 2005b; Cameron et al., 2004). In 24%-44% of the patients administered fluid was reduced (Morita et al., 1999a, 2005b). One study (Fainsinger et al., 1998) reported that no sedated patients received artificial fluid. Some studies reported that mildly sedated patients were able to take in fluids and/or food orally (Müller-Busch et al., 2003; Morita et al., 2005b; Cameron et al., 2004).

DECISION MAKING

Fifteen papers provided information about the decision-making process related to palliative sedation. All of these reported that consent was obtained from almost all patients who were not cognitively impaired (Müller-Busch et al., 2003; Menten, 2003; Ventafridda et al., 1990; Rietjens et al., 2004, 2005, 2006; Chater et al., 1998; Morita, 2004b,c; Chiu et al., 2001; Morita et al., 1996, 1999b, 2005a,b; Cameron et al., 2004). The most important reason for not discussing the decision with competent patients was to protect them from anxiety and/or sudden onset of refractory suffering (Rietjens et al., 2004; Morita et al., 1996, 1999a). In 50%–99% of the cases, the family was involved in the decision-making process (Rietjens et al., 2004; Morita et al., 1996, 1999b; 2002a; Chater et al., 1998; Morita, 2004b,c; Chiu et al., 2001). Seventy-five percent of families felt that the information supplied by healthcare professionals was sufficient, whereas 22% felt it was insufficient (Morita et al., 2002a). Conflicts in opinion between family members, between the patient and family, and between the medical staff and family were observed in 15%, 7.6%, and 9.7%, respectively, of the cases (Morita et al., 2002a). In cases of disagreement between the patient and family, 79% of the time physicians would try to find a compromise, and 20% of the time they would persuade the family to comply

(Morita, 2004b). All physicians surveyed indicated that they would not comply with the wishes of the family or the patient if both parties failed to reach an agreement (Morita, 2004b).

Overall, 78% of families were satisfied with the decision that was made and with the timing of palliative sedation. Twenty-five percent of the families, however, experienced high levels of emotional distress related to palliative sedation, and 30% of the families perceived the decision-making process as burdensome (Morita, 2004d). Factors hampering the decision-making of families were the presence of delirium, the ambivalence of a patient's wishes, and the absence of objectivity in assessing distress (Morita et al., 1999b). The level of family dissatisfaction with palliative sedation seemed to be determined by high levels of persistent distress in patients after sedation, insufficient information, fear of shortening the patients' life, physicians and nurses lacking sufficient compassionate, and lack of discussion with patients (Morita et al., 2004a).

It is clear from the literature that caregivers play a major role in the decision-making process. When asked how they experience the decision, 15% of physicians found it very easy, 27.5% found it to be somewhat easy, and 57.5% found it to be difficult to very difficult (Chater et al., 1998). Caregivers were hindered in making decisions by their lack of objectivity in assessing the distress experienced by patients and by conflicts about the sedation (e.g., between patient and family) (Morita et al., 1999a).

ATTITUDES OF PHYSICIANS TOWARDS PALLIATIVE SEDATION

Seven studies described the attitudes of physicians towards using palliative sedation. In two of seven studies, 78–94% of physicians supported the practice of palliative sedation in cases of intolerable or hopeless distress (Müller-Busch et al., 2004; Kaldjian et al., 2004). Two studies reported that, although physicians advocated palliative sedation, they preferred to administer palliative sedation only in cases of physical suffering rather than in cases of existential suffering (Blondeau et al., 2005; Simon et al., 2007). In the study of Morita et al. (2002a), 83% of physicians stated that patients have a right to receive sedation. Only 5.3% reported that palliative sedation was unnecessary. Less than 15% of physicians had concerns about patient trust and being critiqued by colleagues or by law. However, 37% of physicians associated palliative sedation with a risk of shortening life, and 19% believed that sedation does not sufficiently alleviate patient suffering. Important with regard to the practice of palliative sedation is the finding that 49% of physicians thought that it is difficult to accurately identify medical indications necessitating palliative sedation, and 25% believed that there is a high risk of performing palliative sedation inadequately (Morita et al., 2002a).

One study (Morita et al., 2002a) examined the independent determinants underlying physicians' decisions to choose continuous deep sedation in cases of refractory existential and physical distress. When physicians expressed a stronger preference for symptomatic treatment during their own end-of-life care (odds ratio = 1.53; p = .021) and had more emotional exhaustion (odds ratio = 1.02; p = .014), they more frequently chose continuous deep sedation. Müller-Busch et al. (2004) found that physicians preferred palliative sedation in cases of intolerable or hopeless distress (94%). The vast majority of the physicians that were questioned opposed euthanasia (90.4%). From this, the authors conclude that, according to physicians involved, palliative sedation and euthanasia are very different and palliative sedation is not (slow) euthanasia.

FAMILY EXPERIENCE WITH PALLIATIVE SEDATION

When families were asked about their experience with palliative sedation, 69% believed that patients were very distressed before sedation. Eighty-eight percent of families felt that palliative sedation helped to considerably decrease symptom distress (Morita et al., 2004d). Moreover, 94% of families observed that physicians and nurses visited the patient as much as, or more, than before. They also noticed that the physician or nurse who knew the patient well was the one who performed palliative sedation. Families clearly disagreed with the idea that palliative sedation was not dignified and with the idea that no meaning could be found in being with the sedated patient (Morita et al., 2004d).

Research also showed, however, that families expressed concerns about palliative sedation. These concerns can be categorized as emotions and wishes (Morita et al., 2004a). Families reported guilt, helplessness, and physical and emotional exhaustion. Although they believed that palliative sedation is beneficial for symptom relief, they needed to be certain that no other solutions existed. Families also expressed their need for clear explanations about the risks associated with palliative sedation. Moreover, they wanted time to say goodbye to the patient before sedation was initiated. Families also felt it was important that sedated patients receive the same dignified care as do conscious patients (Morita et al., 2004a).

COMPARISON OF PATIENTS RECEIVING SEDATION AND PATIENTS RECEIVING EUTHANASIA

Based on physician reports, Rietjens et al. (2006) compared the characteristics of patients that received palliative sedation with those of patients that received euthanasia. In hospitals, 49% of palliative

sedation was performed by clinical specialists, 25% was performed by general practitioners, and 26% by nursing home physicians. Euthanasia was mainly performed in home-care situations (55%). Patients who received palliative sedation were significantly older (mean: 72 years; $p<.001$) and suffered less from cancer than patients receiving euthanasia. Symptoms such as anxiety, confusion, depression, bedsores, loss of appetite, unclear consciousness, and inactivity were more frequently observed in patients receiving palliative sedation than in patients receiving euthanasia.

EFFICACY AND SAFETY OF PALLIATIVE SEDATION

Only four papers examined the efficacy and safety of palliative sedation for treating refractory suffering. Morita et al. (2005a) reported that palliative sedation adequately relieved symptoms in 83% of the cases. Full control of the symptoms was reached 60 minutes to 48 hours after sedation was initiated (Menten, 2003; Morita et al., 2005a). Forty-nine percent of patients awakened only once after they entered deep sleep. Time to sedation, however, was significantly shorter when midazolam was used in comparison to when phenobarbital was used ($p=.01$) (Morita et al., 2005a). Serious complications, such as respiratory suppression without arrest, aspiration, and paradoxical reaction, were noted in 22% of the patients (Morita et al., 2005a). Also, higher dosages of midazolam were needed in young patients, in patients lacking icterus, in patients pre-exposed to midazolam, and in patients requiring sedation of long duration (Morita et al., 2005a). Menten (2003) and Chater et al. (1998) reported a success rate of 90-92% and Chiu et al. (2001) reported that in 71% of the cases, physicians were satisfied with the treatment of palliative sedation, 67% of the family was satisfied though 90% of the families agreed that this treatment was the best option for the patient.

DISCUSSION

SUBSTANTIAL FINDINGS

DEFINITION OF PALLIATIVE SEDATION

This systematic review summarizes all available information published (up to 2007) in the medical literature on the practice of palliative sedation. One of our most important findings is the divergence that exists in the literature with regard to the prevalence of palliative sedation. In our view, this is mainly due to the fact that palliative sedation - often for the purpose of the study - is narrowed down to only one form of palliative sedation. For example, Rietjens et al. (2004) examined palliative sedation in terms of continuous deep sedation in combination with the withholding of food and fluids. This clearly differs from the papers of Morita et al. (2001, 2003) who also included mild and

intermittent sedation in their definition. Obviously, prevalence figures are expected to be much higher in the latter case. Other factors that might explain the wide variations in the reported results of this review are the unclear concept of 'refractory symptom', accepted indications for sedation; the fact that studies are carried out in different setting (home care, palliative care units, hospital support teams), the methodology used to assess the prevalence of palliative sedation (retrospective studies are prone to memory bias), patient characteristics, expertise, and progress in symptom control, the country(is there a law on euthanasia or not?), and the culture in which the study took place.

Discussing the different definitions that are used and available in the literature is clearly very interesting and important. This article, however, focuses on the empirical results of primary research. The discussion of the definitions is important and extensive enough to warrant another article. Nevertheless, it is clear that the lack of consensus in defining palliative sedation reflects the broad and varying ways in which palliative sedation is applied (Broeckaert, 2002, 2000; Broeckaert & Nuñez-Olarte, 2002).

Narrowing the concept of palliative sedation, as is done in several empirical studies (e.g., Rietjens, 2004, 2005, 2006; Miccinesi et al., 2006; Chater et al., 1998), jeopardizes the crucial notion of proportionality, which is really at the heart of the concept of palliative sedation: palliative sedation implies that the consciousness is reduced just enough to relieve refractory suffering in an adequate way (Broeckaert, 2002, 2000; Broeckaert & Nuñez-Olarte, 2002; deGraeff & Dean, 2007). The notion of proportionality is crucial to differentiate palliative sedation from euthanasia (Broeckaert, 2002, 2000; Broeckaert & Nuñez-Olarte, 2002).

To be able to give an overall definition that captures all possible forms of palliative sedation occurring in practice, mild and intermittent sedation must be included in the definition of palliative sedation (Broeckaert, 2002, 2000; Broeckaert & Nuñez-Olarte, 2002; Morita et al., 2005a; Peruselli et al., 1999; deGraeff & Dean, 2007). Because little empirical information about palliative sedation is available, an overarching definition is essential if we are to fully understand the practice of palliative sedation. In order to stress, on the one hand, the common goal and intention of the different types of palliative sedation, and on the other hand, the crucial importance of proportionality in all these types of palliative sedation, we have defined palliative sedation as follows:

> *"The intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms" (Broeckaert, 2000, 2002; Broeckaert & Nuñez-Olarte, 2002).*

Starting from this broad definition, further differentiations (mild/deep, continuous/intermittent) can be made (Broeckaert, 2000, 2002; Broeckaert & Nuñez-Olarte, 2002; Morita et al., 2001). Only when clear-cut definitions of palliative sedation are proposed and applied will it be relevant and methodological correct to compare prevalence figures.

NATURE OF REFRACTORINESS

Most studies found that palliative sedation was administered primarily to relieve refractory physical suffering. Some studies, however, found it was used to relieve a combination of refractory physical and psycho-existential suffering (Tables 3, 4). Over the years, researchers have noticed that palliative sedation is increasingly being used solely to control refractory psycho-existential suffering (Müller-Busch et al., 2003; Menten, 2003). According to palliative experts, this is due to the enormous progress in managing physical suffering. Successful treatment of physical suffering (e.g., pain) opens the way for patients to focus more on psycho-existential and spiritual issues or suffering (Menten, 2003). Administering palliative sedation to alleviate psycho-existential suffering remains a controversial issue (NEC, 2006; Morita et al., 2002a), partly because it is difficult to determine when this suffering is refractory (NEC, 2006; Morita et al., 2002a).

DOES PALLIATIVE SEDATION SHORTEN LIFE?

One of the most important controversies that still exist is the presumed life-shortening effect of palliative sedation. Authors that oppose palliative sedation often consider it to be a form of ‘slow euthanasia’, especially when it is combined with the withholding or withdrawing of life-sustaining treatment, such as artificial food and fluids (Billings & Block, 1996). Because this is a much-debated issue, one would expect to find much data on this topic. We found, however, only seven papers that discussed food and fluid intake in sedated patients, again with very different conclusions (cf. above) (Müller-Busch et al., 2003; Menten, 2003; Fainsinger et al., 1998; Miccinesi et al., 2006; Morita et al., 1999a, 2005b; Cameron et al., 2004). A similar argument has been developed by Rousseau (2003). If a patient shows signs of imminent death (e.g. loss of appetite, decreased food/fluid intake) before sedation, it seems irresponsible and unethical to hamper the natural dying process by administering artificial food or fluid during sedation. Moreover, to do so is considered to be a futile treatment for patients suffering from cachexia. This, in combination with research findings showing that survival of sedated patients is not shorter than that of non-sedated patients (Ventafridda et al., 1990; Stone et al., 1997; Kohara et al., 2005; Chiu et al., 2001; Sykes & Thorns, 2001; Morita et al., 2001), suggests that palliative sedation has no proven life-shortening effects. This refutes the argument that palliative sedation is a form of ‘slow euthanasia’ (Simon et al., 2007; Broeckaert, 2000, 2002; Broeckaert &

Nuñez-Olarte, 2002).Although more prospective research on this matter would be needed to corroborate this assertion, it will never give a definite answer. Performing a randomized study is the only way to prove that palliative sedation has no life-shortening effect, but for obvious ethical reasons, this will never be performed.

Another important aspect that relates to a possible life-shortening effect is the safety of palliative sedation. Although palliative sedation has no significant effects on patient survival on a mass level, some patients experience life-threatening complications on an individual level. Morita et al. (2005a) - the only study that examines systematically the safety of palliative sedation - report a higher percentage of serious complications. Therefore, it is essential that palliative sedation, though a normal medical practice, is used with the necessary caution.

MIDAZOLAM: THE DRUG OF CHOICE FOR PALLIATIVE SEDATION

Midazolam appears to be the drug of choice for initiating palliative sedation. Porta Sales (2002) and Menten (2003) strongly defend this choice of drug, because midazolam is easy to titrate, has rapid onset and offset (the latter being very important in cases of intermittent sedation), can be combined with other drugs used in palliative care, and has an antidote (Flumazenil® or Anexate®). Only one study (Morita et al., 1999a) reported opioids as the drug of choice for palliative sedation. This apparently limited use of opioids to induce sedation is probably done in patients that already are on opioids before palliative sedation is started. It must be stressed that the use of opioids to induce palliative sedation has not proven to be the most efficient way to treat refractory suffering. Although they might cause drowsiness in patients, opioids usually do not lead to a loss of consciousness (Verhagen et al., 1999). Three studies reported that barbiturates are still used for palliative sedation (Morita et al., 1996; Fainsinger et al., 2000b; Chater et al., 1998) albeit in a minority of cases. Barbiturates often result in cardiovascular instability, and therefore are less appropriate (Porta Sales, 2002).

In some studies, haloperidol is listed as a sedative (Morita et al., 2001) and described as being used to initiate palliative sedation. Haloperidol, however, is not a sedative and, therefore, should not be used to induce sedation. This clearly indicates that there is still much confusion as to what sedation is and again shows that clear definitions and clinical guidelines are necessary to guarantee the quality and safety of palliative sedation as a therapy for refractory suffering.

In many of the papers we reviewed in which midazolam was listed as the drug of choice for inducing palliative sedation, authors reported ‘mean dosages’ used for sedation to give readers an idea

of the amount of drug needed for sedation. Sedation status, however, cannot be solely based on mean drug dosages, because the effective dosage range varies largely (sometimes up to a factor of ≥10) in different patients. Therefore, it is important that dosages are individually and continuously titrated based on a patient's medical history, the patient's reaction to benzodiazepines, and the intensity of the patient's refractory symptoms (cf. the crucial notion of proportionality) (Menten, 2003; Broeckaert, 2000, 2002; Broeckaert & Nuñez-Olarte, 2002). Thus, palliative sedation requires that the professionals must be competent and must have appropriate clinical experience. In contrast, what should be called slow euthanasia would start at a standard level and be progressively and intentionally titrated up according to a fixed protocol until the patient dies. This practice does not imply expert palliative care or expert clinical experience and betrays a different intention.

INFORMED CONSENT OF PATIENT AND/OR FAMILY

A positive finding of our review is that in the majority of cases, palliative sedation was performed with the explicit consent of the patient and his family. Health care professionals did not obtain informed consent from the patient only in cases of acute physical refractory suffering (e.g. massive bleeding) or when patients were cognitively impaired. When obtaining informed consent to carry out palliative sedation, researchers noted that caregivers and family found the experience of deciding whether to sedate a patient to be very difficult and emotionally burdensome (Chater et al., 1998; Morita et al., 2004d). This finding confirms that palliative sedation, though part of a normal medical practice, is certainly not an ordinary medical act. Indeed, palliative sedation is a serious, well-discussed medical treatment of last resort (Quill et al., 1997, 2000).

METHODOLOGICAL ISSUES

Half of the studies included in this literature review were retrospective in nature (Table 3). Obviously, these studies were influenced by recall (memory) bias. Moreover, the quality of data is determined by the limited data available in patients' charts. Given that retrospective methodology has several limitations, recent studies have shifted to using a prospective, cross-sectional design. Although of better quality, this design does not allow researchers to consider the history of a patient, an aspect that can be extremely interesting when looking at certain issues of palliative sedation, such as food and fluid intake. Moreover, most studies are based on convenience sampling and are carried out in very different settings, making it difficult to compare results.

Implementing the best possible study design, however, remains a difficult task, because a given population of terminally ill patients has certain characteristics that may influence the choice of a

particular study design or may be inextricably linked with bias. Terminally ill patients are very heterogeneous; therefore, it is very difficult to delimit a population of terminally ill patients under study. Additionally, these patients experience many symptoms concurrently, have limited survival, and are confronted with mental and physical exhaustion—all factors that hamper the feasibility of performing studies based on patient interviews or patient self-report questionnaires.

Despite the problems we are confronted with in doing research with terminally ill patients, we believe there is a need for more multicentre, international, prospective, longitudinal studies that use an optimal study design. We must acknowledge, however, that some questions will remain unanswered due to patient characteristics and the ethical issues involved (e.g. life-shortening effect of palliative sedation, effect of hydration).

Another important flaw in the studies we reviewed is that valid and reliable instruments specifically geared to assessing palliative care are lacking. Most of the studies were based on self-developed questionnaires (Tables 3, 4) and questionnaires which underwent little or no validation process. This threatens the quality and generalizability of the results. Additionally, we found that these studies provided very vague information about informed consent procedures. One could argue that using few or no validated instruments and lacking a clear-cut procedure for consent, is unethical. On the other hand this may be a special situation, since we are doing research in patients who are terminally ill and extremely vulnerable.

As mentioned above, comparing data from available studies is very difficult, because most of the research was done in different countries having very different cultures. For example, the practice of palliative sedation probably differs in countries with a law on euthanasia compared to countries without a law on euthanasia. Only multicentre studies, done in different countries will be able to reveal these differences.

CONCLUSIONS

This systematic review shows that much work remains to be done within the domain of palliative sedation. Several gaps in our current understanding still exist with regard to the effect of sedation, the evolving ideas about food and fluid intake in terminally ill patients, the possible effects on shortening life, and the decision-making process, to list a few. Further research should be based on multicentre, prospective, longitudinal, and international studies that use a uniform definition of palliative sedation

and valid and reliable instruments. Only through such research will we be able to resolve some of the ethical issues related to palliative sedation.

REFERENCES

Ahmedzai S. New approaches to pain control in patients with cancer. Eur J Cancer 1997;33:S8-S14.

Billings JA, Block SD. Slow euthanasia. J Palliat Care;12:21-30.

Blondeau D, Roy L, Dumont S, Godin G, Martineau I. Physicians' and pharmacists' attitudes toward the use of sedation at the end of life: influence of prognosis and type of suffering. J Palliat Care 2005;21:238-245.

Boyle J. Medical ethics and double effect: the case of terminal sedation. Theor Med 2004;25:51-60.

Broeckaert B, Nuñez-Olarte JM. Sedation in Palliative care: facts and concepts. In H. Ten Have & D. Clarke, eds. The Ethics of Palliative Care. European Perspectives, Buckingham: Open University Press ('Facing Death Series); 2002. 166-180.

Broeckaert B. Palliative sedation: ethical aspects. In: Gastmans C, ed. Between Technology and Humanity. The Impact of Technology on Health Care Ethics, first ed. Leuven: University Press, 2002:239-255.

Cameron D, Bridge D, Blitz-Lindeque J. Use of sedation to relieve refractory symptoms in dying patients. SAMJ. 2004;94:445-449.

Chater S, Viola R, Paterson J, Jarvis V. Sedation for intractable distress in the dying--a survey of experts. Palliat. Med. 1998;12:255-269.

Cherny NI, Radbruch L, Board of the European Association of Palliative Care. Palliat. Med. 2009; 23:581-593.

Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care. 1994;10:31-38.

Cherny NI. Sedation for the care of patients with advanced cancer. Nat Clin Pract Oncol. 2006;3:492-500.

Chiu TY, Hu WY, Lue BH, Cheng SY, Chen CY. Sedation for refractory symptoms of terminal cancer patients in Taiwan. J.Pain Symptom.Manag, 21, 467-472.

Claessens P, De Blaeser L, Broeckaert B. Palliatieve sedatie. Acta Hosp. 2003;4:37-47.

Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manag. 1994;5: 83-93.

Craig G. Terminal sedation. Cathol Med Q. 2002; February.

Fainsinger R, Miller MJ, Bruera E, Hanson J, MacEachern T. Symptom control during the last week of life on a palliative care unit. J Palliat Care. 1991;7:5-11.

Fainsinger RL, deMoissac D, Mancini I, Oneschuk D. Sedation for delirium and other symptoms in terminally ill patients in Edmonton. J Palliat Care. 2000a;16:5-10.

Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for uncontrolled symptoms in a South African hospice. J Pain Symptom Manage. 1998;16:145-152.

Fainsinger RL, Waller A, Bercovici M, et al. A multicentre international study of sedation for uncontrolled symptoms in terminally ill patients. Palliat Med. 2000b;14:257-265.

Georges J, Onwuteaka BD, van der Heide A, van der Wal G, van der Maas P. Symptoms, treatment and 'dying peacefully' in terminally ill cancer patients: a prospective study. Support Care Cancer. 2005;13:160-168.

Hallenbeck JL. Terminal sedation: ethical implications in different situations. J Palliat Med. 2000;3:313-320.

Hawker S, Payne S, Kerr C, Hardey M, Powell J. Appraising the evidence: reviewing disparate data systematically. Qualitative Health Research. 2002;12:1284-1299.

Hermann C, Looney S. The effectiveness of symptom management in hospice patients during the last seven days of life. J Hosp Palliat Nurs. 2001;3:88-96.

Howland J. Questions about palliative sedation. Ethics Medics. 2005;30:1-2.

Kaldjian LC, Jekel JF, Bernene JL, et al. Internists' attitudes towards terminal sedation in end of life care. J Med Ethics. 2004;30:499-503.

Kohara H, Ueoka H, Takeyama H, Murakami T, Morita T. Sedation for terminally ill patients with cancer with uncontrollable physical distress. J Palliat Med. 2005;8:20-25.

Lo B, Rubenfeld G. Palliative sedation in dying patients. JAMA. 2005;294:1810-1816.

Menten J. Cancer pain: interdisciplinary and comprehensive management (Dissertation). Acco: Catholic University Leuven, 2003.

Miccinesi G, Rietjens JAC, Deliens L, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage. 2006;31:122-129.

Morita T, Tsunoda J, Inoue S, Chihara S. Effects of high dose opioids and sedatives on survival of terminally ill cancer patients. J Pain Symptom Manage. 2001;21:282-289.

Morita T, Akechi T, Sugawara Y, Chihara S, Uchitomi Y. Practices and attitudes of Japanese Oncologists and Palliative Care Physicians Concerning Terminal Sedation: a Nationwide Survey. J Clin Oncol. 2002a;20:758-764.

Morita T, Chinone Y, Ikenaga M, et al. Efficacy and safety of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan. J Pain Symptom Manage. 2005a;30:320-328.

Morita T, Chinone Y, Ikenaga M, et al. Ethical validity of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized care units in Japan. J Pain Symptom Manage. 2005b;30:308-319.

Morita T, Hirai K, Akechi T, Uchitomi Y. Similarity and differences among standard medical care, palliative sedation therapy, and euthanasia: a multidimensional scaling analysis on physicians' and the general population's opinion. J Pain Symptom Manage. 2003;25:357-362.

Morita T, Hirai K, Okazaki Y. Preferences in palliative sedation therapy in the Japanese general populations. J Palliat Med. 2002b;5:375-385.

Morita T, Ikenaga M, Adachi I, et al. Concerns of family members of patients receiving palliative sedation therapy. Support Care Cancer. 2004a;12:885-889.

Morita T, Ikenaga M, Adachi I, et al. Family experience with palliative sedation therapy for terminally ill cancer patients. J Pain Symptom Manage. 2004d;28:557-565.

Morita T, Inoue S, Chihara S. Sedation for symptom control in Japan: the importance of intermittent use and communication with family members. J Pain Symptom Manage. 1996;12:32-38.

Morita T, Tsunoda J, Inoue S, Chihara S. Do hospice clinicians sedate patients intending to hasten Death? J Palliat Care. 1999a;15:20-23.

Morita T, Tsunoda J, Inoue S, Chihara S. The decision-making process in sedation for symptom control in Japan. Palliat.Med. 1999b;13:262-264.

Morita T. Differences in physician-reported practice in palliative sedation therapy. Support Care Cancer. 2004b;12:584-592.

Morita T. Palliative sedation to relieve psycho-existential suffering of terminally ill cancer patients. J Pain Symptom Manage. 2004c;28:445-450.

Müller-Busch HC, Andres I, Jehser T. Sedation in palliative care – a critical analysis of 7 years' experience. BMC Palliat Care. 2003, 2.

Müller-Busch HC, Oduncu FS, Woskanjan S, Klaschik E. Attitudes on euthanasia, physician-assisted suicide and terminal sedation – A survey of the members of the German Association for Palliative Medicine. Med Health Care Philos. 2004;7:333-339.

National Ethics Committee, Veterans' Health Administration. The ethics of palliative sedation as a therapy of last resort. Am J Hosp Palliat Care. 2006;23:483-491.

Peruselli C, Di Giulio P, Toscani F, et al. Home palliative care for terminal cancer patients: a survey on the final week of life. Palliat Med. 1999;13:233-241.

Porta Sales J. Palliative sedation. Clinical Aspects. In: Gastmans C, editor. Between Technology and Humanity. The impact of technology and health care ethics. Leuven: University Press Leuven, 2002:219-237.

Quill TE, Byock IR. Responding to intractable terminal suffering: the role of terminal sedation and voluntary refusal of food and fluids. Ann Intern Med. 2000;132:408-414.

Quill TE, Lo B, Brock DW. Palliative options of last resort. A comparison of voluntary stopping eating and drinking, terminal sedation, physician-assisted suicide and voluntary active euthanasia. JAMA. 1997;278:2099-2104.

Rietjens JAC, van Delden JM, van der Heide A et al. Terminal sedation and euthanasia. A comparison of clinical practices. Arch Intern Med. 2006;166:749-753.

Rietjens JAC, van der Heide A, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. The practice of terminal sedation in the Netherlands. Ned Tijdschr Geneeskd. 2005;149:467-471.

Rietjens JAC, van der Heide A, Vrakking AM, Onwuteaka-Philipsen B, van der Maas PJ, van der Wal G. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med. 2004;141:178-185.

Rousseau P. Palliative sedation and sleeping before death: a need for clinical guidelines? J Palliat Med. 2003;6:425-427.

Simon A, Kar M, Hinz J, Beck D. Attitudes towards terminal sedation: an empirical survey among experts in the field of medical ethics. BMC Palliat Care. 2007;6.

Stone P, Phillips C, Spruyt O, Waight C. A comparison of the use of sedatives in a hospital support team and in a hospice. Palliat Med. 1997;11:140-144.

Tännsjö T. Terminal sedation or voluntary euthanasia? Bull Med Ethics. 2000; November:13-22.

Tännsjö T. Terminal sedation: euthanasia in disguise? Kluwer Academic Publishers: Dordrecht, the Netherlands; 2004.

Taylor RM. Is terminal sedation really euthanasia? Med. Ethics. 2003;10:3-8.

Vainio A, Auvinen A, Members of the Symptom Prevalence Group. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J Pain Symptom Manage. 1996;12:3-10.

Van der Heide A, Onwuteaka-Philipsen B, Rurup ML et al. End-of-Life practices in the Netherlands under the euthanasia act. NEJM. 2007; 356:1957-1965.

Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care. 1990;6:7-11.

Verhagen EH, Eliel MR, De Graeff A, Theunissen SCCM. Sedation in the terminal life phase. Ned Tijdschr Geneeskd. 1999;143:2601-2603.

Vitetta L, Kenner D, Sali A. Sedation and analgesia-prescribing patterns in terminally ill patients at the end of life. Am J Hosp Pall Care 2005;22:465-473.

Zech DFJ, Grond S, Lynch J, Hertel D, Lehman KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. Pain. 1995;63:65-76.

CHAPTER 3: VALIDITY AND RELIABILITY

A man should look for what is,
and not for what he thinks should be.

Albert Einstein

Published: Development and Validation of a Modified Version of the Edmonton Symptom Assessment Scale in a Flemish Palliative Care Population. American Journal of Hospice and Palliative Medicine, 2011, 28:475-482.

ABSTRACT

Patients suffering from a terminal illness often are confronted with severe symptoms during the last phase of their lives. Palliative sedation, although one of the options of last resort, remains a much debated and controversial issue and is often referred to as a form of slow euthanasia or euthanasia in disguise.

A prospective longitudinal and descriptive design was used. Each patient admitted in one of the 8 participating units was included if they met the inclusion criteria and gave written informed consent.

Two hundred and sixty six patients were included. The incidence of palliative sedation was 7;5%. For the group of sedated patients results show that 90% entered the palliative care unit being fully conscious. Two patients were comatose upon arrival. 90% of the patients remained fully conscious up to the day palliative sedation was started. When looking at the effect of palliative sedation on the level of consciousness the analysis strongly suggest that the palliative sedation – as expected- has an impact on the GCS score. Irrespective of the dichotomization of the score the probability of having a lower GCS increases substantially once sedation is initiated. Additionally, results show that once palliative sedation is administered, the level of consciousness gradually goes down up until the day of death.

Palliative sedation is nor slow euthanasia nor an ambivalent practice. It is an intentional medical treatment which is administered in a proportional way when refractory suffering occurs. It occurs in extraordinary situations and at the very end of the dying process.

INTRODUCTION

In her definition of palliative care, the World Health Association (WHO) states that the focus of palliative care is to improve the quality of life of terminally ill patients. According to several researchers, quality of life is affected by the amount of symptoms patients are confronted with and the accompanying symptom distress (Chang et al., 1998; Chiu et al., 2000; Mangan et al., 2003; Tranmer et al., 2003; Walsh et al., 2002). Some studies even show a significant negative effect of symptom occurrence on quality of life ($p<0.001$) (Astradsson et al., 2001; Chang et al., 2000; McMillan & Small, 2002; Tierney et al., 1998). Palliative care, therefore, is focused primarily on symptom control, an essential but often inadequately met need of terminally ill patients (Kutner et al., 2001; Morasso et al., 1999).

Symptom control can only be efficient and well-done if it is based on a systematic and standardized assessment of symptom experience. During the last decades, several instruments to assess different symptoms have been developed (Bruera et al., 1991; de Haes et al., 1996; Portenoy et al., 1994). One of these was the Edmonton Symptom Assessment Scale developed by Bruera et al. (Bruera et al., 1991) which has become one of the most used instruments in palliative care settings (Bruera et al., 1991). However, since the development of this instrument palliative care, more in particular as a result of the significant progress in symptom management and symptom control (Chiu et al., 2001; Heedman & Strang, 2003), has changed. Additionally, the symptom experience of the palliative patient and his family has changed (Mangan et al., 2003), leaving researchers with questions concerning symptom experience in the current palliative care population. Therefore, there is a need to readdress the measurement of the symptom experience of palliative care patients in the 21st century.

This study aims to investigate the validity of a modified version of the Edmonton Symptom Assessment Scale (M-ESAS), an adjusted version of the initial tool (Bruera et al., 1991; Bruera, 1994), in the measurement of palliative care patients' symptom experience. This will be investigated, in particular, through a study of face-validity, content validity, concurrent validity, construct validity and internal consistency.

CONCEPTUAL BACKGROUND

A symptom is described as a perception of a phenomenon in the body of the patient which is perceived by the patient as a characteristic of a disease or disorder (Blacklow, 1983; McDaniel & Rhodes, 1995; Rhodes & Watson, 1987; Zhukovsky et al., 2000). Given that a symptom is a

perception, it is by definition a subjective theme (Bruera, 1996; Kristjanson et al., 1998) and therefore it differs from a sign, which is an objective signal of a disease or disorder (Blacklow, 1983).

Rhodes & Watson (1987) are the first authors who conceptualized the symptom experience of a patient as a multidimensional concept. They described the concept of symptom experience as the combination of symptom occurrence and symptom distress, a conceptualization which, was later adopted by several authors (McMillan & Small, 2002; Ingham & Portenoy, 1996; Rhodes et al., 2000). Symptom experience is an overall perception of and response to the symptom occurrence, while symptom distress is based more on patients' experiences (McMillan & Small, 2002; Rhodes et al., 2000). Symptom occurrence, which is the cognitive component of a symptom experience, contains the frequency, the duration and the intensity of the bodily sensation of the patient (McMillan & Small, 2002; Rhodes & Watson, 1987; Rhodes et al., 2000). Symptom Distress is the emotional component of a symptom experience, and is defined as the degree of physical and/or mental anguish caused by the occurrence of a specific symptom (McMillan & Small, 2002; Kristjanson et al., 1998; Rhodes et al., 2000; Leventhal & Johnson, 1983; Leventhal et al., 1992). This conceptualization of symptom experience is congruent with the theory of self-regulation (Leventhal et al., 1984). This theory states that a person who is confronted with a stimulus (e.g. a bodily sensation) will immediately respond with two simultaneous processes, a cognitive process focused on the development of a coping strategy and an emotional process based on the emotional incorporation of the perceived stimulus (Leventhal et al., 1992; Leventhal et al., 1984).

Therefore, when assessing the symptom experience of a palliative care cancer patient, it is important to regard these two dimensions. Indeed, the presence of a symptom, represented by its frequency, duration or intensity, does not give an insight in the perceived distress patient's experience. Studies have shown that in a sample of hospitalized adult palliative cancer patients, there is a significant difference between intensity and distress (Tranmer et al., 2003; Chang et al., 2000; Rhodes & Watson, 1987; Ingham & Portenoy, 1996). Moreover, distress seems to entail more information regarding the impact of symptoms on quality of life, even though both dimensions of symptom experience are crucial during assessment.

DEVELOPMENT OF A "MODIFIED VERSION OF THE EDMONTON SYMPTOM ASSESSMENT SCALE"

The Edmonton Symptom Assessment Scale developed by Bruera et al. (1991) is a clinical tool used to measure the intensity and frequency of symptoms in a palliative care population (Bruera et al., 1991; Zhukovsky et al., 2000; Cleeland, 2000; Dudgeon et al., 1999; Jenkins et al., 1998; Nekolaichuk et al., 1999; Philip et al., 1998; Bruera et al., 2000). The ESAS is based on self-report with a possibility for the patient to complete the questionnaire with the help of the nurse/family (Bruera et al., 1991; Zhukovsky et al., 2000; Jenkins et al., 1998; Nekolaichuk et al., 1999; Strömgren et al., 2002; Nelson et al., 2001). Initially, the ESAS consisted of 9 Visual Analogue Scales to measure the ad hoc symptom intensity of 9 physical and psychological symptoms (Astradsson et al., 2001; Bruera et al., 1991; Zhukovsky et al., 2000). The symptoms measured include pain, weakness, nausea, depression, anxiety, drowsiness, appetite, sensation of well-being and 1 VAS symptom to be chosen by the patient. Over time, a 10th VAS was added for the symptom 'shortness of breath' and the symptom 'weakness' was replaced by 'activity' and later by 'fatigue' (Bruera et al., 1991; Cleeland, 2000; Bruera et al., 2000; Nelson et al., 2001). The VAS ranges from 0-100mm where 0 reflects the absence of a symptom and 100 reflects the worst intensity of a symptom (Astradsson et al., 2001; Philip et al., 1998; Nelson et al., 2001). Bruera et al. (1991) states that by summing up the individual item scores, researchers can attain an indication of the Global Symptom Distress score of the patient. The ESAS has proven to be a reliable and valid measurement in assessing the symptoms of palliative care patients (Dudgeon et al., 1999; Jenkins et al., 1998; Bruera et al., 2000; Rees et al., 1998; Osaba, 1993). However, there is presently no Dutch version of the ESAS available which has been checked for validity and reliability.

Because of the absence of a clinically useful Dutch questionnaire to score the symptom experience of palliative care patients, we translated the ESAS into Dutch. Based on the conceptualization of Rhodes & Watson's model of symptom experience and the available evidence that confirms that there is indeed a significant difference between symptom intensity and symptom distress (supra), we added 10 more items for measuring the symptom distress patients' experience.

In contrast with Bruera et al. (1991) we did not use the global symptom distress score. The addition of item scores implies that each symptom is regarded as equally important (Streiner & Norman, 1989)) and goes beyond the fact that each patient experiences some symptoms as more or less important than others (Hinds et al., 2002). A total score does reflect the cumulative effect of

symptoms but is not of much use to determine specific interventions, since clinical significant scores on individual items can be masked (Anderson et al., 1996).

METHODOLOGY

A descriptive comparative design was used to test the psychometric features of the modified version of the Edmonton Symptom Assessment Scale (M-ESAS). This took place in three phases. Each phase involved a different convenience sample and followed a different protocol. Phases two and three were based on an approval of the local ethics committee and an informed consent of each participant guaranteeing the anonymity and privacy of the participant.

PHASE 1: CONTENT VALIDITY

A dual procedure was used to test the content validity of the modified and translated version of the ESAS. The first procedure included a systematic literature search of diverse databases (Medline, Cinahl, Invert & Cochrane) in order to assess whether the symptoms that are included in the ESAS are, in fact, those symptoms that are most commonly experienced by hospitalized, palliative care patients. We also examined whether or not each of these symptoms were listed as symptoms and not as signs. Based on the available literature research a survey of the symptoms and their prevalence figures was then assembled. Symptoms were ranked and the 12 most prevalent symptoms were withheld. We chose 12 symptoms due to the necessity of finding a balance between information and workload for the patient considering the fact that we are dealing with very frail patients in the last phase of their lives. This list of symptoms was compared with the symptoms included in the ESAS. Remarks with regard to the ESAS that were made in the articles were withheld and taken into account in the further evaluation of the content validity.

In a second phase, an expert panel, which was composed of 5 physicians and 5 head nurses working in the field of palliative care, was assembled. The members of the panel were carefully selected with the assurance that every province and every type of hospital (private, public, university) was represented in this sample. Each expert received an e-mail that situated the study and was asked to fill out a questionnaire. On the questionnaire, all 9 symptoms of the ESAS were listed together with 11 other symptoms that were proven important. Experts were asked to determine whether or not these symptoms were comprehensible, were relevant for the Flemish palliative care population, and to rank these symptoms according to their relevance. After 10 days a reminder was sent by e-mail to those experts that had not yet answered. Thereafter, possible non-responders were contacted by phone.

When an expert decided not to participate, another expert was contacted from the same province. In that case, the same procedure was repeated.

PHASE 2: FACE VALIDITY

To assess the face validity of the M-ESAS we contacted 5 hospitalized palliative cancer patients, 5 family members and 5 nurses residing/working on the palliative care unit of the university hospitals in Leuven, Belgium. Patients and family members had to meet the following inclusion criteria: oncological patient (or a family member of such a patient), older than 18 years of age, with an understanding and literacy of Dutch, mentally alert, and give oral informed consent. These participants had to determine whether or not they understood what was asked in the M-ESAS, if they thought the symptoms were adequately described and whether or not they observed any important items not included in the list. Participants also received a form on which they had to write their comments and demographic characteristics. All forms were then collected and an overview of the outcomes created. Changes were made to the M-ESAS based on these results.

PHASE 3: CONCURRENT VALIDITY, CONCEPT VALIDITY AND INTERNAL CONSISTENCY

The *concurrent validity* of the M-ESAS was tested based on four hypotheses. First, we wanted to test whether the symptom experience was correlated with the functional status of the patients. For this purpose the Palliative Performance Scale (PPS) (Anderson et al., 1996) was completed for each patient. In accordance with Morita et al. (1999) and Chang et al. (2000), the threshold between a high and low functional status was set at 50. A second hypothesis, which was tested, analyzed the differences between patients with a high or low risk of depression. For this purpose the 5-item Geriatric Depression Scale (GDS) was used (Hoyl et al., 1999). This short and easy to use instrument was developed specifically for geriatric populations (Kok, 1994; Vandevelde et al., 2002) and indicates that patients with a score of 2 or more have a higher risk for developing depression.

The last two hypotheses that were tested were linked with gender and primary diagnoses. It is presumed that females report more frequent and more intense symptom experiences then males (Gijbers et al., 1999; Kroenke et al., 1994; Stenberg & Wall, 1995). Moreover, symptom experience is, according to Donnelly et al. (1995) and Vainio & Auvinen (1996), linked with the primary tumor site. Therefore, both gender and primary tumor site were tested for a possible significant link.

A second type of validity that was tested in this third phase of the study was the *congruent validity*. Two hypotheses were formulated. One stated that symptom occurrence and symptom distress were two related but independent concepts (Rhodes & Watson, 1987; Leventhal et al., 1984). A second hypothesis assumed that healthy controls have lower scores on symptom occurrence and symptom distress than palliative care patients.

A last aspect that was tested was the *internal consistency* of the M-ESAS. Although this might seem unnecessary, considering that different symptoms are assessed which are not necessarily related to one another, we decided to create a correlation matrix in which the size and direction of the correlation was checked. If this correlation matrix would show that not all items are present in a consistent way, this would be an extra argument against the use of the symptom distress scale as postulated by Bruera et al. (1991).

Two samples were used to test these different forms of validity and reliability. The first sample consisted of Flemish palliative care patients admitted to 1 of 3 participating palliative care units. Each patient that was already admitted to these units at the time of the start of the study or was admitted during the study, was asked to participate. Patients had to meet the following inclusion criteria: an oncological patient or a family member of such patient, older than 18 years of age, with an understanding and literacy of Dutch, mentally alert, give oral informed consent. One day after admission, each possible participant was contacted by the researcher and received oral and written information explaining the purpose of the study. After giving informed consent, each participant was asked to fill out the M-ESAS. The GDS was done based on an interview and demographics and PPS were gathered by the researcher. This data collection was done over three consecutive days.

A second sample consisted of healthy controls that were matched for age and gender. These participants had to be healthy and free of cancer, had to be able to read and write Dutch, be mentally alert and give an oral informed consent. For privacy reasons, the patients were contacted by their general practitioners prior to being contacted by the researcher. Each participant was asked to fill out the M-ESAS.

Analysis of these data were based on non-parametric statistics, more specifically the Wilcoxon-Mann-Whitney U-test, Kendall's Tau and Wilcoxon Singed Ranks test (Pett, 1997). All analyses were done with SPSS 9.0 and the level of significance was set at 0.05.

RESULTS

PHASE 1: CONTENT VALIDITY

Based on the literature review and the evaluation of the expert panel (80% response) the researchers decided to withhold all symptoms that were mentioned in the ESAS and completed the list with the symptoms of dry mouth, constipation and disturbed sleep. Since there was unanimity on the indistinctness of the items appetite, well-being and depression, it was decided to rephrase these items. 'Appetite' was changed to 'reduced appetite', 'well-being' was changed to an 'uncomfortable/unhappy feeling' and 'depression' was changed to 'feeling down'. This modified version of the ESAS was used from this point on to test validity and reliability.

PHASE 2: FACE VALIDITY

Almost all participants (n=14; Table 1) were able to understand what was asked of them when they read the instructions that were on the questionnaire. In relation to the formulation and the clarity of the concepts, 'constipation' was the only symptom which appeared difficult to understand. Based on our literary research, we decided to change this item to 'bowel obstruction' *(literal translation of the Dutch term, and thus different from the clinical diagnoses of bowel obstruction)*. Neither patients nor family members mentioned symptoms that were not mentioned on the M-ESAS and thus no extra symptoms were added to the questionnaire.

Table 1
Demographic Characteristics Sample Face Validity

Variables	Prevalence (%)	Median
Nurses (n=5)		
Age		35
Men	2 (40)	
Years' experience		5
Family Members (n=5)		
Age		51
Men	3 (60)	
Relationship with patient		
Spouse	1 (20)	
child	4 (80)	
Patients (n=4)		
Age		80
Men	3 (75)	

PHASE 3: CONCURRENT VALIDITY, CONSTRUCT VALIDITY AND INTERNAL CONSISTENCY

In this study, twenty three cancer patients (38% of admitted patients during time of study) were included on three palliative care units (Table 2). Of these, 52% were male with a median age of 68 year. The majority of patients (82%) had a low functional status (PPS $\leq$ 50) and 56% of the patients had an increased risk for depression (GDS $\geq$ 2). All patients required help from the researcher to fill out the M-ESAS. Of the 23 participants, 8 participants were not able to complete the M-ESAS during three consecutive days, even with the support of the researcher. The high dropout (62%) was mainly due to communication problems (11%), progression of the illness (21%) and patients not meeting the inclusion criteria (60%). However, there were no significant differences between the included/not included patients concerning age (p = 0.089) and gender (p = 0.444). Table 3 summarizes the variance and the prevalence of symptoms on day one, after admission.

Table 2
Demographic Variables Sample of Patients (n=23)

Variables		Prevalence (%)	Median/mean
Age (years)			68
Female		11 (48%)	
Functional status:	30%	4 (17%)	
	40%	8 (35%)	
	50%	7 (30%)	
	60%	2 (9%)	
	70%	2 (9%)	
Risk for depression	0	3 (13%)	
	1	7 (30%)	
	2	8 (35%)	
	3	4 (17%)	
	4	1 (4%)	
Primary tumor site	Kidney	1 (4%)	
	Lung	4 (17%)	
	Breast	3 (13%)	
	Colon	2 (9%)	
	Stomach	1 (4%)	
	Uterus	1 (4%)	
	Thyroid	1 (4%)	
	prostate	3 (13%)	
	Pancreas	5 (22%)	
	Bile	1 (4%)	
	Larynx	1 (4%)	

CONCURRENT VALIDITY

Based on the above hypotheses that were tested, several differences were found between the diverse subgroups of the sample.

Female patients and patients with a low functional status (PPS ≤ 50) had a tendency to report a higher symptom occurrence for pain (p=0.072; p=0.028), reduced appetite (p=0.001; p=0.022) and bowel obstruction (p=0.003; p=0.054). Additionally, females scored higher on nausea (p=0.035) and anxiety (p=0.038), where patients with a low PPS scored higher on dry mouth (p=0.042) and drowsiness (p=0.074). Moreover, patients with a higher risk for depression (GDS ≥ 2) had a higher score for uncomfortable/unhappy feelings (p=0.036). There was no difference found in symptom distress scores except in the categories of pain and low functional status. Patients with a low PPS scored significantly higher for pain than patients with a high PPS (p=0.028).

Table 3
Variance of Symptom Occurrence Scores on Day 1 of the Admission

Symptom Occurrence	Quartile 1	Median	Quartile 3	Times Present (%)
Pain	0	4	52	13 (56.5)
Fatigue	11	47	76	19 (82.6)
Nausea	0	0	32	10 (43.5)
Feeling down	0	0	67	11 (47.8
Anxiety	0	0	34	7 (30.4)
Drowsiness	21	49	72	20 (87)
Reduced appetite	37	70	95	18 (78.3)
Uncomfortable/unhappy feeling	0	20	48	174 (73.9)
Shortness of breath	24	46	81	20 (87)
Bowel obstruction	0	0	33	11 (47.8)
Dry mouth	24	51	80	20 (87)
Disturbed sleep	0	0	32	11 (47.8)

CONSTRUCT VALIDITY

To get an insight in the construct validity of the M-ESAS, we tested if the categories of symptom occurrence and symptom distress were two related but different concepts. Kendall's Tau revealed that there was only a weak to mediocre relationship between symptom occurrence and symptom distress (Table 4). Only for symptom anxiety was there a strong correlation between distress (r=0.782) and occurrence. With a Wilcoxon Signed Ranks Test we examined whether the symptom occurrence scores were higher than the distress scores or vice versa. In 25% of the symptoms, distress

scores were higher than occurrence (pain, nausea and dyspnea) scores. For all other symptoms, occurrence scores were higher than distress.

Table 4
Kendall Tau Correlation Coefficient Between Symptom Occurrence and Symptom Distress

Symptoms	Kendall's Tau
Pain	0.688
Fatigue	0.525
Nausea	0.554
Feeling down	0.667
Anxiety	0.782
Drowsiness	0.516
Reduced appetite	0.268
Uncomfortable/unhappy feeling	0.514
Shortness of breath	0.364
Bowel obstruction	0.518
Dry mouth	0.496
Disturbed sleep	0.669

In a second step, we compared patients' scores with healthy controls conform the 'known group' technique. We found that patients reported higher symptom occurrence and distress for fatigue ($p<0.01$), nausea ($p<0.001$), drowsiness ($p<0.001$), reduced appetite ($p<0.001$), shortness of breath ($p<0.001$) and dry mouth ($p<0.001$) than the healthy controls. Symptom distress was higher for patients when it concerned fatigue ($p<0.01$), nausea ($p<0.01$), drowsiness ($p<0.05$), reduced appetite ($p<0.001$), shortness of breath ($p<0.001$) and dry mouth ($p<0.001$). There was no significant difference between young and old for either the patients nor the healthy controls.

INTERNAL CONSISTENCY

Based on the established correlation matrix, researchers found that both positive and negative correlations were present. Thus, there was no need to calculate a Cronbach's alpha, to determine the internal consistency of this instrument. Moreover, this matrix shows that there is a weak to mediocre relationship between the different symptoms included in the M-ESAS for both symptom occurrence and symptom distress.

DISCUSSION

GENERAL FINDINGS AND CONCLUSIONS

Our findings have revealed that there was a low variance for the symptoms pain, nausea, feeling down, anxiety, bowel obstruction and disturbed sleep. The fact that there was such a low variance and a limited occurrence of these symptoms can be explained by the treatment that is given for these symptoms on palliative care units. All included palliative care units already have a well-established procedure to treat pain, constipation and nausea. Sleep disturbances appeared to be treated systematically. The fact that anxiety scored low is probably due to the fact that patients admitted to palliative care units (albeit coming from another ward, or from home) are well informed by palliative care teams or regional palliative home care teams, thus, resulting in a high percentage of patients having accepted their disease status. Palliative care experts use an open communication and are experienced listeners who are willing to talk about feelings and fears that might accompany admission. Therefore, they are seemingly very successful in comforting the patient and his/her family and in giving the message that health care workers at the PCU will accompany them throughout their illness journey.

Most of the patients were able to fill out the modified version of the Edmonton Symptom Assessment Scale themselves with some assistance from the researcher. This is in contrast with results in other studies which report that 61% – 97.1% could fill out the ESAS independently (Bruera et al., 2000, Chang et al., 2000). However, the functional status of the patients in these studies was higher, with Chang et al. (2000) reporting a PPS of 60-80%, which might explain this difference. Our patients had a much lower PPS score and thus were in a more advanced phase of their disease, making it difficult to fill out questionnaires by themselves.

The attrition in our study was high (62%) in comparison with other studies that reported a maximum of 50% (Osaba, 1993). This is due to our use of very stringent inclusion criteria. We did not include patients with dementia, who are non-native Dutch speakers and non-cancer patients, which would have given an attrition rate that equals 43.9%. But even then, a sizeable group of patients would remain out of consideration. In further studies, it might be interesting to explore how we might use the contribution of nurses, family and physicians to assess the symptom experience of terminally ill, palliative care patients.

An interesting finding in this study was that only two patients refused to participate. This is in contrast with the 'paternalistic' idea, which some palliative care experts express, that it is ethically unacceptable to do research with patients that are dying (Mc. Donald et al., 2004; Crowley et al., 2003). Patients possibly disagree with the 'paternalistic' point of view because their participation in research, may assist in giving meaning to the last days of their lives because their input might benefit other terminally ill patients in the future.

CONTENT VALIDITY

Based on the analysis of the content validity, the ESAS was adjusted. Bowel obstruction, dry mouth and disturbed sleep were newly added symptoms. Well-being, depression and appetite were rephrased. Considering 52% of the patients expressed that bowel obstruction was not a problem for them, one might conclude that this is no longer a relevant symptom to be included in the M-ESAS. This action, however, is not advised considering all palliative care units have a well-established policy and transparent attitude towards preventing constipation. Such a policy emphasizes the importance of assessing constipation in palliative care units. Use of morphine, reduced food and fluid intake and being bedridden makes palliative care patients at a higher risk for developing bowel obstruction. Therefore, it is not advisable to eliminate this item from the M-ESAS.

A second, frequently reported symptom that was added, which is often the cause of considerable distress, was 'dry mouth'. The importance of maintaining this symptom was linked to the reality that palliative care patients are confronted with an extensive medication-intake and reduced fluid intake, which are two aspects that often lead to the symptom of dry mouth. Since there is still a lot of controversy with regard to the withholding or withdrawing of fluid in palliative care patients, partly because of the symbolic meaning that this act has (Printz, 1992; Taylor, 1995), assessing the symptom 'dry mouth' could assist in delineating an individualized policy on fluid intake. Another reason for maintaining this item is that reduced fluid intake influences the M-ESAS items pain, nausea and shortness of breath (Van Orshoven & Menten, 2000).

A last symptom that was added was 'disturbed sleep'. This symptom had a low frequency that could be attributed to the potentially good effects of sleep medication, which is an aspect that was not assessed in this study. The fact that good sleep is beneficial for the well-being of the patients, both physically and psychologically (Sateia & Silberfarb, 1998) is another argument for maintaining this symptom in the M-ESAS.

CONCURRENT VALIDITY

The analysis of the data gathered to test the concurrent validity revealed that the formulated hypotheses were only partly confirmed. Although this is in agreement with what other authors have reported, (Astradsson et al., 2001) there may be some distortion in the results due to the use of a small convenience sample with a high attrition.

CONSTRUCT VALIDITY

The construct validity test was based on two hypotheses. The hypothesis of symptom occurrence and symptom distress as two related but different concepts was clearly confirmed. Moreover, symptom distress scores were higher than symptom occurrence indicating that assessing symptom distress is very important and valuable. The second hypotheses for which comparisons were made between palliative care patients and healthy controls (matched for age and gender) was confirmed in the majority of symptoms. One could argue that those symptoms, that were not significantly different between the two groups, should be omitted from the questionnaire. This however would be premature since all PCU's maintain a policy which focuses on treating these symptoms from day one.

INTERNAL CONSISTENCY

Although dubious, we decided to test the internal consistency of this questionnaire. Based on the correlation matrix it became clear that calculating a Cronbach's alpha was non-beneficial, considering the different relationships and directions that were found between symptoms and that the size of the relationship was small. These findings support the idea of abandoning the global symptom distress score, as introduced by Bruera et al. (1991), and replacing it with independent symptom distress scores. Without a certain number of internal consistency, different items cannot be summarized (Hinds et al., 2002).

METHODOLOGICAL QUALITY

The strength of this study is the use of a prospective design. Moreover the researchers performed a thorough investigation of different forms of validation and reliability prior to beginning the study and decided which forms of validity could be used.

Nevertheless there are also some limitations that should be taken into account when interpreting the results of this study. This study was based on convenience samples which are, due to high attrition, not always representative for the population. The instruments used to test the diverse

hypotheses, namely the Palliative Performance Score and the Geriatric Depression Scale (5-item) were not validated for this patient population and thus, might have caused a certain bias. Moreover, symptom treatment was not assessed, although this might have revealed interesting information. In summary, many interesting findings were established but need to be interpreted within the boundaries of these methodological limitations.

CONCLUSION

This study was intended to develop a clinical instrument which would assess the symptom experience in patients admitted to a Flemish palliative care unit. In order to test this instrument, a validation study was set up in three Flemish palliative care units.

Adding 3 symptoms and a section on symptom distress; revising certain formulations and abandoning the global distress score were measures that found support in the results. Taking into account the current 'new-wave' vision on validity and reliability, the modified version of the Edmonton Symptom Assessment Scale is an accurate instrument to measure the symptom experience of Flemish palliative care patients. More in-depth research remains necessary to further explore the characteristics of this instrument and demonstrate the added value for clinical practice.

REFERENCES

Anderson F, Dowing GM, Hill J, Casorso L, Lerch N. Palliative performance scale: a new tool. J Palliat Care 1996; 12:5-11.

Astradsson E, Granath L, Heedman P-A, Starkhammar H. Cancer patients hospitalized for palliative reasons. Symptoms and needs presented at a university hospital. Support Car Cancer 2001, 9: 97-102.

Blacklow RS. The study of symptoms. In Blacklow RS ed., MacBryde's signs and symptoms: apllied pathologic physiology and clinical interpretation (pp. 1-16). Philadelphia: Lippingcott, 1983.

Bruera E, Kuehn N, Miller MJ, Selmser P McMillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. J Palliat Care 1991;7:2-9.

Bruera E, Neumann C, Brenneis C, Quan H. Frequency of symptom distress and poor prognostic indicators in palliative care patients admitted to a tertiary palliative care unit, hospices, and acute care hospitals. J Palliat Care 2000; 16:16-21.

Bruera E. Ethical issues in palliative care research. Journal of Palliative Care 1994; 10:7-9.

Bruera E. Patient assessment in palliative cancer care. Cancer Treatment Reviews 1996; 22:3-12.

Chang VT, Hwang SS & Feuerman M. Validation of the Edmonton Symptom Assessment Scale. Cancer 2000a; 88:2164-2171.

Chang VT, Hwang SS, Feuerman M, Kasimis BS, Thaler HT. The Memorial Symptom Assessment Scale short form. Validity and reliability. Cancer 2000c; 89:1162-1171.

Chang VT, Hwang SS, Feuerman M, Kasimis BS. Symptom and quality of life survey of emdical oncology patients at a veterans affairs medical center. American Cancer Society 2000b; 88:1175-1183.

Chang, V.T. , Thaler, H.T., Polyak, T.A., Kornblith, A.B. , Lepore, J.M., & Portenoy, R.K. (1998). Quality of life and survival. The role of multidimensional symptom assessment. *Cancer, 8(3),* 173-179.

Chiu TY, Hu WY Chen CY. Prevalence and severity of symptoms in terminal cancer patients: a study in Taiwan. Support Care Cancer 2000; 8:311-313.

Chiu T-Y, Lue B-H, Cheng S-Y, Chen C-Y. Sedation for refractory symptoms of terminal cancer patients in Taiwan. J Pain Symptom Manage 2001; 21:467-472.

Cleeland CS. Cancer-related symptoms. Sem Radiation Oncol 2000; 10:175-190.

Crowley R, Casarett D. Patients' willingness to participate in symptom-related and disease modifying research. Cancer 2003; 97:2327-2333.

de Haes, J.C.J.M. , Oleschewski, M. , Fayers, P. , Visser, M.R.M. , Cull, A. , Hopwood, P., et al. (1996). *Measuring the quality of life of cancer patients with the Rotterdam Symptom Checklist: a manual*. Retrieved October 2, 2003, from the University of Groningen, Northern Centre for Healthcare Research Web site: http://www.coo.med.rug.nl/nch/rscl.pdf

Donnelly S, Walsh D, Rybicki L. The symptoms of advanced cancer: identification of clinical and research priorities by assessment of prevalence and severity. J Palliat Care 1995; 11:27-32.

Dudgeon DJ, Harlos M, Clinch JJ. The Edmonton Symptom Assessment Scale as an audit tool. J Palliat Care 1999; 15:14-19.

Gijbers van Wijk CMT, Huisman H, Kolk AM. Gender differences in physical symptoms and illness behavioral health diary study. Soc Scie Med 1999; 49: 1061-1074.

Heedman P-A, Strang P. Pain and pain alleviation in hospital based home care: demographic, biological and treatment factors. Support Care Cancer 2003; 11:35-40.

Hinds PS, Schum L, Srivastava DK. Is clinical relevance sometimes lost in summative scores? West J Nurs Research 2002; 24:345-353.

Hoyl MT, Alessi CA, Harker JO, Josephson KR, Pietruszka FM, Koelfgen M, et al. Development and testing of a five-item version of the Geriatric Depression Scale. JAGS 1999; 47:873-878.

Ingham JM, Portenoy RK (1996). Symptom assessment. Hematology/Oncoloy Clinics of North America 1996; 10:21-39.

Jenkins CA, Taube AW, Turner K, Hanson J, Bruera E. Initial demographic, symptom, and medication profiles in patients admitted to continuing palliative care units. J Pain Symptom Manage 1998; 16:163-170.

Jubb AM. Palliative care research: trading ethics for an evidence base. J Med Ethics 2002; 28:342-346.

Kok RM. Zelfbeoordelingsschalen voor depressie bij ouderen. Tijdschrift voor gerontologie en geriatrie 1994; 25:150-156.

Kristjanson LJ, Nikoletti S, Porock D, Smith M, Lobchuk M, Pedler P. Congruence between patients' and family caregivers' perceptions of symptom distress in patients with terminal cancer. Journal of Palliative Care 1998; 14:24-32.

Kroenke K, Spitzer RL, Williams JB, Linzer M, Hahn SR, de Gruy FV, et al. Physical symptoms in primary care. Predictors of psychiatric disorders and functional impairment. Arch Family Med 1994; 3:774-779.

Kutner JS, kassner CT, Nowels DE. Symptom burden at the end of life: hospice providers' perceptions. Journal of Pain and Symptom Management 2001; 21:473-480.

Leventhal H, Diefenbach M, Leventhal EA. Illness cognition/using common sense to understand treatment adherence and affect cognition interactions. Cognitive Therapy and Research 1992;16:143-163.

Leventhal H, Johnson JE. Laboratory and filed experimentation. Development of a theory of self-regulation. In Wooldrigde PJ, Schmitt MH, Schipper JK, Leonard RC (eds.). Behavioral science and nursing theory (pp. 189-262). St. Louis: CV Mosby, 1983.

Leventhal H, Nerenz, DR, Steele, DJ. Illness representations and coping with health threats. In Baum A, Taylor, SE, Singer JE (Eds.), *Handbook of psychology and health. Social Psychological aspects of health* (pp. 219-252), 1984.

Mangan PA, Taylor KL, Yabroff KR, Fleming Da, Ingham JM. Caregiving near the end of life: unmet needs and potential solutions. Palliat Support Care 2003; 1:247-259.

McDaniel RW, Rhodes VA. Symptom experience. Seminars in oncology 1995; 11:232-234.

McDonald N, Weijer C. Ethical issues in palliative care research. In: Doyle D, Hanks G, Cherny N, Calman K (Eds.), Oxford textbook of palliative medicine (pp.76-83); 2004. Oxford: Oxford university press.

McMillan SC & Small BJ (2002). Symptom distress and quality of life in patients with cancer newly admitted to hospice home care. Oncology Nursing Forum 2002; 29:1421-1428.

Morasso G, Capelli M, Viterbori P, Di Leo S, Alberisio A, Costantini M et al. Psychological and symptom distress in terminal cancer patients with met and unmet needs. Journal of Pain and Symptom Management 1999; 17:402-409.

Morita T, Tsunoda J, Inoue S, Chihara S. Contributing factors to physical symptoms in terminally-ill cancer patients. J Pain Symptom Manage 1999; 18:338-346.

Nekolaichuk CL, Maguire TO, Suarez-Almazor M, Rogers WT, Bruera E. Assessing the reliability of patient, nurse and family caregiver symptom ratings in hospitalized advanced cancer patients. J Clin Oncol 1999; 17:3621-3630.

Nelson JE, Meier DE, Oei EJ, Nierman Dm, Snezel RS, Manfredi PL et al. Self-reported symptom experience of critically ill cancer patients receiving intensive care. Critical Care Medicine 2001; 277-282.

Osaba D. Self-rating symptom checklists: a simple method for recording and evaluating symptom control in oncology. Cancer Treatment Reviews 1993; 19 (suppl A): 43-51.

Pett MA. Nonparametric statistics for health care research (1st ed.); 1997. California/London/new Delhi: Sage Publications.

Philip J, Smith WB, Craft P, Lickiss N. Concurrent validity of the modified Edmonton Symptom Assessment Scale with the Rotterdam Symptom Checklist and the Brief Pain Inventory. Support Care Cancer 1998; 6:539-541.

Portenoy RK, Thaler HT, Kornblith AB, McCarthy L, Friedlander-Klar H, Coyle N, et al. Symptom Prevalence, characteristics and distress in a cancer population. Qual Life research 1994; 3:183-189.

Printz LA. Terminal dehydration, a compassionate treatment. Arch Intern Med 1992; 152:697-700.

Rees E, hardy J, Ling J, Broadley K, A'hern, R. The use of the Edmonton Symptom Assessment Scale within a palliative care unit in the UK. Palliat Med 1998; 12:75-82.

Rhodes VA, McDaniel RW, Homan, SS, Johnson M & Madsen R. An instrument to measure symptom experience. Cancer Nursing 2000; 23:49-54.

Rhodes VA, Watson PM. Symptom Distress, the concept: past and present. Seminars in Oncology 1987; 3:242-247.

Sateia MJ, Silberfarb PM. Sleep. In: Doyle D, Hanks G, Cherny N, Calman K (Eds.). Oxford textbook of Palliative Medicine (pp. 751-767), 1998, Oxford: Oxford University Press.

Stenberg B, Wall S. Why do women report 'sick building symptoms' more often than men? Soc Scie Med; 40: 491-502.

Streiner DL, Norman GR. Health measurement scales: a practical guide to their development and use (1th ed.), 1989. Oxford: Oxford University Press.

Strömgren AS, Groenvold M, Pederson L, Olsen AK, Sjorgen P. Symptomatology of cancer patients in palliative care: content validation of self-assessment questionnaires against medical records. Eur J Cancer 2002; 38:788-794.

Taylor MA. Benefits of dehydration in terminally ill patients: allowing terminally ill patients to dehydrate is an ethically and legally acceptable therapeutic measure. Geriatric Nursing 1995; 16:271-272.

Tierney RM, Horton SM, Hannan TJ, Tierney WM. Relationships between symptom relief, quality of life, and satisfaction with hospice care. Palliative Medicine 1998; 12:333-344.

Tranmer JE, Heyland D, Dudgeon D, Groll D, Squires-Graham M & Coulson K. Measuring the symptom experience of seriously ill cancer and non-cancer hospitalized patients near the end of life with the Memorial Symptom Assessment Scale. J Pain Symptom Manage 2003; 25:420-429.

Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J Pain Symptom Manage 1996; 12:3-10.

Van Orshoven A, Menten J. Palliatieve zorg, stervensbegeleiding, rouwbegeleiding 2000. Leuven Acco.

Vandevelde E, Milisen K, Steeman E, Godderis J. Depressie bij gehospitaliseerde ouderen. In Milisen K, De Maesschalck L, Abraham I (Eds.) verpleegkundige zorgaspecten bij ouderen (pp. 201-220); 2002. Maarssen: Elsevier Gezondheidszorg.

Walsh D, Ribicki L, Nelson KA, Donnelly S. Symptoms and prognosis in advanced cancer. Support Care Cancer 2002; 10:385-388.

Zhukovsky DS, Abdullah O, Richardson M, Walsh D. Clinical evaluation in advanced cancer. Seminars in Oncology 2000; 27:14-23.

CHAPTER 4: THE PRACTICE OF PALLIATIVE SEDATION

Published: Palliative Sedation, Not Slow Euthanasia: a Prospective, Longitudinal Study of Sedation in Flemish Palliative Care Units. Journal of Pain and Symptom Management, 2011,41, 14-24.

ABSTRACT

Palliative sedation remains a much debated and controversial issue. The limited literature on the topic often fails to answer ethical questions concerning this practice.

The aim of this study was to describe the characteristics of patients who are being sedated for refractory symptoms in palliative care units (PCUs) from the time of admission until the day of death.

A prospective, longitudinal, descriptive design was used to assess data in eight PCUs. The total sample consisted of 266 patients. Information on demographics, medication, food and fluid intake, decision making, level of consciousness, and symptom experience were gathered by nurses and researchers three times a week. If patients received palliative sedation, extra information was gathered.

Of all included patients (n ¼ 266), 7.5% received palliative sedation. Sedation started, on average, 2.5 days before death and for half of these patients, the form of sedation changed over time. At the start of sedation, patients were in the end stage of their illness and needed total care. Patients were fully conscious and had very limited oral food or fluid intake. Only three patients received artificial fluids at the start of sedation. Patients reported, on average, two refractory symptoms, the most important ones being pain, fatigue, depression, drowsiness, and loss of feeling of well-being. In all cases, the patient gave consent to start palliative sedation because of increased suffering.

INTRODUCTION

Palliative sedation, as a therapy for refractory symptoms, remains a much debated and controversial issue both within and outside the palliative care movement (Howland, 2005; Billings & Block, 1996; Cooney, 2005). However, studies report various indications for palliative sedation, with a broad range of frequency of use and inconsistent information with regard to food and fluid intake (Claessens et al., 2007). These diverse findings are because of differences in care settings, in patient populations and caregivers, and in clinical practice, education and culture (Claessens et al., 2008). Hence, the current available literature, although informative, is limited in its ability to accurately answer the ethical questions concerning palliative sedation (Ventafridda et al., 1990; Fainsinger et al., 1991, 1998a,b, 2000; Stone et al., 1997; Chater et al., 1998; Menten, 2003).

Given that care for patients with life-threatening illnesses will become even more important because of an aging population and the subsequent increase in cancer and nonmalignant but chronic incurable disorders (e.g., dementia, respiratory and cardiac failure) (Cannaerts et al., 2000), there is a pressing need for reliable information concerning palliative sedation (Claessens et al., 2007,2008).

The aim of this study was to describe the characteristics of patients who are being sedated for refractory symptoms in palliative care units (PCUs) from the time of admission until the day of death.

METHODOLOGY

DESIGN, SETTING AND STUDY POPULATION

A prospective, longitudinal and descriptive design was used. To assure a representative sample of PCUs, all PCUs in Flanders, the Dutch-speaking, northern part of Belgium, were contacted (n=29). Data gathering required approximately eight minutes per patient per day; eight PCUs (27%) agreed to participate. Other PCUs (80%) refused participation because of the time required. After review of the research protocol, each unit was granted approval for the study by the local ethics committee. The sample consisted of three PCUs in general hospitals, one hospice, one PCU in a university hospital and three PCUs in university-affiliated general hospitals. Five hospitals (62%) had a Roman-Catholic background and three hospitals had no religious affiliation. Euthanasia (decriminalized in Belgium since 2002) was possible in six of the eight PCUs.

Each patient admitted to one of these PCUs between September 2004 and April 2005 who met the inclusion criteria and gave formal written informed consent was asked to participate. The

following inclusion criteria were set: patients had to be older than 18 years and had to be diagnosed with cancer. Twenty-seven percent of the patients refused to participate, 5% of the patient died before informed consent could be obtained, and 16% of the patients were not diagnosed with cancer.

VARIABLES

After an extensive review of the literature and careful consideration with the caregivers in palliative care settings, a list of relevant variables was drawn up. Data were assessed upon patient admission and thereafter every Monday, Wednesday and Friday, until the day of death. To reduce the workload for nurses, the registration of the variables was divided between the nurses and the research team. A researcher visited the unit once every two weeks and gathered the data that were available in the patients' charts. The nurse who was taking care of the patient during the time of assessment noted the other variables, which were based on observations (Table 1).

Table 1

Overview of registered Variables, Measurement Instruments Used, and Data Gatherers

Variable	Measurement instrument	Nurse	Researcher
Functional Status	Palliative Performance Scale	X	
Symptom Occurrence	Modified Edmonton Symptom Assessment Scale	X	
Symptom Distress	Modified Edmonton Symptom Assessment Scale	X	
Level of Consciousness	Glasgow Coma Scale	X	
Demographics	Chart review		X
Oral food and fluid intake	5-point scale		X
Artificial food and fluid intake	Chart review		X
Medication (name, dose/24h)	Chart review		X

Demographic variables (sex, age, nationality, marital status, religious affiliation , date of admission, date of death/discharge) were collected by a member of the research team at the time of admission and completed on the day of death. When patients received palliative sedation, extra information was gathered concerning the refractory suffering involved, the decision making process, the duration of the palliative sedation, and the kind of palliative sedation received. Because it was important to gain an insight into the practice of the use of sedatives in the PCU, no definition of palliative sedation was imposed. This prevented possible conceptual confusion between the PCUs and ensured that all possible cases of palliative sedation were included in the study.

MEASUREMENT INSTRUMENTS (SEE APPENDIX 2)

The oral food and fluid intake was scored based on a 5-point Likert scale (1 = normal food and fluid intake [>1 liter per day (L/day)], 2 = skips meals, normal fluid intake [>1 L/day], 3 = no food intake, drinks small amounts of fluid [<1 L/day], 4 = takes sips of fluid, 5 = no oral intake [mouth care only]). This scale was developed by the research team in close collaboration with head nurses of the PCUs and was understood as being a good representation of the different situations that occur in PCUs. Inter-rater reliability between nurses was evaluated in a pilot study. The intra class correlation coefficient (ICC) was 0.93 (confidence interval [CI] 0.875, 0.962).

Symptom prevalence and symptom distress were registered using the Modified Edmonton Symptom Assessment Scale (M-ESAS) (Claessens et al., 2011; De Blaeser, 2004). The M-ESAS consists of 24 (2x12) visual analogue scales (VAS) ranging from 0-100mm. Each VAS score represents either the symptom intensity or the symptom distress. The following 12 symptoms are included in this instrument: pain, fatigue, nausea, feeling down, anxiety, drowsiness, reduced appetite, uncomfortable/unhappy feeling, shortness of breath, bowel obstruction, dry mouth and disturbed sleep. This modified questionnaire was developed and tested for validity and reliability in a pilot study and proven useful for this patient population (Claessens et al., 2011; De Blaeser et al., 2004).

The Palliative Performance Scale (PPS) (Anderson et al., 1996) was used to record the functional status of the patient. This instrument was developed for use in palliative care populations and was derived from the Karnofsky Performance Status Scale. It is based on the following five parameters: ambulation, activity and evidence of disease, self-care, intake and consciousness level. The PPS score is assigned to the patient in percentages: 100% indicates good functional status while 0% indicates death. The PPS score decreases in 10% increments only. The PPS was translated into Dutch and was subjected to a back translation. Inter-rater reliability between nurses was established in a pilot study and showed a high agreement between nurses (ICC=0.91, CI 0.841, 0.950).

The Glasgow Coma Scale was used by the nurses to evaluate the level of consciousness of the patient (Teasdale & Jennett, 1974). This instrument is frequently used, easy to use and a valid and reliable instrument (Braakman et al., 1977; Fielding & Rowley, 1990; Rowley & Fielding, 1991). In this study, a translated version was used and the inter-rater reliability was assessed between nurses. Intra class correlation was 0.807 (CI 0.671, 0.891).

The medication dosage and the artificial food and fluid intake were assessed based on a chart review. Belgian law requires that this information be documented in the patient's chart.

PROCEDURE

An elaborate research protocol was established (see Appendix 1) in close collaboration with representatives from the different PCUs. Each unit received the final protocol together with a letter of clarification. When further information was wanted, the researcher would visit specific units on site. As soon as the unit agreed to participate, and after obtaining the approval of the local ethics committee, the researcher started a two-day training session for all nurses. First, instructions were given on how to fill out the questionnaires. Explicit attention was given to the importance of obtaining informed consent (e.g., how to obtain, what information must be given) from the patient and/or his/her family. Each patient admitted to the PCU was evaluated in terms of the inclusion criteria. When patients met the criteria, the nurse would meet with the patient, clarify the purpose of the study and ask the patient and/or his/her family for informed consent. Once the informed consent was obtained, data gathering started. Data collection was ended when the patient died, was discharged or when the patient reconsidered his/her participation in the study. Patients who refused to participate were asked why they had made this decision.

ANALYSES

Each patient was assigned a numerical code to maintain anonymity of the data. Only the researcher could access the link between the code and patient information. For the purpose of the analysis, patients receiving palliative sedation were divided into different levels. These levels were based on Broeckaert's definition ("palliative sedation is the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms") (Broeckaert, 2000, 2008a,b).

The following theoretical levels of sedation were distinguished: mild-intermittent, mild-continuous, deep-intermittent in non-acute situations, deep-intermittent in acute situations, deep-continuous in non-acute situations, deep-continuous in acute situations (Table 2). Palliative sedation was distinguished from the use of sedatives for symptom control (sedatives that are administered to treat a symptom without compromising the consciousness of the patient, i.e., delirium) and sleep disturbances (sedatives administered only during the night with the purpose of enhancing the sleep pattern of the patient).

Table 2
Theoretical levels of sedation

Level of sedation	Description
Mild-intermittent	Intermittent, mild reduction of consciousness, patient still reacts to stimuli
Mild-continuous	Continuous, mild reduction of the consciousness, patient still reacts to stimuli
Deep-intermittent, non-acute	Intermittent reduction of the consciousness to treat a non-acute refractory symptom. Patient is unconscious
Deep-intermittent, acute	Intermittent sedation of the patient to unconsciousness to treat an acute, refractory symptom.
Deep-continuous, non-acute	Deep-Continuous sedation for a non-acute symptom. Patient is unconscious
Deep-continuous, acute	Deep- continuous sedation for an acute symptom (e.g. .shortness of breath, haemorrhage), patient is unconscious

All data analyses were performed using SAS (SAS Institute Inc., Cary, NC, USA). Descriptive statistics (mean, median, quartiles) were used to describe the population under study. During the analysis, assistance was obtained from biostatisticians to assure the methodological quality of the study. In this article, no comparisons are made between the sedated and the non-sedated group. The difference in numbers of patients in both groups was huge, and for this reason, the value of these possible statistical differences would be of little value.

RESULTS

Two hundred sixty-six patients were included in this study; 54% were male and the median age was 72 years of age ((Q1=65; Q3=81). The three most important primary diagnoses that occurred in this group were lung cancer (24%), bowel cancer (15.4%) and breast cancer (12.4%). Fifty-one percent of the patients were married, 29% were widowed and 8% divorced. The majority of the patients were Christian (82%). The median follow-up period was twelve days (Q1=5; Q3=26). The median PPS score and Glasgow Coma Score at admission were 40 and 15, respectively, indicating that patients were mainly bedbound, had an extensive disease, needed assistance with care, had a reduced appetite and a normal consciousness.

PREVALENCE OF PALLIATIVE SEDATION AND THE EVOLUTION OVER TIME

Of all included patients (*n*=266), 7.5% (*n*=20) received one of the above-mentioned forms of palliative sedation. Seventy percent of these sedated patients were on sedatives prior to palliative sedation administration, either for symptom control (55%) or for sleep disturbances (15%). Palliative sedation started, on average, 2.5 days before death. For 40% of the patients, sedation started as a mild-

continuous sedation and 40% started as a deep-continuous sedation in non-acute situations. On the day of death, 85% of the patients received deep continuous sedation for non-acute situations, indicating that the nature of palliative sedation evolves over time. Looking at this evolution more in detail, it is clear that in almost half of the patients (45%) that received palliative sedation, the form of sedation changed over time. In the majority of these patients (88%), palliative sedation was started as a mild or intermittent form of sedation, on average, four days before the day of death, and it evolved into deep continuous sedation on average two days prior to the patient's death.

In those patients for whom palliative sedation did not change over time, palliative sedation was started, on average, two days prior to death. Seventy-three percent of these patients received deep continuous sedation for non-acute situations and 27% received mild-continuous or mild-intermittent sedation.

DEMOGRAPHIC VARIABLES FOR THE GROUP OF SEDATED PATIENTS

Of the 20 patients who received palliative sedation, 45% were male. Patients were, on average, 63 years of age. The median period of follow-up was 16 days and 58% of the patients were married, 20% had bowel cancer, 25% had breast cancer and 20% had lung cancer. Moreover, 80% of these cancers were metastasized. The majority of the patients (83%) were Christian and 17% were non-religious. All of the patients in the study died while staying at the palliative care unit (Tables 3 and 4).

FUNCTIONAL STATUS, ORAL FOOD AND FLUID INTAKE AND CONSCIOUSNESS LEVEL

Patients who received palliative sedation during their stay entered the PCU with a moderate to low functional status (median PPS score = 40 [Q1=30; Q3=50]). Patients were in a very advanced stage of their disease, were mostly bedbound, unable to do any activity and needed assistance for self-care. Patients had a normal intake of fluid (> 1 L/day) but skipped meals during the day (median = 2 [Q1=1; Q3=2]) and were fully conscious (median GCS score = 15 [Q1=15; Q3=15]).

At the start of sedation, the functional status of patients had dropped to a median PPS of 20 (Q1=10; Q3=30). Patients were at the end stage of their disease and needed total care. Patients drank only small amounts of fluid (< 1 L/day) and had no meals at all (median = 3 [Q1=3; Q2=4]). The patients were fully conscious (median GCS score = 14 [Q1=13; Q2=15]) and were alert to what was happening around them. Functional status declined further during palliative sedation and equaled a median score of 10 (Q1=10; Q3=30) during the last day of life. The patients were at that moment

unconscious (median GCS = 3 [Q1=3; Q3=7] and received mouth care only (median = 5 [Q1=5; Q3=5].

Table 3
Descriptive Characteristics of the Sedated Patients

Variables		Percentage (100%)	Number of patients (N=20)
Sex ***(no missing)***	Male	45	**9**
	Female	55	**11**
Marital status ***(missing = 1)***	married	57.9	**11**
	Living together with partner	5.3	**1**
	Living together with family member	10.5	**2**
	Single	10.5	**2**
	Widowed	10.5	**2**
	Divorced	5.3	**1**
Primary TumorSite ***(no missing)***	Breast	25	**5**
	Bowel	20	**4**
	Lung	20	**4**
	Pancreas	5	**1**
	Skin	5	**1**
	Lymphoma	5	**1**
	Stomach	5	**1**
	Uterus	5	**1**
	Ovarian	5	**1**
	Gallbladder	5	**1**
Metastases ***(missing=2)***	Yes	80	**16**
	No	20	**4**
Ideology ***(missing=2)***	Roman-Catholic background	83.3	**15**
	Pluralistic background	16.7	**3**

ARTIFICIAL FOOD AND/OR FLUID INTAKE

Only 35% (*n*=7) of the sedated patients received artificial fluid upon admission. This figure is in accordance with the prevalence of artificial fluid in the whole group (28%) of patients included in this study (Claessens et al., submitted) at the time of admission. Only two patients received artificial food when admitted to the PCU. In none of the patients' artificial food/fluids were started during their stay. At the start of sedation, three patients (43%) still received artificial fluids and continued to do so until the day of death. None of the patients received artificial food. The amount of fluids administered during sedation was 500cc/24hours for all patients.

Table 4
Descriptive Characteristics of Continuous Variables in Sedated Patients

Variable	Mean	Std	Q1	Median	Q3
Follow-up	19.65	15.29	12.5	16	**22**
Age	63.40	13.59	51	62.5	**75.5**

SYMPTOM PREVALENCE ON DAY OF ADMISSION, WHEN SEDATION IS STARTED AND AT THE END OF LIFE

The five most prevalent symptoms (Table 5) in this group of patients that were reported on the day of admission were pain (81%), fatigue (81%), depression (75%), drowsiness (75%) and a loss of feeling of well-being (69%). At the start of sedation, an average of five symptoms (range 1-8) were reported per patient, with the most prevalent being pain (55%), fatigue (35%) and a loss of feeling of well-being (40%) (Table 5). When the patient was asked which of these symptoms were decisive in terming the suffering as refractory, the three most important were pain, loss of feeling of well-being and anxiety (Table 6). Each patient reported an average of two symptoms as refractory to treatment.

DECISION MAKING PROCESS

In the majority of cases (70%), patients themselves, in consensus with the family or the caregivers, indicated that they were suffering intolerably. When the problem of refractory suffering arose for the first time, the patient and/or his/her family mentioned this to either nurses or doctors. In none of the cases did patients mention this to other health care workers such as volunteers, pastors or other paramedics.

DISCUSSION

Despite the fact that a very broad definition of palliative sedation was used (both mild, deep, continuous-intermittent and sedation with or without artificial food/fluid were included), this study reveals that only 7.5% of the patients residing in PCUs receive some form of palliative sedation during their stay. This low-prevalence figure is in contradiction to the existing literature, which reports much higher figures (Ventafridda et al., 1990; Stone et al., 1997; Peruselli et al., 1999; Fainsinger et al., 2000a,b; Morita et al., 1996; Müller-Busch et al., 2003; Chiu et al., 2001; Morita et al., 2005; Cameron

Table 5: **Overview of the Frequency of Reporting and Median Symptom Scores on Admission and at Start of Sedation on a Scale from 0-100**

	On admission*				At start palliative sedation			
	Symptom Occurrence/Intensity		Symptom Distress		Symptom Occurrence/intensity		Symptom Distress**	
	Frequency n (%)	*Median (Q1,Q3)*	*Frequency n (%)*	*Median (Q1,Q3)*	*Frequency n (%)¥*	*Median (Q1,Q3)***	*Frequency N (%)*	*Median (Q1,Q3)*
Pain	13 (81)	55 (28,72)	13 (81)	32 (24,81)	11(55)	33.5 (17,70)	9 (75)	83 (18,85)
Fatigue	13 (81)	71 (39,85)	11 (69)	74 (30,84)	7 (35)	87 (70,94)	9 (75)	51 (21,83)
Nausea	8 (50)	16.5 (45,57.5)	8 (50)	25.5 (2.5,72.5)	5 (25)	13.5 (10,32)	6 (50)	23.5 (7,39)
Depression	12 (75)	35.5 (13,63.5)	11 (69)	40 (32,78)	3 (15)	67.5 (47,83)	7 (58)	61 (18,80)
Anxiety	9 (56)	54 (28,72)	7 (44)	64 (34,88)	6 (30)	24 (18,47)	7 (58)	53 (12,68)
Drowsiness	12 (75)	34.5 (19.5,73.5)	11 (69)	64 (18,80)	4 (20)	89 (66,96)	8 (67)	22 (11,78.5)
Reduced appetite	9 (56)	47 (18,63)	8 (50)	33.5 (17.5,42)	6 (30)	91.5 (20,99)	7 (58)	6 (5,28)
Loss of well-being	11 (69)	29 (14,67)	10 (63)	59.5 (25,77)	8 (40)	79 (51,96)	8 (67)	70.5 (30.5,83)
Shortness of breath	8 (50)	40 (17,76.5)	7 (47)†	46 (26,72)	4 (20)	10 (5,56)	4 (33)	34 (17.5,53.5)
Constipation	9 (56)	39 (12,80)	7 (44)	71 (6,87)	3 (15)	55 (27,79)	6 (50	17 (3,53)
Dry mouth	10 (63)	43 (12,76)	9 (56)	47 (9,71)	3 (15)	79.5 (37,89)	7 (58)	61 (16,97)
Disturbed sleep	6 (38)	46 (17,92)	6 (38)	38 (3,85)	5 (25)	80 (38,91)	6 (50)	15 (4,37)

* n=16, missings=4, † n=15, 5 missings, ** n=12, missings=8, ‡ n=13, missings=7, § n=11, missings=9, ¥ n=20, no missings

et al., 2004; Miccinesi et al., 2006), even though in most cases a much more narrow definition of palliative sedation was used (Claessens et al., 2008). The ever-increasing knowledge in symptom management and the expertise that is available in contemporary PCUs results in high quality palliative care that makes palliative sedation redundant in many cases. On the other hand, it becomes clear that, in exceptional cases, symptoms indeed remain insensitive to any treatment (i.e., are refractory) and this almost always occurs when a patient is close to death. Thus, palliative sedation is proven to be an exceptional treatment that is only administered in those cases where patients are close to the end of life and where symptoms are not susceptible to any treatment at all (Claessens et al., 2007, 2011). Another argument, which could be used to explain the low prevalence of palliative sedation in our study, could be the decriminalization of euthanasia in Belgium. For this reason, one could assume that instead of using palliative sedation, euthanasia is recommended for these patients. Our study, however, refutes this argument since only five cases of euthanasia were registered in the participating PCUs.

Table 6
Symptoms Reported as Refractory by Patients

Symptom	Labeled as refractory by patients
Pain	5
Fatigue	3
Nausea	1
Depression	1
Anxiety	4
Drowsiness	1
Reduced appetite	1
Loss of feeling of well-being	5
Shortness of Breath	3
Constipation	
Dry Mouth	
Disturbed sleep	
others	5

An interesting finding of this study is that the symptom distress score, more than the intensity of the symptom, is suggestive of a symptom being labeled as refractory by patients. Since symptom distress is defined as the emotional component of a symptom experience (McMillan & Small, 2002; Rhodes et al., 2000), this finding confirms the ideas of Cassell (1984; 1999), who argues that suffering arises from the meaning that the patient attaches to his or her symptoms. In other words, a higher symptom distress score can be associated with increased suffering of the patient. Therefore, it is crucial to determine symptom distress in order to assess the suffering of a patient and label a symptom as refractory or not. Moreover, this finding suggests that there is no easy distinction between physical and existential symptoms. A person may experience physical pain without suffering, or may

experience suffering without having physical pain (Cassell, 1984; 1999). Thus, palliative sedation is used in those situations where the patient is exposed to refractory suffering because of one or more symptoms. Although this is a very interesting finding, more research is needed to further explore this relationship.

When we look at the number of symptoms that are labeled refractory (median = 2), this is in accordance with other findings (Cowan & Walsh, 2001). However, despite the enormous evolution in pain management, pain remains one of the most important symptoms.

Some authors label palliative sedation as "slow euthanasia," a kind of hidden form of euthanasia (Billings & Block, 1996). This study clearly shows that in the majority of patients, palliative sedation starts as a mild sedation and evolves over time to a deep and/or continuous form of sedation. This illustrates how important and present the *principle of proportionality* is in the decision-making process. The intensity and nature of the suffering determines which form of sedation, and more specifically, what dosage of sedatives will be administered to the patients. Thus, palliative sedation does not presuppose that a patient is sedated until unconsciousness. Palliative sedation means that sedative drugs are administered in dosages and combinations required to reduce consciousness as much as necessary to adequately relieve one or more refractory symptoms (Claessens et al., 2008; Broeckaert , 2008b; Claessens et al., 2007; Broeckaert, 2002). This notion of proportionality is crucial in distinguishing palliative sedation from euthanasia. This study illustrates that the principle of proportionality is present in current medical practice and that, indeed, a clear distinction can be made between palliative sedation and euthanasia.

In this study, almost all patients who later received sedation indicated that they were suffering intolerably. All patients were involved in the decision-making process. In this patient population, palliative sedation was only administered when requested by the patient and consent was given by him or her. This observation goes against the arguments of opponents of palliative sedation who assert that palliative sedation is given to incapacitated patients and without the consent of the patient (Valko, 2002). Because taking away the consciousness of a patient is a very delicate and far-reaching decision, it is not just the doctor who decides. All health care workers, the patient, and the family take part in the decision process. There of course may be exceptional acute cases in which a patient almost instantly receives palliative sedation (e.g., in case of massive hemorrhage or acute terminal dyspnea), but no such cases were found in our study.

Another aspect that is currently debated is food and fluid intake of patients that receive palliative sedation. Must artificial fluid be continued, stopped or started? This study, in accordance with others (Broeckaert, 2008b; Levy & Cohen, 2005; Cowan & Palmer, 2002; Rousseau, 2000), shows that when palliative sedation is being initiated, the oral intake of foods and/or fluids is reduced to a minimum. However, one should keep in mind that an average patient in that stage of his/her illness only takes little sips of fluid and, in most cases, no food whatsoever. Withholding little sips of water because of the decision to sedate (and to withhold artificial hydration) has no proven life-shortening effect. Moreover, our study (n=266) supports the fact that, as stated by different palliative care experts, palliative care patients tend to eat and drink less the more they approach the ends of their lives. This argument is further developed in another article (Claessens et al., submitted) where a comparison is made between the group of sedated and the group of non-sedated patients concerning the oral and artificial food and fluid intake and its evolution over time. This aspect, in combination with the fact that administering artificial fluids to terminal patients has rather a baleful influence on patients' condition, suggests that starting artificial fluids during palliative sedation is futile (Levy & Cohen, 2005). Arguing that withholding artificial hydration would be life shortening is meaningless in these cases.

However, in a minority of cases, patients were receiving artificial food/fluid before sedation was started. Is it then necessary or recommended to withdraw this fluid? Our study shows that, in clinical practice, withdrawing artificial fluids is not a prerequisite for palliative sedation. In 43% of the cases, patients kept on receiving the artificial fluids in the same amount as before sedation was started. In those patients where fluids were withdrawn, this was done with the consent of the patient. Deciding to withhold or withdraw artificial fluid (in cases of palliative sedation) is a totally different discussion from that of deciding to start palliative sedation.

Withholding or withdrawing food and/or fluid is not an intrinsic part of palliative sedation and, therefore, should not be integrated in a definition of palliative sedation. If sedation is combined with the withdrawing of hydration and nutrition, what is done is not just sedation, but sedation AND the withdrawing of hydration and nutrition (Broeckaert, 2008a,b; Rousseau, 2000).

METHODOLOGICAL QUALITY

This is the first study, to our knowledge, that has gathered data prospectively and over a long period of time. By using this design, this study clearly has added value in comparison with other studies that have been done up until now (e.g., Ventafridda et al., 1990; Fainsinger et al., 2000a,b).

Not only can we give a detailed description of the period during which the patient was sedated, but we can also give an accurate description of the period that precedes palliative sedation. We can do this both for the patients who were sedated, as well as for those who were not sedated (which was not the objective of this paper).

Moreover, because nurses have gathered data based on their observations, we are not confronted with the problem of attrition and have valuable data up to, and including, the day of death. It must be taken into account that symptom prevalence and symptom distress is not rated by the patients themselves and, therefore, might not be a true reflection of what the patient feels. A pilot study showed that the agreement between the scores of nurses and patients were moderate ($r = 0.661$) to weak ($r = 0.201$) ($P<0.05$) We found this to be the only way to get valid information on the symptom experience of very weak terminally ill patients (without being confronted with high attrition, and thus useless information), taking into account the burden self-rating would bring about for them, considering they would be asked to score 12 symptoms for intensity and distress three times a week. Therefore, we decided that this was the best possible way to rate the symptom experience of this patient population in the context of this study on palliative sedation.

Because only 27 % of the PCUs participated to this study, and because we only focused on patients admitted to PCUs and who were diagnosed with cancer, the results of this study cannot be extrapolated to other care settings. Nevertheless, we are convinced that this prospective, longitudinal study has a significant added value and presents some interesting findings that need further examination in different patient populations.

REFERENCES

Anderson F, Downing GM, Hill J, Casorso L, Lerch N. Palliative Performance Scale: a new tool. J Palliat Care 1996;12:5-11.

Billings JA, Block SD. Slow euthanasia. J Palliat Care 1996;12:21-30.

Braakman R, Averaat CJ, Maas AI, Roel M, Schouten HJ. Inter observer agreement in the assessment of the motor response of the Glasgow Coma Scale. Clin Neurol Neurosurg 1977; 80:100-106.

Broeckaert B. Ethical issues at the end of life. In: Payne S, Seymour J, Ingleton C, eds. Palliative care nursing. Principles and evidence for practice, 2nd ed. Berkshire: Open University Press, 2008:402-421.

Broeckaert B. Euthanasia and physician assisted suicide. In: Walsh D, ed. Palliative medicine. Philadelphia: Elsevier, 2008:110-115.

Broeckaert B. Palliative sedation defined or why and when terminal sedation is not euthanasia. J Pain Symptom Manage 2000;20:S58.

Broeckaert B. Palliative sedation: ethical aspects. In: Gastmans C, ed. Between technology and humanity. The impact of technology on health care ethics, 1st ed. Leuven: University Press, 2002:239-255.

Cameron D, Bridge D, Blitz-Lindeque J. Use of sedation to relieve refractory symptoms in dying patients. SAJM 2004;94:445-449.

Cannaerts N, Dierckx de Casterlé B, Grypdonck M. Palliatieve zorg- zorg voor het leven. Een onderzoek naar de specifieke bijdrage van residentiële palliatieve zorg. Leuven, Belgium:Academia Press, 2000.

Cassell EJ. Diagnosing suffering: a perspective. Ann Intern Med 1999; 31:531-534.

Cassell EJ. Life as a work of art. Hastings Cent Rep 1984;14:35-37.

Chater S, Viola R, Paterson J, Jarvis V. Sedation for intractable distress in the dying – a survey of experts. Palliat Med 1998; 12:255-269.

Chiu TY, Hu WY, Lue BH, Cheng SY, Chen CY. Sedation for refractory symptoms of terminal cancer patients in Taiwan. J Pain Symptom Manage 2001; 21:467-472.

Claessens P, Genbrugge E, Vannuffelen R, et al. Palliative sedation and nursing: the place of palliative sedation within palliative care. J Hospice Palliat Nurs 2007; 9:100-106.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation: a review of the research literature. J Pain Symptom Manage 2008; 36:310-333.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Starving them to death? Food and fluid intake and palliative sedation in palliative care units: a longitudinal prospective study. Submitted for publication in Progress in Palliative Care.

Claessens P. Food and fluid intake on Flemish palliative care units: an empirical study. Presentation at the 4th Flemish Conference on Palliative Care, May 31, 2007.

Cooney GA. Palliative sedation: the ethical controversy. Available from http://www.medscape.com/viewarticle/499472.

Cowan J, Walsh D. Terminal sedation in palliative medicine: definition and review of the literature. Support Care Cancer 2001;9:403-407.

Cowan JD, Palmer TW. Practical guideline to palliative sedation. Curr Oncol Rep 2002;4:242-249.

De Blaeser L. Validiteit en betrouwbaarheid van de naar het Nederlands vertaalde en herwerkte Edmonton Symptom assessment Scale bij oncologische patiënten in meerdere Vlaamse eenheden voor palliatieve zorg. Doctoral dissertation. Leuven, Belgium: Catholic University of Leuven, 2004.

Fainsinger R, Miller MJ, Bruera E, Hanson J, MacEachern T. Symptom control during the last week of life on a palliative care unit. J Palliat Care 1991;7:5-11.

Fainsinger RL, de Moissac D, Mancini I, Oneschuk D. Sedation for delirium and other symptoms in terminally ill patients in Edmonton. J Palliat Care 2000a; 16:5-10.

Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for uncontrolled symptoms in a South African hospice. J Pain Symptom Manage 1998a;16:145-152.

Fainsinger RL, Waller A, Bercovici M, et al. A multicentre study of sedation for uncontrolled symptoms in terminally ill patients. Palliat Med 2000b;14:257-265.

Fainsinger RL. Use of sedation by a hospital palliative care support team. J Palliat Care 1998b; 14:51-54.

Fielding K, Rowley G. Reliability of assessments by skilled observers using the Glasgow Coma Scale. Aust J Adv Nurs 1990; 7:13-17.

Howland J. Questions about palliative sedation: an act of mercy or mercy killing? Ethics Medics. 2005;30(8):1-2.

Levy MH, Cohen SD. Sedation for the relief of refractory symptoms in the imminently dying: a fine intentional line. Sem Oncol 2005; 32:237-246.

McMillan SC, Small, BJ. Symptom distress and quality of life in patients with cancer newly admitted to hospice home care. Oncol Nurs Forum 2002; 29:1421-1428.

Menten J. Cancer pain: interdisciplinary and comprehensive management. Doctoral dissertation. Leuven, Belgium: Catholic University of Leuven, 2003.

Miccinesi G, Rietjens JAC, Deliens L, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage 2006;31:122-129.

Morita T, Chinone Y, Ikenaga M, et al. Efficacy and safety of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan. J Pain Symptom Manage 2005;30:320-328.

Morita T, Inoue S, Chihara S. Sedation for symptom control in Japan: the importance of intermittent use and communication with family members. J Pain Symptom Manage 1996;12:32-38.

Morita T, Tsunoda J, Inoue S, Chihara S. Do hospice clinicians sedate patients intending to hasten death? J Palliat Care 1999; 15:20-23.

Müller-Busch HC, Andres I, Jehser T. Sedation in palliative care--a critical analysis of 7 years' experience. BMC Palliat Care 2003;2(1):2.

Peruselli C, DiGiulio P, Toscani F, et al. Home palliative care for terminal cancer patients: a survey on the final week of life. Palliat Med 1999; 13:233-241.

Rhodes VA, McDaniel RW, Homan SS, Johnson M, Madsen R. An instrument to measure symptom experience. Cancer Nurs 2000; 23:49-54.

Rousseau P. The ethical validity and clinical experience of palliative sedation. Mayo Clin Proc 2000;75:1064-1069.

Rowley G, Fielding K. Reliability and accuracy of the GCS with experienced and inexperienced users. Lancet 1991; 337:535-538.

Stone P, Phillips C, Spruyt O, Waight C. A comparison of the use of sedatives in a hospital support team and in a hospice. Palliat Med 1997; 11:140-144.

Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 13:81-84.

Valko NG. Should sedation be terminal? Natl Cathol Bioeth Q 2002;2:601-608.

Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care 1990; 6:7-11.

CHAPTER 5: THE RELATIONSHIP BETWEEN FOOD AND FLUID INTAKE AND PALLIATIVE SEDATION

How can I not give him food and water,
You need food and water to live

- Wife of a patient

Article submitted for publication in Progress in Palliative Care

ABSTRACT

Divergent opinions exist on what is correct and morally acceptable when it concerns the management of patients who are terminally ill and unable to maintain their own nutritional and hydration needs. This issue becomes even more problematic when it concerns patients for whom palliative sedation is considered. The aim of this study is to describe the evolution of oral and artificial food and fluid intake of patients residing in Flemish palliative care units (PCU) and the possible effect of palliative sedation. A prospective longitudinal and descriptive design was used. Each patient admitted in one of the 8 participating units was included if they met the inclusion criteria and gave written informed consent.

Two Hundred and sixty six patients were included. The incidence of palliative sedation was 7,5%.The oral food and fluid intake of these patients decreased during their stay and was reduced to a minimum a few days before death. With regard to the artificial food/fluid intake this study reveals that only 28% of patients received artificial food and/or fluid. Moreover it shows that the withdrawal is not a standard policy but is always based on a profound and individual decision making process. An effect of initiating palliative sedation on the fluid intake is found, but is of no clinical relevance, in the sense that it would shorten the life of the patient.

This longitudinal prospective study does not support the argument that palliative sedation amounts to 'slow euthanasia' because it entails the withholding or withdrawing of substantial amounts of food and or fluids, thus having a clear life-shortening effect. This study shows that palliative sedation, in specialized palliative care units, is not slow euthanasia but advanced symptom control during the final days of terminally ill patients' lives who are confronted with refractory suffering.

INTRODUCTION

Providing food and fluid is a fundamental and basic human duty (Kedziera, 2001; Ersek, 2001). There are, however, widely divergent opinions on what is correct and morally acceptable when it comes to the management of patients who are terminally ill and unable to maintain their own nutritional and hydration needs (Kedziera, 2001; Craig, 2002). Differences in opinion might be voiced by relatives, nurses, doctors or other persons involved in the care of the patient. Moreover, in the absence of consistent and convincing research data, the use of hydration in terminally ill patients is more likely to be governed by established practice, tradition and culture (cf. symbolic meaning of food and fluid), physician bias and place of care rather than by a systematic and objective assessment of appropriateness (Kedziera, 2001).

The issue of hydration and nutrition becomes even more problematic when it concerns patients for whom palliative sedation is considered. Patients suffering from a terminal illness are often confronted with severe symptoms during the last phase of their lives (Georges et al., 2005; Hermann & Clooney, 2001). Most of the time these symptoms can be well-controlled (Vainio & Auvinen, 1996; Zech et al., 1995; Ahmedzai, 1997) but for some patients, symptoms remain uncontrollable (Lo & Rubenfeld, 2005; NEC, 2006). These refractory symptoms have a negative impact on patient functioning and well-being (Menten, 2003; Coyle et al., 1994), frequently increase as the patient approaches the end of life (Ventafridda et al., 1991) and may interfere with a peaceful dying process (Claessens et al., 2008). Palliative sedation (Broeckaert, 2000; Broeckaert, 2002a,b; Broeckaert, 2008a,b) therefore, has been placed on the foreground as an option of last resort for refractory suffering (Quill et al., 1997; Quill & Byock, 2000; Cherny, 2006) and is increasingly being implemented in palliative care programs (Claessens et al., 2008; Howland, 2005; Boyle, 2004; Claessens et al., 2007; Murray et al., 2008).

Authors that oppose palliative sedation often consider it to be a form of ‘slow euthanasia’, especially when it is combined with the withholding of artificial food and/or fluids (Quill et al., 1997; Billings & Block, 1996). This controversy is strengthened by the diverse and conflicting definitions of palliative sedation found in literature (Claessens et al., 2008) and the fact that some authors even have defined palliative sedation as having an intrinsic link with the withholding or withdrawing of artificial hydration and nutrition (Quill & Byock, 2000; Taylor, 2003; Gevers, 2003; Rietjens et al., 2004, 2005, 2006; Tännsjö, 2004; Keizer & Swart, 2005).

A review of the available clinical studies on palliative sedation (Claessens et al., 2008) revealed that only 8 out of 37 papers provided information on artificial food and fluid intake in relation to palliative sedation. Moreover, prevalence figures varied significantly. Menten (2003) and Miccinesi et al. (2006) reported that for 35% - 64% of patients, palliative sedation was performed without administering artificial fluids. Morita et al. (1999; 2005) and Cameron et al. (2004) reported information about the circumstances before and after palliative sedation was initiated. Of the patients who received artificial fluids before sedation, 20% - 69% had fluid intake continued during sedation (Morita et al., 2005; Cameron et al., 2004) while 24% - 44% of the patients had their artificial fluids reduced (Morita et al., 1999; 2005). Only one study reported that none of the sedated patients received artificial fluid (Fainsinger et al., 1998). Thus, the strong controversy concerning the life shortening effect of the withholding or withdrawing of artificial food and or fluid in terminally ill patients who receive palliative sedation, is not based on solid scientific evidence, as this is lacking to an important degree.

Therefore, the aim of this study is to describe in detail, the evolution of oral and artificial food and fluid intake of patients residing in Flemish palliative care units (PCU), from their admission until their day of death. In doing so, we specifically want to describe what the effect is of initiating palliative sedation on the oral and/or artificial food and fluid intake of terminally ill patients.

METHODOLOGY

DESIGN, SETTING AND STUDY POPULATION

A prospective, longitudinal and descriptive design was used. 8 PCU's, which were geographically spread over Flanders, agreed to participate. The sample consisted of three PCU's in general hospitals, one hospice, one PCU in a university hospital and three PCU's in general hospitals affiliated with a university. Five hospitals (62%) had a Roman-Catholic background and three were pluralistic. Belgium has legalized euthanasia since 2002 and it was an option in six out of the eight PCU's. The recruitment policy in the participating units was based on the same criteria.

Each unit received, based on the comprehensive research protocol, positive advice from the local ethical committee. Each patient admitted from September 2004 – April 2005 that met the inclusion criteria and gave formal written informed consent, was included in this study. The following inclusion criteria were set: patients had to be older than 18 years of age and had to be diagnosed with incurable cancer. Their life expectancy was less than three months.

VARIABLES

After an extensive review of the literature (Claessens et al., 2008) and after extended discussions with physicians and nurses in palliative care settings, a list of relevant variables to include in this study was created (Table 1). Data were assessed on admission and every Monday, Wednesday and Friday. To reduce the workload for the nurses, the registration of the variables was divided between the nurses and the researcher. The researcher visited the unit once every two weeks and gathered the data that were available in the patients' charts. The other variables, which were based on observations, were registered by the nurse taking care of the patient for the day (Table 1). When patients received palliative sedation extra information was gathered concerning the refractory suffering involved, the decision-making process, the duration of the palliative sedation, and the kind of palliative sedation received. Since it was important to gain an insight into the practice of the use of sedatives in PCU, no definition of palliative sedation was imposed. This prevented possible conceptual confusion between the PCU's and ensured that all possible cases of palliative sedation were included in the study.

Table 1

Overview of registered Variables, Measurement Instruments Used, and Data Gatherers

Variable	Measurement instrument	Nurse	Researcher
Functional Status	Palliative Performance Scale	X	
Symptom Occurrence	Modified Edmonton Symptom Assessment Scale	X	
Symptom Distress	Modified Edmonton Symptom Assessment Scale	X	
Level of Consciousness	Glasgow Coma Scale	X	
Demographics	Chart review		X
Oral food and fluid intake	5-point scale		X
Artificial food and fluid intake	Chart review		X
Medication (name, dose/24h)	Chart review		X

Demographic variables (sex, age, nationality, marital status, religion/worldview, date of admission, date of death/discharge) were collected by the researcher on admission and completed at the day of death. For the purpose of this article we only report on the variables oral food and fluid intake, artificial food and fluid intake and having received palliative sedation or not during the stay on the PCU.

MEASUREMENT INSTRUMENTS

Oral food and fluid intake was scored on a five point Likert scale (Table 2). This scale was developed by the research team in close collaboration with the head nurses in the PCU's and was understood to be a good representation of the different situations that occur in PCU's. Inter-rater reliability between nurses was evaluated in a pilot study. The intra-class correlation coefficient was .93 (CI [.875-.962]).

Artificial food and fluid intake was prospectively assessed based on the patients' charts, that are required by Belgian law to contain this information.

Table 2
Measurement tool for oral food and fluid intake

	Score
1	Normal food and fluid intake (> 1l/day)
2	Skips meals, normal fluid intake (>1 l/day)
3	No food intake, drinks small amounts of fluid (< 1 l/day)
4	Takes sips of fluid
5	No oral intake

PROCEDURE

An elaborate research protocol was established in close collaboration with representatives of different PCU's. Each unit received the final protocol together with a letter of clarification. When further information was needed the researcher visited the site. After the unit agreed to participate and upon obtaining the approval of the local ethical committee, the researcher started a two-day training session for all of the nurses involved in the study. First of all, instructions were given on how to fill out the questionnaires. Explicit attention was given to the importance of obtaining informed consent from the patient and/or his/her family. Each patient admitted to the PCU was evaluated in terms of the inclusion criteria. When patients met the criteria, the nurse explained, to the patient and/or his/her family, the purpose of the study and asked the patient and/or his/her family for an informed consent. Off all eligible patients admitted to the PCU's, 27% of the patients refused to participate, 5% of the patient died before informed consent could be obtained and 16% of the patients were not diagnosed with cancer. Once the informed consent was obtained, data gathering started. Data collection ended when the patient died, was discharged or when the patient reconsidered his/her participation in the study.

ANALYSES

Each patient was assigned a numerical code to maintain the anonymity of the data. The link between the code and patient information could only be accessed by the researcher. For the purpose of this analysis, patients receiving palliative sedation were divided into different levels according to Broeckaert's definition *("palliative sedation is the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms*") (Broeckaert, 2000, 2002a,b, 2008a,b). The following theoretical levels of sedation were distinguished: mild-intermittent, mild-continuous, deep-intermittent in non-acute situations, deep-intermittent in acute situations, deep-continuous in non-acute situations, and deep-continuous in acute situations (Table 3).

Table 3

Different stages of palliative sedation according to the definition of Broeckaert (2000, 2002)

Level of sedation	Description
Mild-intermittent	Intermittent, mild reduction of consciousness, patient still reacts to stimuli
Mild-continuous	Continuous, mild reduction of the consciousness, patient still reacts to stimuli
Deep-intermittent, non-acute	Intermittent reduction of the consciousness to treat a non-acute refractory symptom. Patient is unconscious
Deep-intermittent, acute	Intermittent sedation of the patient to unconsciousness to treat an acute, refractory symptom.
Deep-continuous, non-acute	Deep-Continuous sedation for a non-acute symptom. Patient is unconscious
Deep-continuous, acute	Deep- continuous sedation for an acute symptom (e.g. shortness of breath, hemorrhage), patient is unconscious

Descriptive statistics (mean, median, first (Q1) and third quartile (Q3)). were used to describe the population being studied and to attain further detail of the evolution of the oral food and fluid intake over time. The relation is evaluated between the presence of palliative sedation and the oral food and fluid intake, the latter measured by the aforementioned ordinal score (Table 2). For each patient, multiple scores over time are available, yielding 2125 scores in total. At each moment the sedation status is scored as absent (=0) or present (=1) . Note that for the majority of patients (92.5%), this variable remains zero throughout the total follow-up. Once sedation is initiated, this variable takes value 1 during the rest of the follow-up. A binary logistic regression model has been used separately for each relevant dichotomization of the ordinal score *Y*. More specifically, the following probabilities have been modeled: P(*Y*>2), P(*Y*>3) and P(*Y*>4) resulting in respectively 647, 356 and 208 "events". Time has been expressed as days before the end of the study (death). Restricted cubic

splines (Devlin & Weeks, 1986) have been used to allow non-linearity (on the logit scale) in the evolution over time. The evaluation of the effect of the sedation status can be influenced by differences in patient mix. Therefore, length of the total follow-up time and a binary variable indicating if a patient has ever been sedated are added in the model. Note that the latter variable reflects potential differences in characteristics between patients who will receive sedation and patients who will never receive sedation. Obviously, the 2125 observations are not independent and inference in the logistic regression model should take this into account. Therefore, 'generalized estimating equations' (GEE) have been used resulting in a larger standard error for the effect of sedation. Analyses have been performed using the procedure PROC GENMOD in the SAS software, version 9.2 of the SAS System for Windows. Copyright © 2002 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

RESULTS

OVERALL RESULTS

Two hundred and sixty-six patients were included in this study. 54% were male and the median age was 72 years (Q1=65; Q3=81). The three most important primary diagnoses that occurred in this study were lung cancer (24%), bowel cancer (15.4%) and breast cancer (12.4%). The median follow-up period was 12 days (Q1=5; Q3=26). The median PPS-score (Palliative Performance Scale as measure for functional status) and Glasgow Coma Score at admission were respectively 40 (Q1=30;Q3=50) and 15 (Q1=14; Q3=15) indicating that patients were mainly bed bound, had an extensive disease, needed assistance with care, had a reduced appetite and were fully conscious. In this sample, 7.5% of the patients received some form of palliative sedation (n=20) (Claessens et al., 2011) all other patients (n=246) died on the unit without receiving palliative sedation. 70% of these sedated patients were on sedatives prior to palliative sedation administration, either for symptom control (55%) or for sleep disturbances (15%). Overall palliative sedation started on average 2.5 days before death. For 40% of the patients, sedation started as a mild-continuous sedation and 40% started as a deep-continuous sedation in non-acute situations. On the day of death, 85% of the patients received deep continuous sedation for non-acute situations, indicating that the nature of palliative sedation evolves over time.

ORAL FOOD AND FLUID INTAKE

When patients entered the palliative care unit they had a median score of 2, meaning that they had a normal fluid intake (>1l/day) and occasionally skipped meals (Q1=1; Q3=3). At the end of their life, the oral food and fluid intake was reduced to a minimum and entailed only the intake of little sips of fluid and no intake of food (median = 4; Q1=3; Q3=5). Analysis show that the oral food and fluid intake of palliative patients is susceptible to variation between subjects. One of the explanations for this variation might be that decisions concerning food and fluid intake are made on an individual level. Secondly, these results show that the oral intake of food and fluid changes over time . More specifically, they show that the intake of food and fluid is gradually reduced over time, resulting in patients only taking little sips of fluid during the last days of their lives.

ARTIFICIAL FOOD AND FLUID INTAKE

Of all included patients, 28% received some form of artificial food and/or fluid during their stay on the palliative care unit. 51% of these patients were male and their median age was 63.4. Of this group of patients 96% received artificial fluid and/or flood on the day of admission. 89% received fluids, 4% received drip-feed and 7% received both. The median amount of food and/or fluid that was administered was 1L/24hours.

When we looked at the situation during the last days of life, only 48% (37/76) of those patients that initially received artificial food and/or fluid still received this at the end of their lives. Of these patients, 59% received fluid (22/37), 2% received drip-feed (1/37) and 8% received both (3/37). The amount of food/fluid administered was reduced to a median of 500cc/24 hours. In the majority of cases patients received glucose 5%. The drip-feed varied widely and depended on the unit to which the patient was admitted. Artificial food and/or fluid was not started for any of the included patients, once they entered the PCU.

RESULTS FOR THE GROUP OF SEDATED PATIENTS

In this study, the incidence of palliative sedation was 7.5%. When comparing the demographic characteristics of these patients with those of non-sedated patients, no differences could be found, except for age (median age sedated patients = 62.5, Q1=51, Q2=75,5)(p = 0.015).

ORAL FOOD AND FLUID INTAKE

Oral food and fluid intake had similar results as to those found in the group of non-sedated patients. On the day of admission, sedated patients had a normal fluid intake (>1l/day) and

occasionally skipped meals (median score = 2; Q1=1; Q3=3). Again, a reduction of food and fluid intake could be observed and as expected, these patients received only mouth care during their last days of life.

More important however, is the oral food and fluid intake that was assessed on the day that palliative sedation was started. Since these patients had a low functional status (PPS=20; Q1=10; Q3=30) oral food and fluid intake had dropped to almost nothing. Patients only had little sips of water but were on the other hand fully conscious (GCS=14; Q1=13; Q3=15) and thus very well aware of what was happening around them.

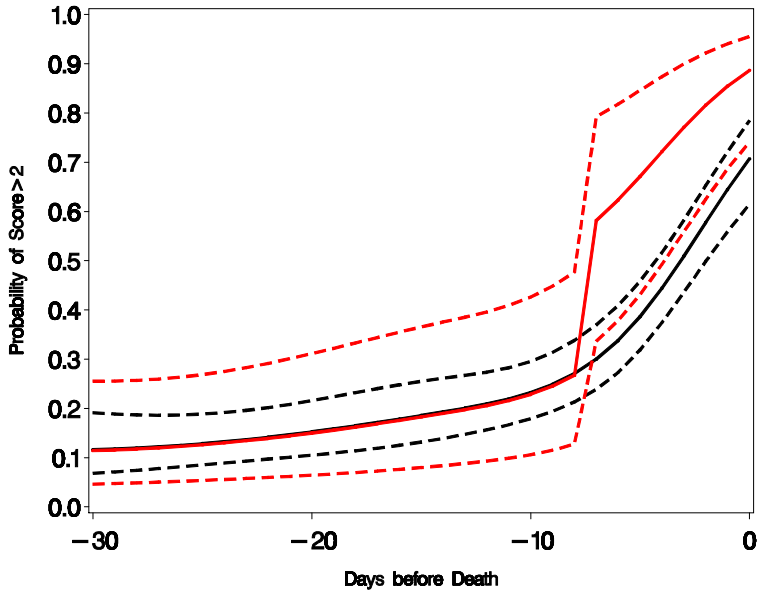
ARTIFICIAL FOOD AND FLUID INTAKE

Of all sedated patients only 35% (n=7) received artificial food and/or fluid on the day of admission (1400cc/24hours). This percentage is slightly higher than the overall prevalence of artificial food and fluid intake in this study (28%). Five patients received artificial fluids (1200cc/24 hours) while two received artificial food and fluids (2000cc/24hours). Artificial food and/or fluid administration was withdrawn during their stay in the PCU in four out of the seven patients and this was on average ten days before palliative sedation was initiated.

At the start of sedation, 3 out of 7 patients (43%) continued to receive artificial fluids. This artificial hydration was maintained until the day of death. No patients received artificial food during the start of sedation. The median amount of fluids administered at the start of and during the palliative sedation was 500cc/24 hours, again similar to the mean in the overall group of patients.

Figure 1

Evolution of the predicted probability that the score is higher than two



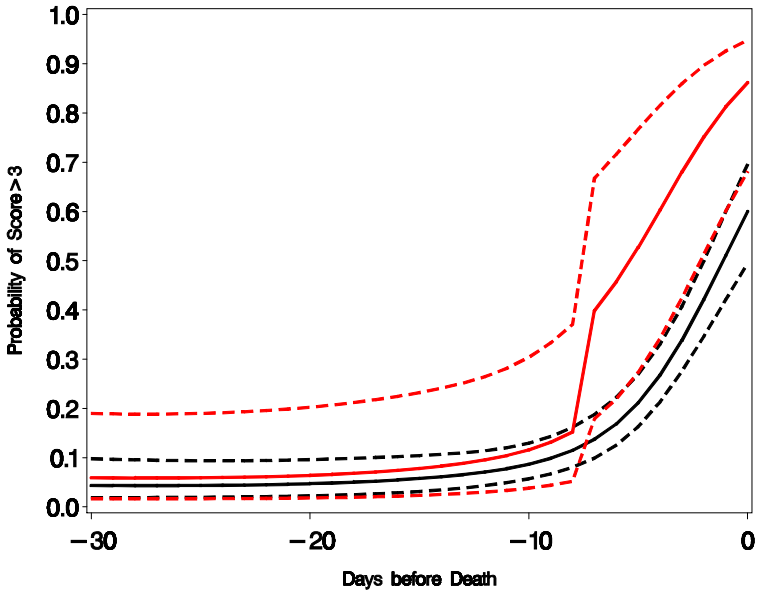
The predictions of two hypothetical subjects are shown, one being sedated 1 week before death (red lines), the other not being sedated (black lines) and both having a median follow-up time. The dotted lines represent the pointwise 95% confidence intervals for these predictions.

EFFECT OF STARTING PALLIATIVE SEDATION ON THE ORAL FOOD AND FLUID INTAKE

When looking at the effect of palliative sedation on the oral food and fluid intake for all three dichotomizations, the analysis indicates that sedation has an impact on the score of oral food and fluid intake. Irrespective of the dichotomization of the score, at the first measurement after the sedation had been initiated, a substantial increase (high actual levels of the odds ratio) in the probability of having a higher score for oral food and fluid intake had been observed. On the probability that the score was higher than 2 the odds ratio equals 3.31 (1.11 – 9.88; 95% confidence interval)(p = 0.032). On the probability that the score was higher than 3 the odds ratio equals 3.00 (0.87-10.35, 95% confidence interval) (p=0.082) and for the probability that the score was higher than 4 the odds ratio equals 5.51 (1.45-20.91, 95% confidence interval) (p=0.037) (Figures 1,2,3).

Figure 2

Evolution of the predicted probability that the score is higher than three.



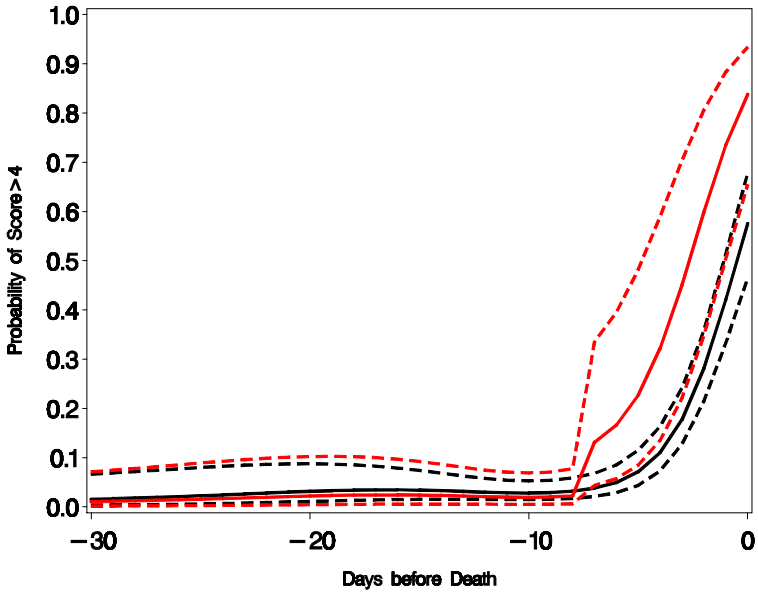
The predictions of two hypothetical subjects are shown, one being sedated 1 week before death (red lines), the other not being sedated (black lines) and both having a median follow-up time. The dotted lines represent the pointwise 95% confidence intervals for these predictions.

DISCUSSION

This longitudinal, prospective study is one of the first studies performed in which there was an assessment of the food and fluid intake, for a substantial sample of palliative care patients (n=266), over time. The food and fluid intake was assessed from admission until the day of death, and this both for sedated and non- sedated patients. Moreover it regarded a representative sample of Flemish palliative care units (geographically spread, euthanasia-no euthanasia, liberal-roman catholic) which enhances the generalizability of the results.

Figure 3

Evolution of the predicted probability that the score is higher than four



The predictions of two hypothetical subjects are shown, one being sedated 1 week before death (red lines), the other not being sedated (black lines) and both having a median follow-up time. The dotted lines represent the point wise 95% confidence intervals for these predictions.

Our results support the hypothesis, based on clinical expertise, that the oral food and fluid intake of terminal patients, admitted to a palliative care unit, decreases during their stay and finally is reduced to a minimum a few days before death. This natural decrease of food and fluid intake, as some authors have named it (Rousseau, 2000; Cowan & Palmer, 2002), is almost always due to the progression of the illness. Although this general tendency can be clearly observed, this study reveals, at the same time, that there is a wide variation within and between subjects. The evolution over time of the oral food and fluid intake of each patients seems, based on the results of this study, highly individual (Rousseau, 2004; deGraeff & Dean, 2007) and therefore should not be generalized.

With regard to the artificial food and fluid intake of patients residing in a palliative care unit, this study reveals that only 28% of patients received artificial food and/or fluid during their stay. 96% of these patients were on artificial food and or fluid when admitted to the palliative care unit. In half of these patients artificial hydration and/or nutrition was withdrawn during their stay in PCU, resulting in only 14% of patients receiving some form of artificial food and/or fluid during the final days of their lives. These results show that there is indeed a tendency to gradually cut down on the artificial food

and or fluid intake in palliative care units and this in concordance with the natural evolution of artificial hydration in non-sedated patients over.

Moreover, since 14% of the patients continue to receive artificial food and or fluid, it is shown that this withdrawal is not a standard policy but is always based on an individual decision making process. On the other hand, the fact that none of the included patients began artificial hydration or nutrition after they were admitted to a PCU, shows that there is a broad consensus that doing so would amount to a futile treatment.

When we look at the group of sedated patients, we see no differences in oral food and fluid intake, when we compare them with the overall group. Moreover, the change over time is similar up until the moment where palliative sedation is initiated. Results show a statistically significant effect of palliative sedation on the oral food and fluid intake, as many types of palliative sedation make oral food and fluid intake impossible. This effect, however, should be put into perspective since our results show that the oral food and fluid intake of these patients was already reduced to a minimum the day before palliative sedation was started: patients only took little sips of fluid and no food at all. Thus, the effect of initiating palliative sedation and thereby withdrawing this very limited amount of fluid intake is of no clinical relevance, in the sense that it would shorten the life of the patient. Nevertheless, the effect of a small amount of fluid must not be ignored or neglected, as it could be a part of mouth care which might prevent possible discomfort. Withholding these drops of fluid has no significant life shortening effect on the patient, moreover since palliative sedation is started on average only 2.5 days before death (Claessens et al., 2011). To this can be added our observation that the artificial food/fluid intake was maintained for those patients receiving it at the moment that palliative sedation was initiated (4/20 patients). Therefore, in the patients we observed whose food/fluid intake was minimal prior to palliative sedation, the palliative sedation did not have a life-shortening effect as a result of withholding of artificial food/fluids.

CONCLUSION

This longitudinal prospective study does not support the argument that palliative sedation amounts to ‘slow euthanasia’ because it entails the withholding or withdrawing of substantial amounts of food and or fluids, thus having a clear life-shortening effect. This study shows that palliative sedation, in specialized palliative care units, is not slow euthanasia but advanced symptom control during the final days of terminally ill patients’ lives who are confronted with refractory suffering. Including the decision to withdraw or withhold artificial fluids as an intrinsic part of the definition of

palliative sedation is not correct, as there is no intrinsic link between the two. The decision to withhold/withdraw artificial hydration is taken independently and this, on average, ten days before the start of sedation. This is in accordance with the view of Broeckaert (Broeckaert, 2002a) who states that "the only correct answer to the problem of withholding hydration and nutrition in sedated patients is to say that this is a totally different discussion". If palliative sedation is combined with the withdrawing of hydration and nutrition, what is done is not just palliative sedation, but sedation AND the withdrawing of hydration and nutrition (Broeckaert, 2000, 2002a).

Although these results are only representative for patients who are admitted to palliative care units and cannot be extrapolated to other care settings. Nevertheless, we are convinced that this prospective, longitudinal study has a significant surplus value and presents some interesting findings that need further examination in different patient populations.

REFERENCES

Ahmedzai S. New approaches to pain control in patients with cancer. Eur J Cancer 1997;33:S8-S14.

Billings JA, Block SD. Slow euthanasia. J Palliat Care.1996;12:21-30.

Boyle J. Medical ethics and double effect: the case of terminal sedation. Theor Med 2004;25:51-60.

Broeckaert B, Nuñez-Olarte JM. Sedation in Palliative care: facts and concepts. In H. Ten Have & D. Clarke, editors The Ethics of Palliative Care. European Perspectives, Buckingham: Open University Press (‘Facing Death Series); 2002b: p. 166-180.

Broeckaert B. Ethical issues at the end of life. In: Payne S, Seymour J, Ingleton C, editors. Palliative Care Nursing. Principles and evidence for practice. Second edition Birkshire: Open University Press, 2008:402-21.

Broeckaert B. Euthanasia and physician assisted suicide. In: Walsh D, editor. Palliative medicine. Philadelphia: Elsevier, 2008:110-5.

Broeckaert B. Palliative Sedation Defined or Why and When Terminal Sedation is Not Euthanasia. J Pain Symptom Manage 2000;20:S58.

Broeckaert B. Palliative sedation: ethical aspects. In: Gastmans C, ed. Between Technology and Humanity. The Impact of Technology on Health Care Ethics, first ed. Leuven: University Press, 2002a:239-255.

Cameron D, Bridge D, Blitz-Lindeque J. Use of sedation to relieve refractory symptoms in dying patients. SAMJ. 2004;94:445-449.

Cherny NI. Sedation for the care of patients with advanced cancer. Nat Clin Pract Oncol. 2006;3:492-500.

Claessens P, Genbrugge E, Vannuffelen R, Broeckaert B, Schotsmans, P, Menten J. Palliative sedation and nursing: the place of palliative sedation within palliative nursing care. J Hospice Palliative Nurs. 2007; 9:100-106.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation: a review of the research literature. J Pain Symptom Manage, 2008; 36:310-33.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation, not slow euthanasia: a prospective, longitudinal study of sedation in Flemish palliative care units. J Pain Symptom Manage. 2011; 41:14-24.

Cowan JD, Palmer TW. Practical Guideline to Palliative Sedation. Curr Oncol Report 2002;4:242-249.

Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manag. 1994;5: 83-93.

Craig G. Terminal sedation. Cathol Med Q. 2002; February.

de Graeff, A., & Dean, M. Palliative Sedation Therapy in the last weeks of life: a Literature Review and Recommendations for Standards. J Palliat Med 2007;10:67-85.

Devlin TF, Weeks BJ. (1986). Spline functions for logistic regression modelling. Proc Eleventh Annual SAS Users Group International. Cary NC:SAS Institute, Inc., pp.646-51.

Ersek M. The meaning of hope and dying. In: Rolling Ferrell B & Coyle N (eds.) Textbook of Palliative Nursing. Oxford: Oxford University Press; 2001: pp 339-351.

Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for uncontrolled symptoms in a South African hospice. J Pain Symptom Manage. 1998;16:145-152.

Georges J, Onwuteaka BD, van der Heide A, van der Wal G, van der Maas P. Symptoms, treatment and 'dying peacefully' in terminally ill cancer patients: a prospective study. Support Care Cancer. 2005;13:160-168.

Gevers S. Terminal Sedation: a Legal Approach. Eur J Health Law 2003;10:359-367.

Hermann C, Looney S. The effectiveness of symptom management in hospice patients during the last seven days of life. J Hosp Palliat Nurs. 2001;3:88-96.

Howland J. Questions about palliative sedation. Ethics Medics. 2005;30:1-2.

Janssen LA, Sulmasy DP. Sedation, Alimentation, hydration and Equivocation: Careful Consideration about Care at the End of Life. Ann Intern Med 2002;136:845-849.

Kedziera P. Hydration, thirst and nutrition. In: Rolling Ferrell B & Coyle N (eds.) Textbook of Palliative Nursing. Oxford: Oxford University Press; 2001: pp 156-163.

Keizer AA, Swart SJ. Palliatieve sedatie, het sympathieke alternatief voor euthanasia? [Palliative sedation, the sympathetic alternative for euthanasia?]. Ned Tijdsch Geneeskd 2005;149:449-451.

Lo B, Rubenfeld G. Palliative sedation in dying patients. JAMA. 2005;294:1810-1816.

Loewy E. Terminal Sedation, Self-Starvation, and Orchestrating the End of Life. Arch Intern Med 2001;161:329-332.

Menten J. Cancer pain: interdisciplinary and comprehensive management (Dissertation). Acco: Catholic University Leuven, 2003.

Miccinesi G, Rietjens JAC, Deliens L, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage. 2006;31:122-129.

Morita T, Chinone Y, Ikenaga M, et al. Efficacy and safety of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan. J Pain Symptom Manage. 2005;30:320-328

Morita T, Tsunoda J, Inoue S, Chihara S. Do hospice clinicians sedate patients intending to hasten Death? J Palliat Care. 1999;15:20-23.

Murray SA, Boyd K, Byock I. Continuous deep sedation in patients nearing death. BMJ. 2008;336:781-782.

National Ethics Committee, veterans' Health Administration. The ethics of palliative sedation as a therapy of last resort. Am J Hosp Palliat Care. 2006;23:483-491.

Quill TE, Byock IR. Responding to intractable terminal suffering: the role of terminal sedation and voluntary refusal of food and fluids. Ann Intern Med. 2000;132:408-414.

Quill TE, Lo B, Brock DW. Palliative options of last resort. A comparison of voluntary stopping eating and drinking, terminal sedation, physician-assisted suicide and voluntary active euthanasia. JAMA. 1997;278:2099-2104.

Rietjens JAC, van Delden JM, van der Heide A et al. Terminal sedation and euthanasia. A comparison of clinical practices. Arch Intern Med. 2006;166:749-753

Rietjens JAC, van der Heide A, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. The practice of terminal sedation in the Netherlands. Ned Tijdschr Geneeskd. 2005;149:467-471.

Rietjens JAC, van der Heide A, Vrakking AM, Onwuteaka-Philipsen B, van der Maas PJ, van der Wal G. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med. 2004;141:178-185.

Rousseau P. The Ethical Validity and Clinical Experience of Palliative Sedation. Mayo Clin Proc 2000; 75: 1064-1069.

Rousseau P. The ethics of palliative sedation. Caring 2004;23:14-19.

Tännsjö T. Terminal sedation: euthanasia in disguise? Kluwer Academic Publishers: Dordrecht, the Netherlands; 2004.

Taylor RM. Is terminal sedation really euthanasia? Med. Ethics. 2003;10:3-8.

Vainio A, Auvinen A, Members of the Symptom Prevalence group. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J Pain Symptom Manage. 1996;12:3-10

Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care. 1990;6:7-11.

Zech DFJ, Grond S, Lynch J, Hertel D, Lehman KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. Pain. 1995;63:65-76.

CHAPTER 6: THE RELATIONSHIP BETWEEN PALLIATIVE SEDATION AND THE LEVEL OF CONSCIOUSNESS OF PATIENTS ADMITTED AT PALLIATIVE CARE UNITS

We are such stuff
As dreams are made off
And our life
Is rounded
With a sleep

Shakespeare, The Tempest Act 4

Published: Claessens P, Menten J, Schotsmans P, Broeckaert B. Level of Consciousness in Dying Patients. The Role of Palliative Sedation: a Longitudinal Prospective Study. American Journal of Hospice and Palliative Medicine. 2012; 29:195-200.

ABSTRACT

Patients suffering from a terminal illness often are confronted with severe symptoms during the last phase of their lives. Palliative sedation, although one of the options of last resort, remains a much debated and controversial issue and is often referred to as a form of slow euthanasia or euthanasia in disguise.

A prospective longitudinal and descriptive design was used. Each patients admitted in one of the 8 participating units was included if they met the inclusion criteria and gave written informed consent.

Two hundred and sixty six patients were included. The incidence of palliative sedation was 7.5%. For the group of sedated patients results show that 90% entered the palliative care unit being fully conscious. Two patients were comatose upon arrival. Ninety percent of the patients remained fully conscious up to the day palliative sedation was started. When looking at the effect of palliative sedation on the level of consciousness the analysis strongly suggest that the palliative sedation – as expected – has an impact on the GCS score. Irrespective of the dichotomization of the score the probability of having a lower GCS increases substantially once sedation is initiated. Additionally, results show that once palliative sedation is administered, the level of consciousness gradually goes down up until the day of death.

Palliative sedation is nor slow euthanasia nor an ambivalent practice. It is an intentional medical treatment which is administered in a proportional way when – in extraordinary situations and at the very end of the dying process - refractory suffering occurs.

INTRODUCTION

Patients suffering from a terminal illness often are confronted with severe symptoms during the last phase of their lives (Georges et al., 2005; Hermann & Looney, 2001). Most of the time these symptoms can be well-controlled (Vainio & Auvinen, 1996; Zech et al., 1995; Ahmedzai, 1997) but for some patients symptoms remain uncontrollable (Lo & Rubenfeld, 2005; NEC, 2006). These refractory symptoms have a negative impact on patient functioning and well-being (Menten, 2003; Coyle et al., 1994), frequently increase as the patient nears the end of life and may interfere with a peaceful dying process (Menten, 2003).

Palliative sedation holds a prominent place as one of the options of last resort when patients are confronted with refractory suffering (Quill et al., 1997; 2000; deGraeff & Dean, 2007; Juth et al., 2010) and as such is increasingly implemented in different hospice programs all over the world (Boyle, 2004; Howland, 2005; Plonk & Arnold, 2005).

Palliative sedation, however, remains a much debated and controversial issue within and outside palliative care (Jansen, 2010; Hasselaar et al., 2007; Vissers et al., 2007) and is often referred to as a form of slow euthanasia or euthanasia in disguise (Howland, 2005; Jansen, 2010; Billings & Block, 1996; Cooney, 2005; Craig, 2002; Taylor, 2003).

Palliative sedation remains a topic of discussion because indeed it is an extraordinary measure which has per definition a serious impact on the consciousness of patients and thus on his ability to think, feel and interact with others. However, an important reason for much of the ongoing debate on palliative sedation is the lack of solid scientific evidence on the current practice (Claessens et al., 2008; 2011).

Therefore, the aim of this paper, which is a report of a part of a prospective, longitudinal study on palliative sedation (Claessens et al., 2011), is to describe in detail the evolution of the level of consciousness of patients residing in palliative care units (PCUs) from admission until their day of death. In doing so, we specifically want to find out what the impact is of palliative sedation/use of sedatives on the level of consciousness of terminally ill patients. By providing this information, a number of empirical claims in the palliative sedation controversy will be assessed.

METHODOLOGY

DESIGN, SETTING AND STUDY POPULATION

A prospective, longitudinal and descriptive design was used. 8 PCU's, which were geographically spread over Flanders and covered the different religious backgrounds, participated in this study. The sample consisted of three PCU's in general hospitals, one hospice, one PCU in a university hospital and three PCU's in general hospitals affiliated with a university. Five hospitals (62%) had a Roman-Catholic background and three were pluralistic. Belgium has legalized euthanasia since 2002 and it was an option in six out of the eight PCU's.

Each unit received, based on the comprehensive research protocol (see appendix 2), positive advice from the local ethical committee. Each patient admitted from September 2004 – April 2005 that met the inclusion criteria and gave formal written informed consent, was included in this study. The following inclusion criteria were set: patients had to be older than 18 years of age and had to be diagnosed with incurable cancer. Their life expectancy was less than three months.

VARIABLES

After an extensive review of the literature and after extended discussions with physicians and nurses in palliative care settings, a list of relevant variables was created. Data were assessed on admission and every Monday, Wednesday and Friday. To reduce the workload for the nurses, the registration of the variables was divided between the nurses and the researcher. The researcher visited the unit once every two weeks and gathered the data that were available in the patients' charts. The other variables, which were based on observations, were registered by the nurse taking care of the patient for the day. A special form, including additional information, was filled out by the attending nurse when palliative sedation was initiated. Demographic variables (sex, age, nationality, marital status, religion/worldview, date of admission, date of death/discharge) were collected by the researcher on admission and completed at the day of death. In this article we will focus on the variable level of consciousness and compare sedated and non-sedated patients.

MEASUREMENT INSTRUMENTS

The Glasgow Coma Scale was used by the nurses to evaluate the level of consciousness of the patient (Teasdale & Jennet, 1974). This scale evaluates the level of consciousness of a patient based on 3 subscales (eyes-movement-verbal reaction). The score can range from 15 'normal consciousness' to 3

'deep comatose'. Nurses scored the level of consciousness three times a week and this from admission until day of death. This instrument is internationally well known, frequently used, easy to use and a valid and reliable instrument (Braakman et al., 1977; Fielding & Rowley, 1990; Rowley & Fielding, 1991) which is not subject to interpretation. It is internationally accepted that a patient with a score < 8 is comatose.

In this study, a translated version, based on a back-to-back translation, was used. The interrater reliability was assessed between nurses in a pilot study. Intraclass correlation was .807 (CI [.671-.891]).

PROCEDURE

An elaborate research protocol was established in close collaboration with representatives of different PCU's (see appendix 2). Each unit received the final protocol together with a letter of clarification. When further information was needed the researcher visited the site. After the unit agreed to participate and upon obtaining the approval of the local ethical committee, the researcher started a two-day training session for all of the nurses involved in the study. First of all, instructions were given on how to fill out the questionnaires. Explicit attention was given to the importance of obtaining informed consent from the patient and/or his/her family. Each patient admitted to the PCU was evaluated in terms of the inclusion criteria. When patients met the criteria, the nurse explained, to the patient and/or his/her family, the purpose of the study and asked the patient and/or his/her family for an informed consent. Once the informed consent was obtained, data gathering started. Data collection ended when the patient died, was discharged or when the patient reconsidered his/her participation in the study.

ANALYSES

Each patient was assigned a numerical code to maintain the anonymity of the data. The link between the code and patient information could only be accessed by the researcher. For the purpose of this analysis, the researchers divided patients receiving palliative sedation into different levels according to Broeckaert's definition of palliative sedation (Broeckaert, 2000, 2002, 2008a,b). The following theoretical levels of sedation were distinguished: mild-intermittent, mild-continuous, deep-intermittent in non-acute situations, deep-intermittent in acute situations, deep-continuous in non-acute situations, and deep-continuous in acute situations.

All data analysis were performed using SAS (SAS institute Inc., Cary, NC, USA). Descriptive statistics (mean, median, quartiles) were used to describe the population under study and to attain further detail of the evolution of the level of consciousness over time. During the analysis, assistance was obtained from biostatisticians to assure the methodological quality of the study.

To assess the impact of the initiation of palliative sedation on the level of consciousness, a logistic regression model, with generalized estimating equations to account for the repeated measurements per subject, was used to model various dichotomized versions [1] of the scale. Specifically, these six different models[2] were used to model separately the probabilities: P(score<15), P(score<14), P(score<13), P(score<12), P(score<11) and P(score<10). For the other dichotomizations, fitting the model was not possible.

Time has been expressed as days before the end of the study (death). Restricted cubic splines (Devlin & Weeks, 1986) have been used to capture and visualize potential nonlinearity (on the logit scale) for the evolution over time. In general, splines are polynomials within intervals of time that are connected across the different intervals of time. Specifically, time has been divided into six intervals (based on observed percentiles) and a cubic polynomial has been used within each interval, except for the outer intervals, in which the relationship was restricted as linear. Sedation was entered in this model as a time-varying binary predictor, equating value 1 as the moment of first sedation. The account for heterogeneity (not due to the moment of sedation) in the probability level, the square root of the length of the follow-up time and the binary variables indicating if the patient has ever been sedated, are entered as baseline variables. Formally, the model is:

$$\text{logit}\big(P(Y=1)\big) = f(t, FU) + \beta_1 ES + \beta_2 S$$

[1] A proportional odds model could be appropriate to model an ordinal score. However, we have not used this model since the small number of patients with sedation and the sparse number of sedation moments does not allow to verify the proportional odds assumption made in this model, i.e. the assumption that the effect of sedation is the same over the whole range of the scale.

RESULTS

OVERALL DESCRIPTIVE RESULTS

Two hundred and sixty-six patients were included in this study. 54% were male and the median age was 72 years (Q1=65; Q3=81). The three most important primary diagnoses that occurred in this study were lung cancer (24%), bowel cancer (15.4%) and breast cancer (12.4%). The median follow-up period was 12 days (Q1=5; Q3=26). The median PPS-score (Palliative Performance Scale as measure for functional status) and Glasgow Coma Score at admission were respectively 40 (Q1=30;Q3=50) and 15 (Q1=14; Q3=15) indicating that patients were mainly bed bound, had an extensive disease, needed assistance with care, had a reduced appetite and were fully conscious. In this sample, 7.5% of the patients received some form of palliative sedation (n=20) (Claessens et al., 2011). All other patients (n=246) died on the unit without receiving palliative sedation. 70% of these sedated patients received some form of benzodiazepines, narcoleptics, neuroleptics prior to palliative sedation administration, either for symptom control (e.g. delirium) (55%) or for sleep disturbances (15%). Overall palliative sedation started on average 2.5 days before death. For 40% of the patients, sedation started as a mild-continuous sedation and 40% started as a deep-continuous sedation in non-acute situations. On the day of death, 85% of the sedated patients received deep continuous sedation for non-acute situations, indicating that the nature of palliative sedation evolves over time.

Looking at this evolution more in detail, it is clear that in almost half of the patients who received palliative sedation, the form of sedation changed over time. In most of the patients, palliative sedation was started as a mild or intermittent form of sedation, on average four days before the day of death, and it evolved into deep-continuous sedation on average two days before the patient's death. In those patients for whom palliative sedation did not change over time, palliative sedation was started, on average, two days before death. Seventy-three percent of these patients received deep-continuous sedation for non-acute situations, and 27% received mild-continuous or mild-intermittent sedation.

LEVEL OF CONSCIOUSNESS FOR THE GROUP OF NON-SEDATED PATIENTS

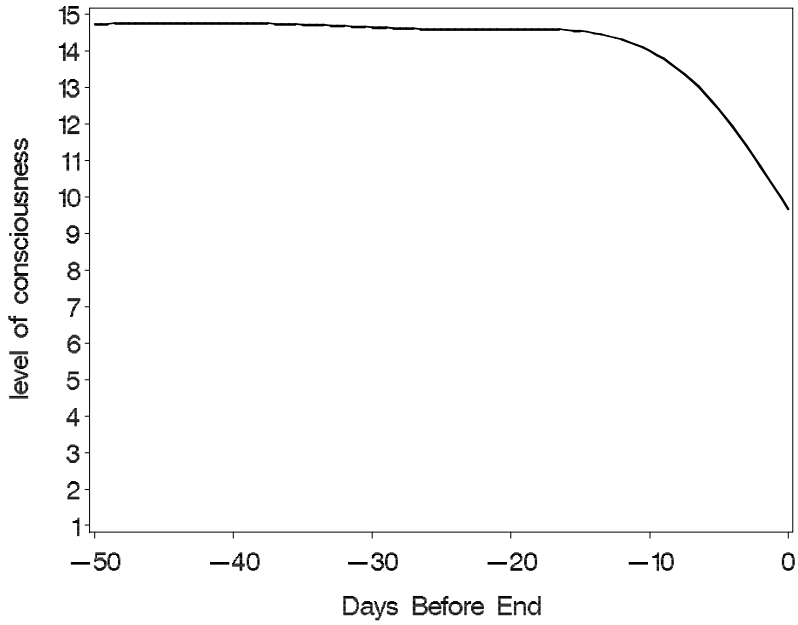
When looking at the level of consciousness for the group of non-sedated patients (n=246) it becomes clear that all patient were fully conscious when admitted to the palliative care unit (median=15; Q1=14; Q3=15). The evolution over time of the GCS score clearly shows that from around day 10 before death the GSC score progressively declines (Figure 1). On the day of death the

median score of the GCS is 9 (Q1=4; Q3=15) indicating that patients are in a state of near coma (8 being the cut-off score).

LEVEL OF CONSCIOUSNESS FOR THE GROUP OF SEDATED PATIENTS

When patients (n=20) entered the palliative care unit 90% were fully conscious (mean GCS = 15).Two patients were comatose upon arrival (GCS of 3 and 7). 90% of the patients remained fully conscious (mean GCS=15 (Q1=15; Q3=15)) up to the day palliative sedation was started and as became clear in another part of this study (Claessens et al. 2011) palliative sedation started on average two and a half days before the day of death. Level of consciousness changed according to the level of sedation that was initiated. For the patients receiving deep continuous sedation during the last days of their life the level of consciousness dropped from 15 to 3 once the sedation was initiated. When patients received some form of intermittent sedation the level if consciousness dropped until levels of 12 meaning that patients had a reduced level of consciousness but were not comatose.

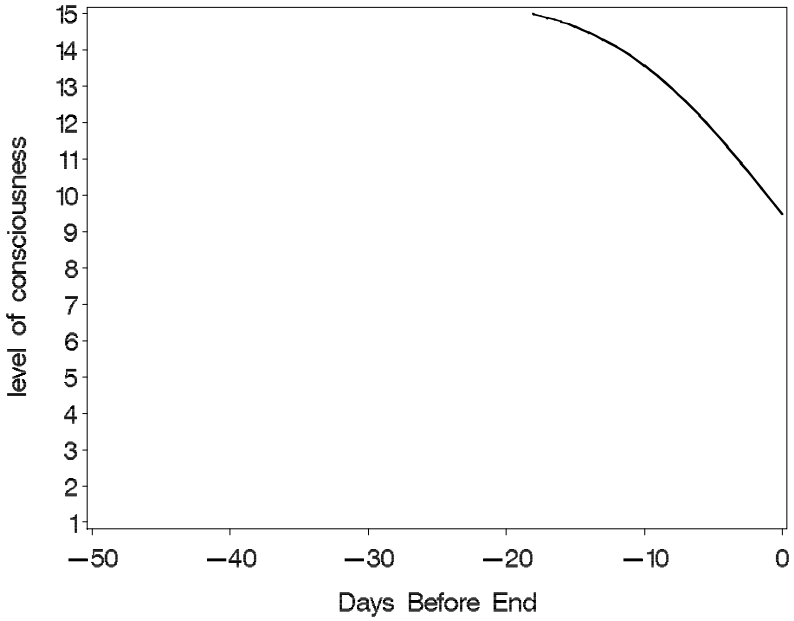
Figure 1
Mean evolution over time for non-sedated patients admitted to the PCU



Although 70% of the sedated patients received some form of benzodiazepines, narcoleptics, neuroleptics for symptom control or sleep disturbances prior to palliative sedation administration this was not reflected in the GCS scales (Figure 2).

Figure 2

Mean evolution of the level of consciousness for patients receiving palliative sedation



EFFECT OF PALLIATIVE SEDATION ON THE LEVEL OF CONSCIOUSNESS

When looking at the effect of palliative sedation on the level of consciousness a comparison was made between sedated and non-sedated patients. This comparison was made based on 6 dichotomizations (cf. supra). The analysis strongly suggest that the palliative sedation – as expected - has an impact on the GCS score. Irrespective of the dichotomization of the score, at the first measurement after sedation has been initiated, the probability of having a lower GCS increases substantially. For all considered dichotomizations, this increase was significant (Table 1). Thus, only the intentional administration of palliative sedation results in a drop of the level of consciousness (Figure 2). Additionally, this figure shows that, once palliative sedation is administered, the level of consciousness gradually goes down up until the day of death.

Table 1

Effect of sedation on level of consciousness for sedated and non-sedated patients

Dichotomisation	Odds ratio	Lower bound	Upper Bound	P-value
P(GCS <10)	15.58	2.44434	99.3664	0.0037
P(GCS <11)	17.57	3.17518	97.1884	0.0010
P(GCS <12)	13.82	2.45530	77.8306	0.0029
P(GCS <13)	13.26	1.86373	94.3213	0.0098
P(GCS <14)	10.04	1.99048	50.6753	0.0052
P(GCS <15)	9.67	3.08976	30.2845	<.001

DISCUSSION

Although palliative sedation is more and more accepted as a medical treatment for refractory symptoms within palliative care, it still is and remains a practice which is saved for those extraordinary situations in which symptoms cannot be relieved in any other way (Hasselaar et al., 2007; Claessens et al., 2011). Because the intentions of physicians can be multiple, ambiguous and uncertain when administering high doses of medication to terminally ill patients (Jansen, 2010), palliative sedation is often referred to as 'slow euthanasia' (Jansen, 2010; Hasselaar et al., 2007; Billings & Block, 1996). This study, however shows that the intentions of physicians can be clearly read from the different levels of consciousness that are observed in patients residing at a palliative care unit. If the intention of the doctor is to administer palliative sedation, a drop in GCS-score is clearly observable. When, however, sedatives are administered for other reasons then palliative sedation (e.g. in order to control delirium directly), the drop in the level of consciousness is very limited, indicating that the intention here is to treat the symptom and not to reduce the level of consciousness. Additionally, this result is even strengthened by the fact that once palliative sedation is administered, there is again a gradual decline in the level of consciousness up until the day of death. Thus, arguing that palliative sedation is administered with the intention to hasten death (as a form of slow euthanasia) (Howland, 2005; Jansen, 2010; Billings & Block, 1996; Cooney, 2005; Craig, 2002; Taylor, 2003) is in contrast with the findings of this study.

Moreover, this study yields that palliative sedation is not only about creating a comatose condition. Palliative sedation is used in different ways (intermittent, acute) and different dosages (mild, deep). When a mild sedation was opted for (40 % of the cases), the level of consciousness dropped only until levels of 12 (meaning that the patient had a reduced level of consciousness but was not comatose at all). In another paper Claessens et al. (2011) report that for the majority of sedated patients, sedation was started as a mild sedation and evolved over time to a deep and/or continuous form of sedation, proving that deep continuous sedation is only administered when the intention of the symptoms necessitates this action (Jansen, 2010; Hasselaar et al., 2007; Vissers et al., 2007). Our findings thus do not suggest ambivalence or a lack of clarity in intentions. Moreover, it shows that assuming that palliative sedation is, by definition, deep continuous sedation (e.g. Rietjens et al., 2006), is meaningless.

In earlier articles Broeckaert has defined palliative sedation as:

> *"the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms (Broeckaert 2000, 2002, 2008a,b)."*

These results suggest, in contrast with what some authors claim (Billings & Block, 1996; Tännsjö, 2004), that in practice too palliative sedation is administered in a proportional way. The use of sedatives and the use of palliative sedation within palliative care is thus clearly based on the intensity and nature of the suffering. Thus, although this study yields a clear effect of palliative sedation on the level of consciousness, sedatives are titrated up according to the intensity of the symptoms. This proportional approach enables the patient to remain conscious for as long as possible given his specific situation and to continue to participate in the decision making process for as long as possible (Claessens et al., 2011). Palliative sedation is nor slow euthanasia nor an ambivalent practice. It is an intentional medical treatment which is administered in a proportional way when refractory suffering occurs. It occurs in extraordinary situations and at the very end of the dying process.

The evolution over time of the GCS score for non-sedated patients, shows that, even though these patients did not receive palliative sedation during their stay, they too have a clear drop in their level of consciousness, occurring approximately 10-7 days before death and progresses downwards up until the day of death. In other words, losing consciousness is often an inherent part of the dying process. Though it is and should be an option of last resort only (Quill et al., 2009) , as the intentional lowering of the level of consciousness is a very serious thing, one should realize at the same time that having a low or very low level of consciousness at the end of life is not an extraordinary or unnatural situation at all.

METHODOLOGICAL QUALITY

This is the first study, to our knowledge, that has gathered data prospectively and over a long period of time. By using this design this study clearly has a surplus value in comparison with other studies that have been done up until now (e.g. Fainsinger et al., 2000; Chiu et al., 2001). Not only can we give a detailed description of the period during which the patient was sedated, but can also give an accurate description of the period that precedes palliative sedation. Moreover this can be done both for the patients that were sedated, as well as for those that were not sedated.

Since nurses have gathered data based on their observations, the problem of attrition is reduced to a minimum. This yields valuable data up to, and including the day of death.

These results are only representative for patients who are admitted to palliative care units and can-not be extrapolated to other care settings. Nevertheless, we are convinced that this, prospective, longitudinal study has a significant surplus value and presents some interesting findings that need further examination in different patient populations.

REFERENCES

Ahmedzai S. New approaches to pain control in patients with cancer. Eur J Cancer 1997;33:S8-S14.

Billings JA, Block SD. Slow Euthanasia. Journal of Palliative Care 1996;12:21-30.

Boyle J. Medical Ethics and Double Effect: The Case of Terminal Sedation. Theories in Medicine 2004;25:51-60.

Braakman R, Averaat CJ, Maas AI, Roel M, Schouten HJ. Inter observer agreement in the assessment of the motor response of the Glasgow Coma Scale. Clin Neurol Neurosurg. 1977; 80:100-106.

Broeckaert B, Nuñez-Olarte JM. Sedation in Palliative Care. Facts and Concepts. In Ten Have, H. & Clarke, D. (Eds.). The Ethics of Palliative Care. European Perspectives. Buckingham: Open University Press, 2002; pp.166-180.

Broeckaert B. Ethical issues at the end of life. In: Payne S, Seymour J, Ingleton C, editors. Palliative Care Nursing: principles and evidence for practice. Second edition. Birkshire: Open University Press, 2008:402-21.

Broeckaert B. Euthanasia and physician assisted suicide. In : Walsh D, editor. Palliative Medicine. Philadelphia: Elsevier, 2008:110-5.

Broeckaert B. Palliative Sedation Defined or Why and When Terminal Sedation is Not Euthanasia. Journal of Pain and Symptom Management 2000;20:S58.

Chiu TY, Hu WY, Lue BH, Cheng SY, Chen CY. Sedation for Refractory Symptoms of Terminal Cancer Patients in Taiwan. Journal of Pain and Symptom Management 2001;21:467-472.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative Sedation: a review of the literature. Journal of Pain and Symptom Management 2008,36:310-333.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative Sedation, not slow euthanasia: a prospective, longitudinal study of sedation in Flemish Palliative Care Units. Journal of Pain and Symptom Management, 2011, 1: 14-24.

Cooney GA. Palliative Sedation: The Ethical Controversy, from http://www.medscape.com/viewarticle/499472, 2005.

Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manag. 1994;5: 83-93.

Craig G. Terminal Sedation. Cathol Med Q 2002; February.

de Graeff, A., & Dean, M. Palliative Sedation Therapy in the last weeks of life: a Literature Review and Recommendations for Standards. Journal of Palliative Medicine 2007;10:67-85.

Devlin TF, Weeks BJ. (1986). Spline functions for logistic regression modelling. Proc Eleventh Annual SAS Users Group International. Cary NC:SAS Institute, Inc., pp.646-51.

Fainsinger RL, de Moissac D, Mancini I, Oneschuk D. Sedation for Delirium and Other Symptoms in Terminally Ill Patients in Edmonton. Journal of Palliative Care 2000a;16:5-10.

Fainsinger RL, Waller A, Bercovici M, Bengston K, Landman W, Hosking M, Nuñez-Olarte JM, de Moissac D. A Multicentre Study of Sedation for Uncontrolled Symptoms in Terminally Ill Patients. Palliative Medicine 2000b;14:257-265.

Fielding K & Rowley G. Reliability of assessments by skilled observers using the Glasgow Coma Scale. Aust J Adv Nurs. 1990; 7:13-17.

Georges J, Onwuteaka BD, van der Heide A, van der Wal G, van der Maas P. Symptoms, treatment and 'dying peacefully' in terminally ill cancer patients: a prospective study. Support Care Cancer. 2005;13:160-168.

Hasselaar J, Reuzel R, Verhagen S, de Graeff A, Vissers K, Crul B. Improving prescription in Palliative Sedation. Archives of Internal Medicine 2007;167:1166-1171.

Hermann C, Looney S. The effectiveness of symptom management in hospice patients during the last seven days of life. J Hosp Palliat Nurs. 2001;3:88-96.

Howland J. Questions about Palliative Sedation. Ethics Medics 2005;30:1-2.

Jansen LA. Disambiguating clinical intention: the ethics of palliative sedation. Journal of Medical Philosophy 2010;35:19-31.

Juth et al. European Association for Palliative Care (EAPC) framework for palliative sedation: an ethical discussion. BMC Palliative Care 2010; 9:20.

Lo B, Rubenfeld G. Palliative Sedation in Dying Patients. Journal of the American Medical Association 2005;294:1810-1816.

Menten J. Cancer Pain: Interdisciplinary and Comprehensive Management. Doctoral Dissertation, Catholic University of Leuven, 2003; Leuven, Belgium.

National Ethics Committee, Veterans' Health Administration. The ethics of palliative sedation as a therapy of last resort. Am J Hosp Palliat Care. 2006;23:483-491.

Plonk WM, Arnold RM. Terminal Care: the Last Weeks of Life. Journal of Palliative Medicine 2005;8:1042-1054.

Quill TE, Byock I.R. Responding to Intractable Terminal Suffering: the Role of Terminal Sedation and Voluntary Refusal of Food and Fluids. Annals of Internal Medicine 2000;132:408-414.

Quill TE, Lo B, Brock DW, Meisel A. Last-resort options for palliative sedation. Annals of Internal Medicine 2009;151:421-424.

Quill TE, Lo B, Brock DW. Palliative Options of Last Resort. A Comparison of Voluntary Stopping Eating and Drinking, Terminal Sedation, Physician-Assisted Suicide and Voluntary Active Euthanasia. Journal of the American Medical Associations 1997;278:2099-2104.

Rietjens JAC, van Delden JM, van der Heide A, Vrakking AM, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. Terminal Sedation and Euthanasia. A Comparison of Clinical Practices. Archives of Internal Medicine 2006;166:749-753.

Rowley G & Fielding K. Reliability and accuracy of the GCS with experienced and inexperienced users. Lancet 1991; 337:535-538.

Tännsjö T. Terminal sedation: Euthanasia in disguise? The Netherlands: Kluwer Academic Publishers, 2004.

Taylor RM. Is Terminal Sedation Really Euthanasia? Medical Ethics 2003;10:3-8.

Teasdale G & Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 13:81-84.

Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J PainSymptom Manage 1996; 12:3-10.

Vissers KC, Hasselaar J, Verhagen SA. Sedation in Palliative Care. Current Opinions in Anaesthesiology 2007;20:137-142.

Zech DFJ, Grond S, Lynch J, Hertel D, Lehman KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. Pain. 1995;63:65-76.

CHAPTER 7: PALLIATIVE SEDATION AND NURSING

Published: Palliative Sedation and Nursing: The Place of Palliative Sedation within Palliative Nursing care. Journal of Hospice and Palliative Nursing, 2007, 9, 100-108.

ABSTRACT

Despite the fact that palliative sedation can be considered a gradually accepted form of therapy within palliative care, research has shown that palliative sedation often involves a heavy emotional burden for care providers, more specifically, for nurses (Morita et al., 2001). It is chiefly the nurse who, after the palliative sedation has been initiated, is assigned the largest share of the subsequent follow-up and care of the sedated patient and his or her family.

Factors such as a patient's unclear wishes as to palliative sedation, difficult-to-diagnose refractory symptoms, insufficient knowledge of palliative sedation, insufficient skills to deal with sedated patients and their families, differences in opinion between doctors and nurses, and conflicts between patient and family, and ethical uncertainties contribute to causing the extra burdens that the nurses experience in these situations and give rise to a certain form of incomprehension or distrust of the method of treatment.

For these reasons, we wish to explain in this article the way in which palliative sedation as a therapy fits into the care perspective of palliative nursing care, the way in which decision-making and the practical procedure of palliative sedation may be carried out (based on a step-by-step plan), and, more specific, the role the nurse can play.

INTRODUCTION

An essential element in palliative care is striving for the best possible quality of life for each terminally ill patient and his or her family. To accomplish this goal, it is important to relieve the patient as much as possible of unpleasant physical, psychological, social, or spiritual problems (Sepulveda et al., 2002; Cannaerts et al. 2000). In recent years, a positive evolution has been noticed regarding the treatment of such physical symptoms as pain (Chater et al., 1998). Research shows that on the whole, palliative care succeeds in adequately treating a number of symptoms, mainly physical (Vainio & Auvinen, 1996; Zech et al., 1995; Ahmedzai, 1997), but at the same time it is evident that many symptoms, although treated, are not accounted for sufficiently. Sometimes these symptoms concern physical problems but increasingly they include spiritual and existential problems (Menten, 2003). These inadequately manageable symptoms are also called 'refractory symptoms' and can be distinguished from other symptoms that are difficult to treat because contrary to the advice of many clinical experts, they cannot be treated without compromising the patient's consciousness (Menten, 2003; Cherny & Portenoy,1994). These refractory symptoms often can have a significant adverse effect on the functioning and well-being of a patient (Cherny & Portenoy, 1994; Coyle et al., 1990) and increase in intensity as the patient approaches death (Ventafridda et al., 1990). Since 1990, some have begun to consider palliative sedation as the final therapeutic possibility (Schotsmans, 1999).

Despite the fact that palliative sedation can be considered a gradually accepted form of therapy within palliative care, research has shown that palliative sedation often involves a heavy emotional burden for care providers, more specifically, for nurses (Morita et al., 2001). It is chiefly the nurse who, after the palliative sedation has been initiated, is assigned the largest share of the subsequent follow-up and care of the sedated patient and his or her family. Morita et al. (2001) surveyed 3187 nurses with the objective of identifying the extent of the emotional burden when confronted with the care of a patient who is undergoing palliative sedation. This research group also identified which factors possibly influence the emotional burden experienced. The study shows that 12 % of the nurses experience palliative sedation as an additional burden, 12% feel helpless when a case of palliative sedation occurs, 11% try to avoid situations in which palliative sedation occurs, and 4 % consider palliative sedation to be pointless (Morita et al., 2001).

Factors such as a patient's unclear wishes as to palliative sedation, difficult-to-diagnose refractory symptoms, insufficient knowledge of palliative sedation, insufficient skills to deal with sedated patients and their families, differences in opinion between doctors and nurses, and conflicts between patient and

family, and ethical uncertainties contribute to causing the extra burdens that the nurses experience in these situations and give rise to a certain form of incomprehension or distrust of the method of treatment.

For these reasons, we wish to explain in this article the way in which palliative sedation as a therapy fits into the care perspective of palliative nursing care, the way in which decision-making and the practical procedure of palliative sedation may be carried out (based on a step-by-step plan), and, concretely, the role the nurse can play.

DOES PALLIATIVE SEDATION CONSTITUTE GOOD NURSING CARE?

A question often raised when nurses discuss palliative sedation is whether this therapy fits in with 'good nursing care', more specifically, good palliative nursing care. Opinions on this vary greatly among palliative nurses. These differences are mainly a consequence of the many misapprehensions that still exist about palliative sedation which, in turn, lead to practices that equally cannot always be distinguished from euthanasia or other forms of end-of-life decisions (ie, improperly increasing certain medication) (Broeckaert & Claessens, 2003). Consequently, nurses occasionally raise serious ethical questions about this form of symptom treatment. A great deal of work has been carried out recently regarding the interpretation and the meaning of the concept of palliative sedation, however (Broeckaert & Claessens, 2003).

Although there is no national or international consensus on the definition of palliative sedation, several essential points appear in the many definitions. The most important elements of most of the definitions are terms such as "proportionality", "refractory symptoms and consciousness" and "terminal condition of the patient". Proportionality refers to the fact that the extent of sedation (as a side-effect of the treatment) must be in proportion to the severity of the symptoms the patients is exhibiting. This rules out considering as palliative sedation the increased use of opioids, among other pain relievers, without taking account of the severity of symptoms. Practice has shown that high dosages of opioids may result in drowsiness, but this effect can never manifest itself to such an extent that it offers a solution for refractory symptoms. In fact, that symptoms, that are treated with palliative sedation are strictly refractory symptoms. In other words, palliative sedation is never used to suppress difficult-to-treat symptoms but is used when a patient is confronted with physical and psychological forms of untreatable suffering. This clearly shows that it is related to controlling symptoms and not euthanasia or any other form of end-of-life decisions under which circumstances the intention is to end life rather than treat refractory suffering (Broeckaert, 2002).

The implementation of palliative sedation is a moral duty in the exceptional cases of untreatable symptoms and cannot be a source of concern to nurses. Denying this therapy to a small group of patients who suffer unnecessarily from refractory symptoms would be immoral if the nurse, in such situation, were not to take into account the ethical foundation of good medical care, namely, patient-oriented care and therapy with respect for the person and, as its most important goal, the patient's comfort (Woods, 2004; Claessens et al., 2003). This does not mean that palliative sedation is to be considered an ideal. On the contrary, this form of therapy may be used only when the care provider has no other possibilities and regular palliative care seems to be insufficient for the patient. In other words, it is important that the nurse, working with the multidisciplinary team, establishes that it concerns a case of refractory suffering and not symptoms that are difficult to treat. Palliative sedation, then, becomes a moral duty in accordance with the values and standards of good medical palliative care (eg. Comfort, patient-oriented care, respect).

In the context of the University Hospitals Leuven, Belgium, we elaborate on the nurse's role in coming to a decision on palliative sedation, carrying out palliative sedation, caring further for the patient, and counseling the family; In doing so, the focus on the multi-disciplinary character of the decision-making process and how the emotional burden of the several care providers can be diminished in this way.

PROCEDURE FOR PALLIATIVE SEDATION AND THE ROLE OF THE NURSE

HISTORY AND DEVELOPMENT OF THE PROTOCOL

In 1999, a palliative care unit was opened in the University Hospitals of Leuven, Belgium. The physician in charge, who was a medical director of the palliative support team since 1992, brought his considerable experience with regard to palliative sedation to the unit, and palliative sedation was elaborately discussed and applied where indicated in concrete circumstances of refractory symptoms. However, this application resulted in many questions from nurses and other care providers, and soon it became clear that there was a need for more a refined procedure concerning the decision-making process and the initiation and execution of palliative sedation. Based on a multidisciplinary consultation and ethical reflection (continuous evaluation of the protocol was carried out by the ethics committee of the hospital), they managed to refine the procedure, and the definition, indications, and procedure were drafted into a protocol for the department (Bruntink, 2001; Vermoesen, 2002;

Menten et al., 2004). After a patient received palliative sedation, there was an extensive evaluation, and certain adaptations to the protocol were implemented. For instance, after a concrete request for palliative sedation, there was a waiting period of 24 hours initiated between the request and the start of the procedure. The possibility of a parting moment was incorporated, because a particular patient had not clearly understood the information provided about palliative sedation and as a result the patient had not been able to say farewell to his friends. Because all questions of palliative sedation were discussed in the multidisciplinary team, the team's consensus and experience in palliative sedation and symptom control grew. Communication with and counselling of the patient and family were more profound and better founded, and spiritual suffering was better recognized and identified. The quality of palliative care increased and requests for palliative care were dealt with transparently. The protocol was progressively adjusted and a flowchart now clarifies the different steps that are to be observed in the decision-making process. The team had grown and was convinced that when a decision for palliative sedation had to be made according to this protocol, this was the only correct solution to treat the refractory symptoms. This certainty creates an undeniable peace of mind of the nurse and the other care providers and supports the nurse and doctor in carrying out palliative sedation.

DEFINITION OF THE CONCEPT OF PALLIATIVE SEDATION

Palliative sedation in this unit was defined as "inducing a terminally ill palliative patient's full loss of consciousness through intermittent or continuous application of medication at the patient's request because there was no other way to gain control over one or more refractory symptoms. The untreatable illness continues evolving naturally during the palliative sedation and the patient will spontaneously and almost always die within a few days.

The palliative sedation, carried out *lege artis*, does not seek to nor shall it cause death and it is not the intention to speed up or slow down the process of dying (Menten, 2003).

Acute sedation of the patient in case of an acute life-threatening hemorrhage or acute respiratory distress is a specific part of the definition and is in this case referred to as 'good clinical practice'. There are specific standard procedures, a standing order, for these acute situations. Palliative sedation, as defined in this unit, is always carried out at the request of the terminally ill palliative patient who is suffering from one or more refractory symptoms for which all therapeutic possibilities for physical, psychological, spiritual, and social comfort have been exhausted. A patient also must have been adequately informed and have understood what this treatment involves.

It must be emphasized that palliative sedation is and hopefully will remain an exceptional measure. Therefore, it is important to incorporate enough steps, conditions, and controls to prevent mistakes, pitfalls and abuses.

THE PROCEDURE

Nurses, alongside other care providers, play a crucial role because they, as the only ones of the multidisciplinary team, are there with the patient and his/her family 24 hours a day.

PHASE 1: PREVENTION OF PALLIATIVE SEDATION: OPTIMIZING PALLIATIVE CARE

Because palliative sedation is an exceptional measure that is only appropriate in cases in which suffering is refractory in form, the first and foremost element of palliative care is the prevention of palliative sedation. The nurses must quickly recognize and acknowledge the needs of the patient (ie, physical, social, psychological, and spiritual) and communicate them to the appropriate care provider (ie, doctor, nurse, psychologist, physiotherapist, pastor, moral counselor). This way, timely intervention is ensured and the suffering of the patient is reduced to a minimum. In this context it is essential that nurses are unconditionally heard by other care providers of the team. Practice has shown that when there is a quick reaction to symptoms, they often can be kept under control and the need for palliative sedation often disappears.

For other patients who exhibit refractory suffering, discussing palliative sedation as a possible therapy is a reassurance in itself. The patient realizes that help is available if the suffering is effectively no longer bearable for him or her. The certainty of a possible solution relaxes the patient and creates a feeling of control. The patient contributes to the decision of his or her further treatment. The nurse plays more of an informing, reflecting, communicating, and explaining role with the patient.

PHASE 2: WHEN REFRACTORY SYMPTOMS PERSIST AND CANNOT BE BORNE BY THE PATIENT

In some rare circumstances, the patient's treatment no longer suffices and signs of continued refractory symptoms remain or the patient explicitly requests palliative sedation. When the nurse or another care provider is asked this question (sometimes the question is also put to a nonmedical team member because he or she is viewed as less intimidating), it first must be heard and thoroughly explored. Why does the patient request this now? What does this question mean and what needs are behind it (is this a real request for palliative sedation or is there another question behind it?)? Are there perhaps other answers to this question? After the request is heard, it is passed on to the medical team and all aspects of it are discussed by the members of the multidisciplinary team, who gather weekly. If

there is an urgent matter, an *ad hoc* interdisciplinary team can be called together. The most important element of discussion is whether the patient is effectively exhibiting refractory symptoms and whether there are any other possible solutions to these symptoms. Only when the team (including every discipline) is satisfied that all other solutions have failed can they further consider the request for palliative sedation. Every decision that is made by the multidisciplinary team must be well reasoned and clearly communicated to the patient and his or her family and must be included in the patient's file.

There is always a nurse present during the discussions between doctors and patients on palliative sedation so that the nurse can come back to it at any time and give further explanations when necessary. The family also receives necessary information from the doctor. Afterward, the nurse ensures that the explanation was clear and well understood by both the patient and the family and determines whether there were any misunderstandings or further questions.

Sometimes the family makes the request for palliative sedation without such request being formulated by the patient, sometimes even without the patient being aware of the request. This question also must be heard and reported to the multidisciplinary team. It is more likely an indication of the family's loss of spirit and a plea for extra support from the whole team. A request made uniquely by the family can never be a reason to initiate palliative sedation with a patient.

PHASE 3: PREPARING THE PATIENT AND FAMILY

The decision to initiate palliative sedation is always taken at a multidisciplinary level. It can never be an individual decision taken by one member of the team alone. The patient and the entire team must agree once all attempts to treat the refractory symptom have been made. The family must be closely involved or at least be fully informed of the decision making process.

The doctor or doctors communicate the decision and the procedure to the patient and family in presence of a nurse; It is also necessary to clearly communicate to the patient a decision not to resort to palliative sedation. The goal of the sedation and the consequences of such are clearly explained, and the team confirms whether the patient wishes to be sedated intermittently or continuously. The nurse also evaluates whether anything is unclear, or the patient or family has any questions. Clear communication with the patient and family is essential. Terminology such as 'putting to sleep' can cause confusion and be unwitting reference to euthanasia. It is important to use clear and simple language, repeat certain elements regularly, and explain them thoroughly. It is also crucial to ask the patient to repeat in his or her own words what he or she has understood from the explanations.

There is a 24-hour period between the request for palliative sedation and its final execution. This period gives the patient and family the opportunity to consider fully the treatment, perhaps make certain arrangements, and part from loved ones. The nurse might, with the patient and family, verify whether there are any financial, notarial, or other practical issues that need arranging. Does the patient wish to phone or see certain people, such as family, friends, doctors, psychologists, pastor, social worker, or notary? Is there a need for a parting moment or ritual? Does the patient wish to make certain arrangements concerning his or her funeral?

Once the decision is taken to proceed to palliative sedation, the patient often experiences a certain feeling of calmness. The end of the suffering is nearing; there is the prospect that it will all end.

PHASE 4: INITIATING PALLIATIVE SEDATION

When palliative sedation is initiated, it must be well organized and well structured. The doctor must be accessible at all times. In consultation with the patient, the nurse inquires who of the family wishes to be present at the start of the sedation and possibly who wants to 'keep watch'. What can be expected from the initiation and the course of the palliative sedation is always discussed with the patient and the family beforehand. It is explained that the palliative sedation is initiated through a continuous subcutaneous (under the skin) drip with Midazolam. At the same time a single injection of Midazolam is given that, on average, induces sleep after about 10 minutes. We explain to the patient and family that this is an initial dose that might still have to be adjusted if the patient's sleep is not adequately deep (observable through handling or nursing) but the appropriate action will be taken immediately at every such episode so that the patient's wish is respected to the greatest extent possible. The nurse continues to be responsible for the patient's comfort and monitors all possible symptoms. Until the moment of death and beyond, the patient is cared for with respect and dignity. A doctor sees the patient daily or more frequently when necessary. The family is followed and supported during the whole process by the multidisciplinary team so that this last phase remains bearable for them, too. Not infrequently the family indicates that this phase is draining because their patience is often put to the test.

The initiation of the sedation itself is an emotional moment during which deep and genuine emotions often surface with the patient and the family. The nurse ensures that this time remains a moment of serenity in the memory of the surviving relatives. Allowing the patient and the family to determine the right time to start is sometimes emotionally difficult, and making the decision is often assumed by the team. Having the sedation initiated by two nurses may ensure that it is a shared experience. The nurse, at that moment, is aware that he or she is carrying out an important turning point, both for that patient and

relatives. Nurses must support each other in this undertaking but also must feel supported by the decision the team has taken. When necessary, nurses must not hesitate to ask for the supporting presence of doctors; doctors must be able to provide this support by inducing the sleep themselves if necessary. This kind of delicate treatment requires meticulousness that is typical of any medical treatment. A well-developed and implemented protocol provides emotional and ethical support, peace of mind for nurses, and prevents improvisation. The initiation of the palliative sedation is often experienced as liberating, not only by the patient but also by the nurse and the family; the patient's suffering is finally over. This sentiment is regularly communicated to the nurses by the family. As a result, the nurses and the team feel supported in the decision they have made and experience a feeling of contentment. This liberating effect and the resulting satisfaction not infrequently wash away any possible uncertainties or even negative feelings that nurses may have. This way, there is often compensation for the emotional burden experienced by nurses directly before or during the initiation of palliative sedation.

Phase 5: Care for the patient and support for the family during the sedation

During the phase in which the patient is in sedated sleep, meticulous medical observation is of the utmost importance to track and report any possible disrupting symptoms in time. The medical care can be adjusted proactively to the anticipated needs of the patient. A bladder catheter can be placed, a antidecubitus mattress provided, and the repositioning schedule adjusted. The nurse checks whether the patient is lying quietly, comfortably, and safely. Mouth care is performed regularly and sometimes can be taught, partly or wholly, to the family keeping watch, which often makes them feel that their presence has more use. In doing so, the mouth is moistened to prevent dehydration and a suitable salve is applied to the lips. If the eyes are open, eye drops or salve prevents local discomfort.

During nursing and handling, the nurse carefully observes the patient's reactions. What is the facial expression? Does the patient moan? Does he or she attempt to resist? Do the eyes open? The level of consciousness must be keenly observed. Is the patient always a sleep, does he or she react to external stimuli such as sound, touch, repositioning? These reactions require immediate (remedial) attention so that the dose required for the optimal treatment of the refractory symptoms is found quickly.

During the course of palliative sedation, the nurse must involve and support the family but also ensure that the patient's room is peaceful and quiet. The family may, if they wish and feel it is appropriate, be involved in caring for the patient. The importance of being present here and now can be emphasized if the family considers it pointless. The nurse also should point out that it is equally important to leave the room, and this request should not be accompanied by feelings of guilt. A question that is often

asked and should be approached with the necessary empathy and perspective is: “How much longer is this going to carry on?” This question can be an expression of the heavy burden the family is experiencing and must be received properly by the care providers. Only then can the family retain a positive feeling from the patient’s final but important stage of life.

PHASE 6: AFTERCARE FOR FAMILY AND NURSE

After the patient has died, there is an assessment conversation with the family members involved. All possible needs are addressed and a further follow-up by a psychologist can be organized. Homecare and the family physician are notified so that they can take over and further assist the surviving relatives. The role of the nurse is fairly limited in this phase. Within the team, the course of the sedation is also assessed. How was it for the patient and the family How have the nurses experienced this period? What are the positive and less positive aspects and what lessons can be drawn? If necessary, a debriefing is organized and a protocol adjustment is discussed.

EVALUATION OF THE PREVALENCE OF PALLIATIVE SEDATION AND THE EFFECT OF USING A PROTOCOL

Since the palliative sedation unit opened (1999) and the protocol was entered into use (2001), there has been a clear decrease in prevalence of palliative sedation on the palliative care unit. Whereas palliative sedation was carried out with approximately 7% of the patients in 1999, this percentage fell to 2.5% in 2005. This decrease can be attributed to an increased expertise concerning the symptom treatment of terminally ill palliative patients. The expertise has evolved to such an extent that most patients are not or rarely confronted with physical refractory suffering. As a result, the demand for sedation with regard to physical refractory suffering has declined sharply. Furthermore, there is clarity among all care providers on how requests for palliative sedation are dealt with in the palliative care unit. This way, the patient receives the same information from all disciplines, which has a positive influence on a patient’s trust because everybody is speaking the same language. As a result, fewer patients are inclined to proactively request palliative sedation, even before the symptomatology becomes a heavy burden, and they wait until they are confronted with refractory suffering.

The development of this step-by-step plan and the precise definition of palliative sedation have made it clear when palliative sedation is and is not an issue. The narrow definition of palliative sedation that is used in this article is partly the cause of the low prevalence compared to some other reported statistics in the international literature (Beel, 2002; Cowan & Walsh, 2001).

CONCLUSION

It should be made clear that nurse play a pivotal role in the prevention of palliative sedation, the decision making process, the execution and follow-up during the palliative sedation, and the aftercare of the family and the team. They are, as it were, the hub between the patient and the family on the one hand and several disciplines on the other hand since they are available with the patient 24 hours a day. Therefore they are often the first to be confronted with the many problems and questions of the patient. It is logical and necessary that the nurse receives professional training regarding palliative sedation, has an opportunity to gain professional experience and that he/she feels supported by the entire team. Only when these conditions are met, will the nurse be able to function optimally for the patient and family. In other words, the nurse is able to ensure, with dignity and respect, the necessary comfort the patient needs in the final stage of life.

Unfortunately, there are many medical and ethical misconceptions concerning the indications, procedures, and courses of palliative sedation. These misconceptions explain why nurses experience this form of treatment as emotionally draining. It is essential that more attention is paid to being more explicit about and ban any misconceptions with regard to palliative sedation.

REFERENCES

Ahmedzai S. New approaches to pain control in patients with cancer. Eur J Cancer 1997;33:S8-S14.

Beel A, McClement SE, Harlos M. palliative Sedation Therapy: a review of definitions and usage. Int J Palliat Nurs. 2002; 8:190-199.

Broeckaert B, Claessens P. Medisch begeleid Sterven: van euthanasie tot het stopzetten van een levensverlengende behandeling. Acta Hosp. 2003; 4:9-20.

Broeckaert B. Palliative sedation: ethical aspects. In: Gastmans C, ed. Between Technology and Humanity. The Impact of Technology on Health Care Ethics, first ed. Leuven: University Press, 2002:239-255.

Bruntink R. Palliatieve Sedatie: Ziekenhuis Leuven stelt procedure op voor palliatieve sedatie. Pallium, 2001; 3:7-11.

Cannaerts N, Dierckx de Casterlé B, Grypdonck M. Palliatieve zorg- zorg voor het leven. Een onderzoek naar de specifieke bijdrage van residentiële palliatieve zorg. Leuven, Belgium: Academia Press, 2000.

Chater S, Viola R, Paterson J, Jarvis V. Sedation for intractable distress in the dying--a survey of experts. Palliat. Med. 1998;12:255-269.

Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care. 1994;10:31-38.

Claessens P, Dierckx de Casterlé B. Skilled Companionship: Verpleegkundige zorg vanuit een zorgethisch perspectief. Tijdschrift voor Gezondheidszorg en Ethiek, 2003; 13:76-80.

Cowan J, Walsh D. Terminal sedation in palliative medicine: definition and review of the literature. Support Care Cancer 2001;9:403-407.

Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manag. 1994;5: 83-93.

Menten J, Van Oosterom A, Vandenbogaert W, et al. Palliatieve Sedatie voor refractaire symptomen bij terminale patiënten: procedure en resultaten van het palliatief support team en de palliatieve zorgeenheid van de Universitaire Ziekenhuizen Leuven. Tijdschrift voor Geneeskunde. 2004;60:164-173.

Menten J. Cancer pain: interdiciplinary and comprehensive management (Dissertation). Acco: Catholic University Leuven, 2003.

Morita t, Miyashita M, Kimura R, Adachi I, Shima Y. Emotional burden of nurses in palliative sedation therapy. Palliat Med. 2001;15:550-557.

Schotsmans P. Een discussie-advies omtrent gecontroleerde sedatie. Ethische Perspectieven, 1999;9:29-34.

Sepúlveda C, Marlin A, Yoshida T, Ullrich A. Palliative Care: The World Health Organization's Global Perspective. Journal of Pain and Symptom Management, 2002; 24:91-96.

Vainio A, Auvinen A, Members of the Symptom Prevalence group. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J Pain Symptom Manage. 1996;12:3-10.

Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care. 1990;6:7-11.

Vermoesen K. Palliatieve sedatie: een menswaardig alternatief. Campuskrant 2002; 13:5.

Woods S. Is terminal sedation compatible with good nursing care at the end of life? Int J Palliat Nurs. 2004;10:244-247.

Woods S. Terminal Sedation: A nursing perspective. In: Tännsjö T, editor. Terminal Sedation: Euthanasia in disguise. Dordrecht, The Netherlands: Kluwer Academic Publishers; 2004. P. 43-56.

Zech DFJ, Grond S, Lynch J, Hertel D, Lehman KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. Pain. 1995;63:65-76.

CHAPTER 8: GENERAL DISCUSSION

OVERALL RESULTS

PREVALENCE OF PALLIATIVE SEDATION

Despite the fact that a very broad definition of palliative sedation was used (both mild-deep, continuous-intermittent and sedation with or without artificial food/fluid were included), this study reveals that only 7.5% of the patients residing in PCUs (palliative care units) receive some form of palliative sedation during their stay. This low prevalence figure is in contradiction to the existing literature, which reports much higher figures (Stone et al., 1997; Peruselli et al., 1999; Fainsinger et al., 2000a en b; Chiu et al., 2001; Morita et al., 2005; Cameron et al., 2004; Chambaere et al., 2010; Rietjens et al., 2008; Rietjens et al., 2008; Elsayem et al., 2009; Alonso-Babarro et al., 2010), even though in most cases a much more narrow definition of palliative sedation was used. Several reasons can be pointed out to explain these differences in numbers. First of all our study involves highly specialized and experienced palliative care units which are – on a daily basis– confronted with dying patients with complex symptoms that are often difficult to treat (Menten, 2003; Broeckaert 2011). Their ever-increasing knowledge in symptom management and the expertise that is available in contemporary PCUs results in high quality palliative care that makes palliative sedation redundant in many cases (Menten, 2003; Broeckaert, 2011; Broeckaert, 2009).

Some methodological issues may be raised to explain the differences in prevalence figures. Since most of the available literature reports on large retrospective studies, these prevalence figures represent what the clinician says he remembered or what was available in the patients' files (Chambaere et al., 2010; Anquinet et al., 2011; Hasselaar et al, 2008; Elsayem et al., 2009; Löfmark et al., 2008; Alonso-Babarro et al., 2010; Caraceni et al., 2012; Rietjens et al., 2008). This might result in prevalence figures that do not really match with the real practice. This is even strengthened by the fact that we are dealing here with a very delicate issue and that often health care workers still do not know what palliative sedation is all about (Broeckaert, 2011).

Another hypothetical argument which could explain the low prevalence of palliative sedation in our study, could be the decriminalization of euthanasia in Belgium. One could assume that, because of the legalization of euthanasia, more patients with refractory symptoms choose for euthanasia instead of asking for palliative sedation. Our study, however, shows no significant increase in the prevalence of euthanasia on PCU's. The only PCU where the number of palliative sedations is available for many years shows that the percentage palliative sedations dropped from 7,5 in 1999 (the

year of starting the PCU) to 2,4% in 2002, the year of the Belgian Euthanasia law. After 2002, the percentage of palliative sedation in that PCU was stable on 2 %. The decrease was probably caused by progressively delivering better palliative care (PhD Thesis Menten 2003 p 98 figure 20) and the euthanasia law did not change that percentage till 2011. It can be hypothesized that patients with an active demand for euthanasia are not transferred to the PCU, but we lack data to confirm this hypothesis . Since euthanasia was an option in most of the participating palliative care units, the access to these units would not be problematized by an active demand for euthanasia.

HOW PALLIATIVE SEDATION IS INITIATED AND HOW IT EVOLVES OVER TIME

This study shows that, in exceptional cases, symptoms remain refractory to any treatment and that this occurs almost exclusively when a patient is close to death. Palliative sedation is thus proven to be an exceptional treatment for patients close to the end of life and whose symptoms are not susceptible to any classical treatment (Cassell & Rich, 2010; Jansen, 2010; Cunningham, 2008; Hasselaar et al., 2008; Cherny et al., 2010). This contrasts with the perception of some authors who label palliative sedation as “slow euthanasia,” a kind of hidden form of euthanasia (Billings & Block, 1996; Tännsjö, 2004; Materstvedt & Bosshard, 2009).

Since palliative sedation starts, in the majority of patients, as a mild and/or intermittent sedation and evolves over time to a deep and/or continuous form of sedation this study illustrates how important and present the *principle of proportionality* is in the decision-making process (Broeckaert, 2000; 2002). The intensity and nature of the suffering determine which form of sedation, and more specifically, which dosage of sedatives is chosen by the treating physician in dialogue with the patients. Thus, palliative sedation does not presuppose that a patient is sedated until unconsciousness. Palliative sedation means that sedative drugs are administered in titrated dosages and individual chosen combinations required to reduce consciousness as much as needed to effectively relieve one or more refractory symptoms (Broeckaert, 2008; Morita et al., 1996; Hasselaar et al., 2009). This notion of proportionality is crucial in distinguishing palliative sedation from euthanasia. This study illustrates that the principle of proportionality is present in current medical practice in palliative care units and that indeed, a clear distinction can and has to be made between palliative sedation and euthanasia (Federatie Palliatieve Zorg, 2011).

SYMPTOM OCCURRENCE AND SYMPTOM DISTRESS – REFRACTORY SYMPTOMS

The observations in this study illustrate that palliative sedation is only administered for those patients who are confronted with intense suffering that cannot be alleviated by standard care. A median of five symptoms was reported on the day that palliative sedation was started, at least two of them were labeled as refractory.

A surprising finding of this study is that the symptom distress score, more than the intensity of the symptom, is suggestive of a symptom being labeled as refractory by patients. Since distress is defined as the emotional component of a symptom experience (Rhodes & Watson; 1987), this finding confirms the ideas of Cassell (1982), who argues that suffering arises from the meaning that patients attach to symptoms. A higher symptom distress score can be associated with increased suffering by the patient. Therefore, it is crucial to determine symptom distress in order to better assess better the suffering of a patient and to evaluate a symptom more correctly as refractory or not. As such, this study confirms the conceptual model of Rhodes & Watson (1987) and supports the idea that a symptom distress score should be included in the assessment of symptoms. This suggests that it is not easy to distinguish physical and existential symptoms . To elucidate this issue: a person may experience physical pain without suffering, or may experience suffering without having physical pain (Valko, 2002; Levy & Cohen, 2005). Based on these observations, this study supports the idea that mind and body are indistinctively entangled with each other (Cassell & Rich, 2010). Even more, it supports the suggestion that suffering is a priori existential. By using this symptom distress score as indicator of refractoriness, the discussion on the subjectivity of the refractoriness gets another meaning (Juth et al;, 2010; Cassell & Rich, 2010; Bruce & Boston, 2011). It overcomes the problem defined by Seymour et al (2007), in which she states that the definition of refractoriness has much to do with the environment and the context of care. By incorporating the assessment of the symptom ”distress score” in daily clinical practice a more adequate evaluation of the refractoriness of the suffering can be made. Although a very interesting observation, more research is needed to further explore this relationship between symptom intensity and symptom distress.

Looking at the number of symptoms that were labeled as refractory and the nature of the refractoriness, our study revealed similar results as reported in the international literature. Pain, despite an enormous evolution in pain management possibilities (Menten, 2003; Hermann & Looney; 2001; Fowell et al., 2006) still remains an important symptom to initiate palliative sedation (Oosten et al.,

2011; Hasselaar et al., 2009; Ventafridda et al., 1990; Rietjens et al., 2004, 2005, 2006; Stone et al., 1997; Morita et al., 1996; Kohara et al., 2005; Chater et al., 1998; Morita, 2004; Elsayem et al., 2009).

DECISION MAKING PROCESS – INFORMED CONSENT

Almost all patients in this study who received palliative sedation indicated themselves that they were suffering intolerably. Moreover, all patients included in this study were actively involved in the decision-making process and gave there informed consent. This is in accordance with other research literature on this matter (Müller-Bush, 2003; Menten, 2003; Ventafridda et al., 1990; Rietjens, 2004,2005,2006; Morita et al., 1996; Chater et al., 1998; Morita, 2004a,b) and accords with recommendations made in several clinical guidelines (KNMG, 2005; Broeckaert et al., 2011; Braun et al., 2003; deGraeff & Dean, 2007; AAHPM, 2002; HPNA, 2003; Morita et al., 2005). This contradicts suggestions that palliative sedation is given to incapacitated patients and is initiated without the consent of the patient (Valko, 2004).

Making a patient unconsciousness is a very delicate and far-reaching decision (Cherny et al., 2010). Therefore it is not only the doctor who decides. All health care workers, the patient, and the family have to be involved in the decision making process and the informed consent of the competent patient is a prerequisite. Of course there may be exceptional acute situations in which a patient almost instantly needs palliative sedation as part of good clinical practice (e.g., in case of massive hemorrhage or acute terminal dyspnea), but no such cases were found in our study.

ARTIFICIAL FOOD AND FLUID INTAKE

Another aspect that is often debated is food and fluid intake of patients that receive palliative sedation. Has artificial fluid been continued, stopped or started? Our study supports the hypothesis, based on clinical registration, that oral food and fluid intake decreases progressively and spontaneously during the stay and finally is reduced to a minimum or even totally stopped a few days before death. This natural decrease of food and fluid intake is thus linked to the progression of the illness and there is no causal relationship with the administration of sedative medication or analgesics (Cunningham, 2008). Only a very limited number of patients receive artificial fluid/food when entering the palliative care unit, which is frequently stopped during the stay and long before palliative sedation is an option of possible treatment. These observations suggest that, in contrast with what some authors claim (Billings & Block, 1996; Tännsjö, 2004; Battin, 2008), withholding artificial hydration has no proven life-shortening effect . This aspect, in combination with the fact that

administering artificial fluids to terminal patients has rather a baleful influence on patients' condition, suggests that starting artificial fluids during palliative sedation is futile (Cowan & Palmer, 2002). Arguing that withholding artificial hydration would be life shortening is meaningless in these cases (Hauser & Walsh, 2010). The majority of experienced clinicians are convinced that patients don't die because they stop drinking or eating, they don't drink or eat anymore because they are dying (Menten, 2003).

However, a few patients still received artificial food/fluid before sedation was started. Is it then necessary or recommended to withdraw this fluid? Our study shows that, in clinical practice, withdrawing artificial fluids is not a prerequisite for palliative sedation. In 14% of the sedated patients artificial fluids were continued in the same amount as before sedation. In those patients where fluids were withdrawn, this was only done on request or with the consent of the patient. The statement that palliative sedation is intrinsically linked with the withholding/withdrawing of artificial foods and fluids , is contradicted by the observations in this study (Quill et al., 1997; Battin, 2008).

LEVEL OF CONSCIOUSNESS

Another important controversial aspect of the debate about palliative sedation is whether this practice is ethically acceptable (Rietjens et al., 2008). Although palliative sedation is more and more accepted as a normal medical treatment (De Graeff & Dean, 2007), the debate whether palliative sedation is slow euthanasia (Jansen, 2010; Hasselaar, 2007; Vissers, 2007; Billings & Block, 1996) or, on the contrary, a palliative intervention that should be clearly distinguished from euthanasia, is still ongoing (Rietjens et al., 2008; Hasselaar et al., 2009; Materstvedt & Bosshard, 2009). This ethical discussion remains alive because the intentions of physicians can be multiple, ambiguous and uncertain when administering high doses of medication to terminally ill patients (Jansen, 2010) and are difficult to assess in an objective way. Literature on this topic focuses strongly on deep, continuous sedation. Authors state that this type of sedation has an important impact on the patient and his/her family: the social life of a patients is actually ended (Materstvedt & Bosshard, 2009).

This study, however shows that the intentions of physicians and patients can be clearly assessed from the different levels of consciousness that are observed in patient residing at a palliative care unit. If the intention of the doctor is to administer palliative sedation, a drop in GCS-score (Glasgow Coma Scale) is clearly observable. When, however, sedatives are administered for other reasons then palliative sedation (e.g. in order to control delirium directly), the drop in the level of consciousness is very limited, indicating that the intention here is to treat the symptom and not to

reduce the level of consciousness. Additionally, this result is even strengthened by the fact that once palliative sedation is administered, there is again a gradual decline in the level of consciousness up until the day of death. Thus, the suggestion that palliative sedation is, a priori, administered with the intention to hasten death (as a form of slow euthanasia) (Howland, 2005; Jansen, 2010; Billings & Block, 1996; Cooney, 2005; Craig, 2002; Taylor, 2003) is not supported by this study.

This study yields that the point of palliative sedation is not to create a comatose condition. Palliative sedation is used in different ways (intermittent, acute) and different dosages (mild, deep). When a mild sedation was opted for (40 % of the cases), the level of consciousness dropped only until levels of 12 (meaning that the patient had a reduced level of consciousness but was not comatose at all). Moreover, for the majority of sedated patients, sedation was started as a mild sedation and evolved over time to a deep and/or continuous form of sedation, proving that deep continuous sedation is only administered when the intensity of the symptoms necessitates this action (Jansen, 2010; Hasselaar, 2007; Vissers, 2007). Our observations do not suggest ambivalence or a lack of clarity in intentions. It shows on the contrary that the idea that palliative sedation by definition is deep continuous sedation (e.g. Rietjens et al., 2006), is not correct.

In earlier articles Broeckaert has defined palliative sedation as:

> *"the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms (Broeckaert, 2000; 2002; 2008a,b)."*

Our results suggest, in contrast with what some authors claim (Billings & Block, 1996; Tännsjö, 2004) that not only in ethical studies but in actual medical practice too palliative sedation implies the proportional administration of sedative medication. The use of sedatives and the use of palliative sedation in palliative care units is clearly based on the intensity and nature of the suffering. Although this study yields a clear effect of palliative sedation on the level of consciousness, sedatives are titrated up according to the intensity of the symptoms. This proportional approach enables the patient to remain conscious for as long as possible, given his specific situation and to continue to participate in the decision making process for as long as possible. Palliative sedation is nor slow euthanasia nor an ambivalent practice. It is an intentional medical treatment which is administered in a proportional way when in extraordinary situations and at the very end of the dying process refractory suffering occurs.

The evolution over time of the GCS score for non-sedated patients, shows a clear drop in their level of consciousness, occurring approximately 10-7 days before death and progresses downwards up until the day of death. Progressive loss of consciousness is thus an inherent part of the natural dying process. Palliative sedation is and should be an option of last resort only (Quill et al., 2009), as the intentional lowering of the level of consciousness is a very serious issue. However, at the same time one should realize that having a low or very low level of consciousness at the end of life is not an extraordinary or unnatural situation at all.

METHODOLOGICAL QUALITY

This is the first study, to our knowledge, that has gathered comprehensive bedside data about palliative sedation prospectively and over a long period of time. By using this design, this study clearly has added value in comparison with other studies (mostly retrospective) that have been done up until now (e.g., Peruselli et al., 1999; Stone et al., 1997; Rietjens et al., 2004). Not only can we give a detailed description of the period during which the patient was sedated, but we can report an accurate description of the period that precedes palliative sedation. We have these data for both the patients who were sedated, as well as for those who were not sedated. The strength of this methodology is that data gathering is not based on what physicians say, remember and think, but on what is clearly observed by nurses, patients and researchers (those who took part in the data gathering). Since nurses, together with patients, have gathered most of the data based on their observations, we are not confronted with the problem of attrition and have valuable data up to, and including, the day of death. Additionally, the quality of the data is guaranteed since most of the instruments used in this study were tested for validity and had a good reliability.

Nevertheless, this study has some methodological weaknesses that must be taken into account when interpreting the results. Although a total sample size of 266 patients was included, the group of sedated patients (n = 20) was rather small. In terms of describing the practice as such this is not a problem. However, this small sample becomes problematic when comparisons are made between the sedated and non-sedated patients. Since the focus of this study was on the description of the practice, no statistical comparisons were made (on the level of descriptive statistics) between sedated and non-sedated patients.

Another important limitation of this study concerns the assessment of the symptom prevalence and symptom distress. This score was not obtained using solely a self-rating scale. When the patient was able to do so he/she scored symptom prevalence and symptom distress himself. However, in most

cases, due to the burden for these terminally ill patients, the score was assessed by the nurse together with the patient. Therefore, it might not be a true reflection of what the patient feels. A pilot study showed that the agreement between the scores of nurses and patients were moderate (r = 0.661) to weak (r = 0.201) (P<0.05). However, this was the only way to get valid information on the symptom experience of very weak terminally ill patients (without being confronted with high attrition, and thus useless information), taking into account the burden self-rating would bring about for them, considering they would be asked to score 12 symptoms for intensity and distress three times a week. Therefore, we decided that this was the best possible way to rate the symptom experience of this patient population in the context of this study on palliative sedation.

During this study no definition of palliative sedation was given to the PCU's to prevent possible conceptual confusion between PCU's and to ensure that all possible cases of palliative sedation were included in the study. Important here is that nurses were asked to fill out an extra questionnaire for each patient that received palliative sedation, conform the practice on the ward. The purpose of this questionnaire was to enrich further our data. Nurses received an elaborate education on how and when to fill out the different questionnaires, informed consent, … and were clearly instructed to fill out this extra questionnaire in all cases were sedatives were used for refractory symptoms. The number of palliative sedation cases and the types of sedation were determined by a specialized physician and a specialized researcher on the basis of a meticulous review of all the cases in which sedative medication was used. Since this information can be found in the general files of the patients we were able to classify all use of sedative medication in different categories. This classification was not based on the perception of the nurses (and the fact that they did or did not fill out the extra sedation questionnaire), but on a thorough assessment of each use of sedative medication. It is thus clearly not correct that in our study cases which were not perceived as palliative sedation by the nurses, were not included – which would explain the low incidence of sedation in our study (Chambaere et al., 2011).

Our study shows that on the included palliative care units, there is a clear distinction between palliative sedation and euthanasia. They use different drugs and in palliative sedation the drug dose is up-titrated in proportion to the symptom. Thus, the hypothesis that palliative sedation is a form of slow euthanasia is not supported by our data. It needs to be said that this conclusion is based on a quantitative observational design which cannot 'prove' the good intention of the physician. However, by combining the results of several well documented outcomes, as there are the decision making process, registration of artificial food and fluid intake, …, a quite thorough view is available on the

process. Of course, the combination of these registrations with a qualitative research design could have contributed to a better understanding of the decision making process, more specific on the aspect of 'good intention' and might have resulted in a more solid conclusion on this matter.

Because we only focused on cancer patients admitted to PCUs , the results of this study cannot be extrapolated to other care settings. Generalization of these results is limited since only 8 PCU's, still 27% of the Flemish PCU's, participated in this study. Moreover, our sample consisted of 8 PCU's that were geographically spread over Flanders and represented both Catholic and pluralistic institutions. Therefore, we are convinced that this prospective, longitudinal study has a significant added value and presents some interesting findings that need further examination in different patient populations.

IMPLICATIONS FOR FURTHER RESEARCH

This study has shown that prospective research in a delicate patient population is feasible.

First of all it is necessary that home care, nursing homes, general hospital based wards are explored with regard to palliative sedation. By comparing different care settings it can become clear what the benefit is of guidelines for the decision making process, what the prevalence of palliative sedation is in relation to euthanasia and how specialized palliative care can influence the quality of palliative sedation practice.

A combination of quantitative and qualitative research methods can offer a better insight in the intention of the physician and the experiences of patients, nurses and families. These results can be used to refine and optimize existing guidelines and practices.

One of the key questions about palliative sedation is its supposed life shortening effect. More rigorous research must be done to answer this question scientifically. Randomized controlled trials could substantially enhance the body of evidence but are unethical (Maltoni et al., 2012). Comparing patients who – despite their refractory suffering – do not choose for palliative sedation with patients choosing for palliative sedation might be an alternative research design, but can hardly be called realistic. It is however very difficult to find these patients for prospective follow-up and registering the different items that are needed to answer the question

The most important question, however, should be: "Will evidence of a (non)-life shortening effect be of clinical importance, i.e. will it change the treatment of refractory suffering?" Suppose we

can prove –our data suggest otherwise- that palliative sedation, an act which as such occurs at the very end of a dying process, indeed shortens life, will we then withhold palliative sedation because of this finding to patients who are suffering intolerably? Is it not enough to know and to show that the palliative sedation procedure is carefully looked at from and interdisciplinary point of view and only used in those patients where a team of health care workers believes that this is the only option to ensure a humane death?

With regard to the question if randomized controlled trials are relevant in answering the question on the life shortening effect of the withholding of hydration during the palliative sedation following remarks can be given.

Although our study shows that the decision to withdraw or withhold hydration is taken apart from the decision to initiate palliative sedation and taken into account that most of the patients have stopped eating or drinking at the start of sedation, carrying out a randomized controlled trial could substantially contribute to the body of knowledge on this topic. Although not an evident choice, carrying out randomized controlled trials with regard to the effect of hydration could be an option and would allow to optimize the practice with regard to the use of artificial hydration near the end of life. Clearly this would imply an informed consent of the patient.

CLINICAL IMPLICATIONS

During the past years palliative sedation has become a normal and widespread accepted practice in palliative care units. This study clearly shows that palliative sedation is only used for those patients who are confronted with severe and refractory suffering at the end of their lives and as such is congruent with findings of recent literature on this topic (Rietjens et al., 2008; Oosten et al., 2011; Alonso-Babarro et al., 2010).

Palliative sedation can be experienced as a technique which has a major impact on the personhood of patients (Materstvedt & Bosshard, 2009; Hasselaar et al., 2009). It intervenes with the possibility of communicating with the patient and as such is often very hard to bear for the family. Therefore, it is of the utmost importance that the decision to initiate palliative sedation is taken based on clear guidelines and with the informed consent of the patient (De Graeff & Dean, 2007). Making sure that both patient and family clearly understand the consequences and possible side effects of palliative sedation can only have a positive effect on the lived experience of both patient and/or his family. Since nurses are closely involved in the procedure of palliative sedation (Gran & Miller, 2008)

as is shown in our protocol (see chapter 7), they will play a crucial role in supporting both patient and family through the process of palliative sedation. Administering and monitoring medications, assessing the effectiveness of treatments, and providing compassionate support for both patients and families are essential tasks for a nurse (Gran & Miller, 2008). Although nurses strongly believe that palliative sedation significantly contributes to the 'quality of death' of the patient (Rietjens et al., 2007), they often experience that their role is complicated because patients are unable to communicate their experiences of pain or other distressing symptoms (Gran & Miller, 2008). Other factors that complicate the role of the nurse are the patient not having participated in the decision making (a situation we did not find in our own study), unclear reasons for administering palliative sedation, limited experience with palliative sedation and the use of palliative sedation for nonphysical symptoms (Rietjens et al., 2007). It is clear that to guarantee the quality of care in relation to palliative sedation, extra attention should be given to support the nurses. Organizational support, educational sessions on the assessment of symptom distress and on giving skilled care for patients that receive palliative sedation and emotional support for nurses might ease the extra burden that is experienced with this type of care (Gran & Miller, 2008; Rietjens et al, 2007). Since the experience of nurses during palliative sedation was not measured or studied in this research project, we are unable to offer new data on this important issue.

The crucial ethical and practical difference between palliative sedation and euthanasia or slow euthanasia lies, as this study clearly showed, in the notion of proportionality. This notion of proportionality, clearly present in palliative sedation, implies highly specialized expertise with regard to symptom assessment and management. Unfortunately, the majority of dying patients do not reside on such a specialized unit and one can wonder whether the distinction between palliative sedation and euthanasia is as clear there as it is in PCU's. This study provides not the data to answer this question but literature shows that, despite the availability of several clinical guidelines on palliative sedation, the practice of palliative sedation in other settings (e.g. home care, nursing home, …) varies widely (Reuzel et al., 2008). Due to a lack of expertise/knowledge the distinction between palliative sedation and slow euthanasia sometimes can fade. Therefore it is of the utmost importance that palliative knowledge and skills become more taught and implemented in the wider setting of end-of-life care (Reuzel et al., 2008). In other words, to avoid a slippery slope (Billings & Block, 1996) the use and development of guidelines, education of health care workers and the involvement of palliative support teams or specialized physicians is a necessity for improving the quality of palliative sedation practices (Reuzel et al., 2008).

Although a lot of literature is available on the practice of palliative sedation, little clear cut answers are available with regard to several ethical questions. We are convinced that in this regard our prospective, longitudinal study presents some interesting findings, that of course need further examinations in different patient populations and larger sample sizes to be conclusive.

REFERENCES

Alonso-Babarro A, Varela-Cerdeira M, Torres-Vigil I, Rodríguez-Barrientos R, Bruera E. At-home palliative sedation for end-of-life cancer patients. Palliat Med. 2010 Jul;24(5):486-92.

American Academy of Hospice and Palliative Medicine (2002). Statement on the sedation at the end of life, from http://www.aahpm.org/postions.sedation.html.

Anquinet L, Rietjens JAC, Van Den Block L, Bossuyt N, Deliens, L. general practitioners report of continuous deep sedation until death for patients dying at home: a descriptive study from Belgium. Eur J Gen Pract. 2011 Mar;17:5-13.

Battin MP. Terminal sedation: pulling the sheet over our eyes. Hastings Cent Rep. 2008;38:27-30.

Billings JA, Block SD. Slow euthanasia. J Palliat Care. 1996; 12:21-30.

Boyle J. Medical ethics and double effect: the case of terminal sedation. Theor Med 2004;25:51-60.

Braun TC, Hagen NA, Clark T. Development of a Clinical Practice Guideline for Palliative Sedation. J Palliat Med. 2003;6:345-350.

Broeckaert B, Nuñez-Olarte JM. Sedation in Palliative care: facts and concepts. In H. Ten Have & D. Clarke, editors The Ethics of Palliative Care. European Perspectives, Buckingham: Open University Press (‘Facing Death Series); 2002. p. 166-180.

Broeckaert B. Ethical issues at the end of life. In: Payne S, Seymour J, Ingleton C, eds. Palliative care nursing. Principles and evidence for practice, 2nd ed. Berkshire: Open University Press, 2008:402-421.

Broeckaert B. Federation TF. Treatment decisions in advanced disease: a conceptual framework. Indian J Palliat Care. 2009;15:30-6.

Broeckaert B. Palliative sedation defined or why and when terminal sedation is not euthanasia. J Pain Symptom Manage 2000;20:S58.

Broeckaert B. Palliative Sedation Defined or Why and When Terminal Sedation is Not Euthanasia. J Pain Symptom Manage 2000;20:S58.

Broeckaert B. Palliative sedation, physician-assisted suicide, and euthanasia: "same, same but different"? Am J Bioeth. 2011 Jun;11(6):62-4.

Broeckaert B. Palliative sedation: ethical aspects. In: Gastmans C, ed. Between Technology and Humanity. The Impact of Technology on Health Care Ethics, first ed. Leuven: University Press, 2002:239-255.

Bruce A, Boston P. Relieving existential suffering through palliative sedation: discussion of an uneasy practice. J Adv Nurs. 2011;67:2732-40.

Cameron D, Bridge D, Blitz-Lindeque J. Use of sedation to relieve refractory symptoms in dying patients. SAMJ. 2004;94:445-449.

Cannaerts N, Dierckx de Casterlé B, Grypdonck M. Palliatieve zorg- zorg voor het leven. Een onderzoek naar de specifieke bijdrage van residentiële palliatieve zorg. Leuven, Belgium: Academia Press, 2000.

Caraceni A, Zecca E, Martini C, Gorni G, Campa T, Brunelli C, De Conno F. Palliative sedation at the end of life at a tertiary cancer center. Support Care Cancer. 2012 Jun;20(6):1299-307.

Carver AC, Foley KM. The Wein article reviewed. Oncology, 2000;14:597-598.

Cassell EJ, Rich BA. Intractable end-of-life suffering and the ethics of palliative sedation. Pain Med. 2010;11:435-438.

Cassell EJ. The nature of suffering and the goals of medicine. N Engl J Med. 1982;306:639-645.

Chambaere K, Rietjens JA, Cohen J, Sterckx S, Mortier F, Deliens L. Palliative sedation in Flemish palliative care units. J Pain Symptom Manage. 2011 Jun;41(6):e1-2; author reply e2-5.

Chater S, Viola R, Paterson J, Jarvis V. Sedation for intractable distress in the dying--a survey of experts. Palliat. Med. 1998;12:255-269.

Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care. 1994;10:31-38.

Cherny NI, Radbruch L, Board of the European Association for Palliative Care (EAPC). European Association for Palliative care recommended framework for the use of sedation in palliative care. PAlliat Med. 2009;23:581-593.

Chiu TY, Hu WY, Lue BH, Cheng SY, Chen CY. Sedation for refractory symptoms of terminal cancer patients in Taiwan. J Pain Symptom Manag., 2001; 21: 467-472.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation: a review of the research literature. J Pain Symptom Manage 2008; 36:310-333.

Cooney GA. Palliative sedation: the ethical controversy. Available from http://www.medscape.com/viewarticle/499472.

Cowan JD, Palmer TW. Practical guideline to palliative sedation. Curr Oncol Rep 2002;4:242-249.

Craig G. Terminal sedation. Cathol Med Q. 2002; February.

Cunningham J. A review of sedation for intractable distress in the dying. Ir Med J. 2008;101:87-90.

de Graeff, A., & Dean, M. Palliative Sedation Therapy in the last weeks of life: a Literature Review and Recommendations for Standards. Journal of Palliative Medicine 2007;10:67-85.

Elsayem A, Currie E, Boohene J, Munsell MF, Calderon B, Hung F, Bruera E. Use of palliative sedation for intractable symptoms in the palliative care unit of a comprehensive cancer center. Support Care Cancer 2009;17:53–59.

Enck RA. Drug-induced terminal sedation for symptom control. American Journal of Hospice and Palliative care. 1991;8:3-5.

Fainsinger R, Miller MJ, Bruera E, Hanson J, Maceachern T. Symptom control during the last week of life on a palliative care unit. J Palliat Care. 1991;7:5-11.

Fainsinger RL, deMoissac D, Mancini I, Oneschuk D. Sedation for delirium and other symptoms in terminally ill patients in Edmonton. J Palliat Care. 2000a;16:5-10.

Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for uncontrolled symptoms in a South African hospice. J Pain Symptom Manage. 1998a;16:145-152.

Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for uncontrolled symptoms in a South African hospice. J Pain Symptom Manage 1998b;16:145-152.

Fainsinger RL, Waller A, Bercovici M, et al. A multicentre international study of sedation for uncontrolled symptoms in terminally ill patients. Palliat Med. 2000b;14:257-265.

Fondras J-C. Sedation and ethical contradiction. European Journal of palliative care 1996;3:17-20.

Fowell A, Johnstone R, Russell I, Russell D, Finlay I. Reported symptoms in the last days of life: the need for robust research. Palliat Med. 2006;20:845-6.

Greene WR, Davis WH. Titrated intravenous barbiturates in the control of symptoms in patients with terminal cancer. South American Journal 1991;84:332-337.

Hasselaar J, Reuzel R, Verhagen S, de Graeff A, Vissers K, Crul B. Improving prescription in Palliative Sedation. Archives of Internal Medicine 2007;167:1166-1171.

Hasselaar J, Verhagen S, Reuzel R, van Leeuwen E, Vissers K. Palliative sedation is not controversial. Lancet Oncol. 2009 Aug;10(8):747-8.

Hasselaar JG, Reuzel RP, van den Muijsenbergh ME, Koopmans RT, Leget CJ, Crul BJ, Vissers KC. Arch Inter Med. 2008; 168:537-543.

Hauser K, Walsh D. Palliative sedation: welcome guidance on a controversial issue. Palliat Med. 2009;23:577-9.

Hermann C, Looney S. The effectiveness of symptom management in hospice patients during the last seven days of life. J Hosp Palliat Nurs. 2001;3:88-96.

Hospice and Palliative Nurses Association (2003). Position Statement: Palliative sedation at the end of life, from http://www.hpna.org.

Howland J. Questions about palliative sedation. Ethics Medics. 2005;30:1-2.

Jackson WC. Palliative sedation versus terminal sedation: What's in a name? American Journal of Hospice and Palliative care 2002;19:81-82.

Jansen LA. Disambiguating clinical intention: the ethics of palliative sedation. Journal of Medical Philosophy 2010;35:19-31.

Janssen LA, Sulmasy DP. Sedation, Alimentation, hydration and Equivocation: Careful Consideration about Care at the End of Life. Ann Intern Med 2002;136:845-849.

Juth et al. European Association for Palliative Care (EAPC) framework for palliative sedation: an ethical discussion. BMC Palliative Care 2010; 9:20.

Keizer AA, Swart SJ. Palliatieve sedatie, het sympathieke alternatief voor euthanasie? [Palliative sedation, the sympathetic alternative for euthanasia?]. Ned Tijdsch. Geneeskd. 2005;149:449-451.

Kirk TW, Mahon MM. Palliative Sedation Task Force of the National Hospice and Palliative Care Organization Ethics Committee. National Hospice and Palliative Care Organization (NHPCO) position statement and commentary on the use of palliative sedation in imminently dying terminally ill patients. J Pain Symptom Manage. 2010;39:914-23.

Koh YH, Lee OK, Wu HY. "Palliative" and not "terminal" sedation. J Pain Symptom Manage. 2009;37:e6-8.

Kohara H, Ueoka H, Takeyama H, Murakami T, Morita T. Sedation for terminally ill patients with cancer with uncontrollable physical distress. J Palliat Med. 2005;8:20-25.

Krakauer E. Responding to intractable terminal suffering. Annals of Internal Medicine. 2000;133:560.

Levy MH, Cohen SD. Sedation for the relief of refractory symptoms in the imminently dying: a fine intentional line. Sem Oncol 2005; 32:237-246.

Lo B, Rubenfeld G. Palliative Sedation in Dying Patients. Journal of the American Medical Association 2005;294:1810-1816.

Löfmark R, Nilstun T, Cartwright C, Fischer S, van der Heide A, Mortier F, Norup M, Simonato L, Onwuteaka-Philipsen BD; EURELD Consortium. Physicians' experiences with end-of-life decision-making: survey in 6 European countries and Australia. BMC Med. 2008 Feb 12;6:4.

Maltoni M, Scarp E, Rosati M, Derni S, FAbbri L, Martini F, Amadori D, Nanni O. Palliative sedation in end-of-life care and survival: a systematic review. J Clin Oncol. 2012;30:1378-1383.

Materstvedt LJ, Bosshard G. Deep and continuous palliative sedation (terminal sedation): clinical-ethical and philosophical aspects. Lancet Oncol. 2009;10:622-7.

Menten J. Cancer pain: interdisciplinary and comprehensive management (Dissertation). Acco: Catholic University Leuven, 2003.

Morita T, Chinone Y, Ikenaga M, et al. Ethical validity of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized care units in Japan. J Pain Symptom Manage. 2005b;30:308-319.

Morita T, Ikenaga M, Adachi I, et al. Concerns of family members of patients receiving palliative sedation therapy. Support Care Cancer. 2004a;12:885-889.

Morita T, Ikenaga M, Adachi I, et al. Family experience with palliative sedation therapy for terminally ill cancer patients. J Pain Symptom Manage. 2004b;28:557-565.

Morita T, Inoue S, Chihara S. Sedation for symptom control in Japan: the importance of intermittent use and communication with family members. J Pain Symptom Manage. 1996;12:32-38.

Morita T, Tsunoda J, Inoue S, Chihara S. Do hospice clinicians sedate patients intending to hasten Death? J Palliat Care. 1999;15:20-23.

Morita T. Differences in physician-reported practice in palliative sedation therapy. Support Care Cancer. 2004a;12:584-592.

Morita T. Palliative sedation to relieve psycho-existential suffering of terminally ill cancer patients. J Pain Symptom Manage. 2004b;28:445-450.

Müller-Bush HC, Andres I, Jehser T. Sedation in Palliative Care: a critical analysis of 7 years' experience. BMC. 2003;2:2.

Olsen ML, Swetz KM, Mueller PS. Ethical decision making with end-of-life care: palliative sedation and withholding or withdrawing life-sustaining treatments. Mayo Clin Proc. 2010;85:949-54.

Oosten AW, Oldenmenger WH, van Zuylen C, Schmitz PI, Bannink M, Lieverse PJ, Bromberg JE, van der Rijt CC. Higher doses of opioids in patients who need palliative sedation prior to death: cause or consequence? Eur J Cancer. 2011;47:2341-6.

Peruselli C, Di Giulio P, Toscani F, et al. Home palliative care for terminal cancer patients: a survey on the final week of life. Palliat Med. 1999;13:233-241.

Porta Sales J. Palliative sedation. Clinical Aspects. In: Gastmans C, editor. Between Techonolgy and Humanity. Leuven: University Press Leuven, 2002:219-237.

Quill TE, Byock IR. Responding to intractable terminal suffering: the role of terminal sedation and voluntary refusal of food and fluids. Ann Intern Med. 2000;132:408-414.

Quill TE, Lo B, Brock DW, Meisel A. Last-resort options for palliative sedation. Annals of Internal Medicine 2009;151:421-424.

Quill TE, Lo B, Brock DW. Palliative options of last resort. A comparison of voluntary stopping eating and drinking, terminal sedation, physician-assisted suicide and voluntary active euthanasia. JAMA. 1997;278:2099-2104.

Reuzel RPB, Hasselaar GJ, Vissers KCP, van der Wilt GJ, Groenewoud JMM, Crul BJP. Inappropriateness of using opioids for end-stage palliative sedation: a Dutch study. Palliat Med. 2008;22:641-646.

Rhodes VA, Watson PM. Symptom Distress, the concept: past and present. Seminars in Oncology 1987; 3:242-247.

Rietjens JA, Buiting HM, Pasman HR, van der Maas PJ, van Delden JJ, van der Heide A. Deciding about continuous deep sedation: physicians' perspectives: a focus group study. Palliat Med. 2009;23:410-7.

Rietjens JA, van Zuylen L, van Veluw H, van der Wijk L, van der Heide A, van der Rijt CC. Palliative sedation in a specialized unit for acute palliative care in a cancer hospital: comparing patients dying with and without palliative sedation.J Pain Symptom Manage. 2008 Sep;36(3):228-34.

Rietjens JAC, van Delden JM, van der Heide A et al. Terminal sedation and euthanasia. A comparison of clinical practices. Arch Intern Med. 2006;166:749-753.

Rietjens JAC, van der Heide A, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. The practice of terminal sedation in the Netherlands. Ned Tijdschr Geneeskd. 2005;149:467-471.

Rietjens JAC, van der Heide A, Vrakking AM, Onwuteaka-Philipsen B, van der Maas PJ, van der Wal G. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med. 2004;141:178-185.

Rietjens JAC, Hauser J, van der Heide A, Emanuel L. Having a difficult time leaving: experiences and attitudes of nurses with palliative sedation. Palliat Med. 2007;21:643-649.

Rousseau P. The ethical validity and clinical experience of palliative sedation. Mayo Clin Proc 2000;75:1064-1069.

Rousseau P. The ethics of palliative sedation. Caring 2004;23:14-19.

Rousseau P. The ethics of palliative sedation. Caring 2004;23:14-19.

Royal Dutch Medical Association (KNMG) (2005). Guideline Palliative Sedation. Utrecht, The Netherlands.

Salacz ME, Weismann DE. Controlled sedation for refractory suffering: part I and II. J Palliat Med. 2005;8:136-137.

Seymour JE, Janssens R, Broeckaert B. Relieving suffering at the end of life: practitioners' perspectives on palliative sedation from three European countries. Soc Sci Med. 2007;64:1679-91.

Stone P, Phillips C, Spruyt O, Waight C. A comparison of the use of sedatives in a hospital support team and in a hospice. Palliat Med. 1997;11:140-144.

Tännsjö T. Terminal sedation or voluntary euthanasia? Bull Med Ethics. 2000; November:13-22.

Taylor RM. Is terminal sedation really euthanasia? Med. Ethics. 2003;10:3-8.

Valko NG. Should sedation be terminal? Nat. Cathol Bioeth. Q. 2002;2:601-608.

van Delden JJ. Terminal sedation: source of a restless ethical debate. J Med Ethics. 2007;33:187-8.

Venke Gran S & Miller J. Norwegian nurses' thoughts and feelings regarding the ethics of palliative sedation. Int J Palliat Nurs. 2008;14:532-538.

Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care 1990; 6:7-11.

Vermylen J, Schotsmans P.(2000) Ethiek in de Kliniek: 25 jaar adviezen van de Commissie Medische Ethiek, Faculteit Geneeskunde, KU Leuven, University Press.

Vissers KC, Hasselaar J, Verhagen SA. Sedation in Palliative Care. Current Opinions in Anesthesiology 2007;20:137-142.

Wein S. Sedation in the Imminently Dying Patient. Oncology 2002;14:582-592

ABSTRACT

Context: Palliative sedation remains a much debated and controversial issue. The limited literature on the topic often fails to answer ethical questions concerning this practice.

Objectives: The aim of this study was to describe the characteristics of terminally ill patients who are being sedated for refractory symptoms in palliative care units (PCUs) from the time of admission until the day of death.

Methods: A prospective, longitudinal, descriptive design was used to assess data in 8 PCUs. The total sample consisted of 266 patients. Information on demographics, medication, food and fluid intake, decision making, level of consciousness, and symptom experience were gathered by nurses and researchers three times a week. If patients received palliative sedation, extra information was gathered.

Results: Of all included patients (n=266), 7.5 % received palliative sedation. Sedation started on average, 2.5 days before death and for half of these patients the form of sedation changed over time. At the start of sedation, patients were on, the end stage of their illness and needed total care. Patients were fully conscious and have very limited oral food and fluid intake. Only three patients received artificial fluids at the start of sedation. Patients reported, on average, two refractory symptoms, the most important ones being pain, fatigue, depression, drowsiness, and loss of feeling of well-being. In all cases, the patient gave consent to start palliative sedation because of increased suffering.

APPENDIX 1: RESEARCH PROTOCOL

ONDERZOEKSPROTOCOL : SYMPTOOMPREVALENTIE EN SYMPTOOMBEHANDELING BIJ PATIËNTEN DIE VERBLIJVEN OP EEN PALLIATIEVE EENHEID. WAT IS DE ROL VAN SEDATIE?

Onderzoekers: Patricia Claessens, MSN, RN, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Kristel Marquet, MSN, RN, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Promotoren: Prof. P. Schotsmans, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Co-promotoren: Prof. B. Broeckaert, Interdisciplinair Centrum voor Religiestudie, K.U.Leuven

Prof. Dr. J. Menten, Palliatieve eenheid, Oncologie-Radiotherapie Universitaire Ziekenhuizen Leuven

Correspondentieadres: Patricia Claessens
Centrum voor Biomedische Ethiek en Recht
Kapucijnenvoer 35/3
3000 Leuven
Tel.: 016/33.29.22
Fax: 016/33.69.52
E-mail: patricia.claessens@med.kuleuven.ac.be

PROBLEEMSTELLING

Essentieel in de palliatieve zorg is het bereiken van een aanvaardbare kwaliteit van leven voor iedere patiënt met een terminale, levensbedreigende ziekte en zijn familie. Om dit te realiseren is het belangrijk dat bij de patiënt alle hinderlijke fysieke, psychische, sociale en spirituele symptomen of problemen zoveel als mogelijk opgeheven worden (1;2). In de voorbije jaren is dan ook heel wat aandacht uitgegaan naar het adequaat bestrijden van symptomen bij patiënten met een levensbedreigende ziekte. Dit bracht een sterke positieve evolutie op het vlak van symptoomcontrole teweeg en dit voornamelijk wat betreft de behandeling van fysieke symptomen. Pijn bleek hierbij het best te behandelen symptoom (3).

Onderzoeken tonen aan dat de palliatieve zorg er grosso modo in slaagt symptomen adequaat te behandelen (4;5;6), maar kunnen tezelfdertijd niet ontkennen dat een aantal van deze symptomen alhoewel behandeld, toch oncontroleerbaar blijven (bij 20 % van de kankerpatiënten blijkt de pijn bijvoorbeeld niet volledig onder controle te brengen (6)). Het gaat hierbij dan niet uitsluitend om fysieke symptomen maar steeds meer en meer om spirituele, existentiële problemen (7). Deze oncontroleerbare symptomen worden ook *refractaire symptomen* genoemd en onderscheiden zich van *moeilijk te behandelen* symptomen omdat zij, ondanks het advies van verschillende klinische experten, niet behandeld kunnen worden zonder dat het bewustzijn van de patiënt wordt gecompromitteerd (7;8). In het omgaan met deze *refractaire symptomen*, die een belangrijk nadelig effect hebben op het functioneren en het welzijn van de patiënt en zijn omgeving (8;9) en vaak toenemen in intensiteit naarmate de patiënt dichter bij de dood komt (10), wordt gedurende de laatste decennia steeds vaker *sedatie* als laatste therapeutische mogelijkheid naar voren geschoven (11). Euthanasie is in België sinds 2002 een ander wettelijk toegelaten alternatief voor patiënten die uitzichtloos lijden.

Toch blijft deze vorm van sedatie een veelbesproken en omstreden onderwerp binnen en buiten de palliatieve zorg en roept hij bij velen niet te verwaarlozen ethische vragen op. Deze worden bovendien versterkt door de tegenstrijdigheden en onduidelijkheden in de onderzoeksresultaten van de verschillende retrospectieve studies die m.b.t. dit onderwerp gepubliceerd zijn (3;8;10-19). Naast een brede waaier aan mogelijke definities voor sedatie, is er ook een zeer grote spreiding wat betreft de frequentie van toepassing en de indicaties voor deze vorm van symptoombestrijding. Bovendien zijn de aangewende geneesmiddelen en doses sterk variabel van onderzoek tot onderzoek. Deze uiteenlopende bevindingen zijn voor een groot deel het gevolg van verschillende onderzoeksdesigns, variatie in settings, patientenpopulaties en hulpverlenende teams en een verschil in klinische praktijk

en opleiding. Het is dan ook dringend noodzakelijk ter zake meer duidelijkheid te scheppen, temeer omdat de vraag naar zorg voor patiënten met een levensbedreigende ziekte zal toenemen in de komende decennia ten gevolge van o.a. de veroudering van de bevolking en de daarmee samenhangende stijgende incidentie van kanker en andere chronische deteriorerende niet geneesbare aandoeningen (o.a. dementie, respiratoire en cardiale insufficiëntie) (2).

Er is met andere woorden nood aan systematisch en methodologisch correct onderzoek waarbij sedatie belicht wordt tegen de achtergrond van symptoomvoorkomen en symptoombehandeling, waarbij aan de hand van eenduidige kaders de praktijk met betrekking tot sedatie in kaart wordt gebracht en waarbij wordt nagegaan hoe en wanneer deze behandeling kan aangewend worden bij patiënten die lijden aan een terminale aandoening.

METHODOLOGIE

DOELSTELLINGEN VAN HET ONDERZOEK

Dit onderzoek beoogt een beschrijving te geven van de patiënten zoals deze in diverse Vlaamse palliatieve zorgeenheden verblijven in termen van functionele toestand, symptoomvoorkomen en -intensiteit, symptoomongemak, bewustzijnsniveau, voedsel- en vochttoediening, medicatiegebruik en demografische variabelen. Extra aandacht zal hierbij uitgaan naar het beschrijven van de praktijk van sedatie, zoals deze de dag van vandaag voorkomt op de palliatieve eenheden in Vlaanderen. Er zal getracht worden een antwoord te formuleren op volgende onderzoeksvragen:

1. Wat is het profiel van een patiënt die op een palliatieve zorgeenheid verblijft in termen van demografische variabelen, functionele toestand, bewustzijnstoestand en voedsel- en vochttoediening bij opname en doorheen het verblijf?
2. Wat is het profiel van een patiënt die op een palliatieve zorgeenheid verblijft in termen van symptoomvoorkomen en symptoomongemak?
3. Wat is de ernst, frequentie en mate van ongemak van de symptomen die als refractair kunnen worden bestempeld en aanleiding geven tot het starten van sedatie?
4. Bij hoeveel van de terminale patiënten op een palliatieve eenheid wordt sedatie toegepast?
5. In welke mate verschillen patiënten die palliatieve sedatie ontvangen van deze patiënten die geen sedatie ontvangen op basis van:

a. demografische gegevens
b. functionele status bij opname en doorheen het verblijf
c. symptoomprofiel bij opname en doorheen het verblijf
d. bewustzijnsniveau bij opname en doorheen het verblijf
e. medicatiegebruik bij opname en doorheen het verblijf
f. voedsel- en vochtinname bij opname en doorheen het verblijf

6. Welke medicatie wordt aangewend om sedatie te realiseren?
7. Welke medicatie ontvangt een patiënt op een palliatieve eenheid?
8. Welke soort sedatie (intermittent of continu, mild of diep,…) wordt aangewend en waarom?
9. In welke mate krijgt de patiënt voedsel en/of vocht tijdens de sedatie en waarom? Hoe verhoudt dit zich tot situatie vóór de sedatie?

CONCEPTUEEL RAAMWERK

SYMPTOOMVOORKOMEN EN SYMPTOOMONGEMAK

Palliatieve zorg wordt door de Wereld Gezondheidsorganisatie (WHO) gedefinieerd als:

> *Een zorgbenadering die de kwaliteit van leven van de patiënt en zijn familie, die geconfronteerd worden met problemen gelinkt aan een levensbedreigende ziekte, verbetert door preventie en behandelen van lijden en dit door vroegtijdige vaststelling, accuraat beoordelen en behandelen van pijn en andere problemen, zowel fysiek, psychosociaal als spiritueel (WHO, 2002).*

Aan de hand van deze definitie wordt duidelijk dat symptoomcontrole een cruciale doelstelling is van palliatieve zorg teneinde de kwaliteit van leven van de palliatieve patiënt te verbeteren. Om een goede symptoomcontrole te kunnen uitvoeren, moeten artsen en verpleegkundigen dan ook zicht hebben op de symptomen die zich bij de patiënten manifesteren.

Symptomen worden beschreven als zijnde subjectieve indicatoren van een ziekte of van een wijziging in de gezondheidstoestand (20). Volgens Rhodes & Watson (1987) zijn symptomen individuele ervaringen, vaststellingen van iedere patiënt die als het ware een veruitwendiging vormen van het probleem dat zich stelt. Het ervaren van symptomen wordt in de literatuur vaak voorgesteld aan de hand van twee aparte componenten, namelijk symptoomvoorkomen en symptoomongemak (20). *Symptoomvoorkomen* wordt hierbij gedefinieerd als de frequentie, duur en intensiteit waarmee een symptoom zich voordoet (20). *Symptoomongemak* wordt beschreven als de mate van fysieke of

mentale last die een patiënt rapporteert ten gevolge van een symptoom. Symptoomongemak is als het ware de menselijke reactie op symptoomvoorkomen. Ondanks de link die reeds meermaals aangetoond is tussen symptoomvoorkomen en -ongemak (20;21) wordt in de literatuur meestal slechts één van beide componenten beschreven. Theoretische modellen zoals de 'theory of self-regulation' van Leventhal en Johnson (1983) benadrukken en verklaren echter dat om een accuraat beeld te krijgen van de symptoomervaring zicht op beide aspecten noodzakelijk is. Daarom worden in deze studie zowel het symptoomvoorkomen (in termen van intensiteit) als het symptoomongemak in kaart gebracht. Dit zal toelaten een zo accuraat mogelijk beeld te krijgen van de symptoomervaring van patiënten op een palliatieve eenheid.

SEDATIE IN DE PALLIATIEVE ZORG

Wanneer artsen sederende medicatie toedienen om een refractair of onbehandelbaar symptoom onder controle te brengen wordt dit in de praktijk en in de literatuur heel divers benoemt. Enck (1991) spreekt over 'terminal sedation', anderen over gecontroleerde sedatie (22) en nog anderen over palliatieve sedatie (23;24). Duidelijk is dat er noch qua terminologie, noch qua definiëring duidelijkheid bestaat in de nationale en internationale literatuur. Dit heeft tot gevolg dat er geen algemeen aanvaardbare definitie bestaat omtrent sedatie die hier als standaard naar voren geschoven kan worden. Vandaar dat, om een realiteitsgetrouw beeld te krijgen van de huidige praktijk omtrent het gebruik van sedatie in de palliatieve zorg, het aangewezen is geen definitie van sedatie op te leggen aan de verschillende palliatieve eenheden. Dit zou immers leiden tot een te strenge afbakening van de studie waardoor een groot deel van de huidige praktijk niet in kaart wordt gebracht, afbreuk wordt gedaan aan het algemeen beschrijvend karakter van dit onderzoek en de vooropgestelde doelstellingen niet worden bereikt.

DESIGN

Er wordt gekozen voor een prospectieve, longitudinale, comparatieve en beschrijvende studie. Deze studie zal de evoluties van palliatieve patiënten, op Vlaamse palliatieve eenheden, beschrijven met betrekking tot de bevraagde variabelen. Het profiel van niet-gesedeerde patiënten zal vergeleken worden met het profiel van gesedeerde patiënten. Mogelijke verschillen in de evoluties op vlak van symptoomongemak, symptoomintensiteit, bewustzijnsniveau, voedsel- en vochttoediening, medicatiegebruik en functionele status worden beschreven.

SETTING EN STEEKPROEF

Deze studie zal doorgaan op Vlaamse palliatieve eenheden die bereid zijn om aan deze studie deel te nemen. Alle palliatieve eenheden, die wensen deel te nemen en waar een positief advies van de Commissie Medische Ethiek is verkregen, worden in de steekproef opgenomen. Data worden verzameld bij de eerste 50 patiënten (gelegenheidssteekproef) die zich op iedere deelnemende afdeling aanbieden, die voldoen aan de inclusiecriteria en die bereid zijn om, op basis van een informed consent, deel te nemen aan de studie. Volgende inclusiecriteria worden voor deze studie opgesteld:

- Patiënten zijn 18 jaar of ouder
- Patiënten hebben een oncologische aandoening
- Patiënten hebben een levensverwachting van minder dan 3 maanden

GEGEVENSVERZAMELING

Na een grondige literatuurstudie en overleg met artsen en verpleegkundigen werkzaam in de palliatieve zorg, is een lijst van in kaart te brengen variabelen opgesteld. Een overzicht van de variabelen, bijhorend meetinstrument, betrouwbaarheid en validiteit van de meetinstrumenten, wie de variabele registreert en de frequentie waarop deze variabele in kaart worden gebracht, vindt u in tabel 1 tot en met 3.

Ondanks het feit dat voor variabelen als symptoomvoorkomen en symptoomongemak de patiënt als ‘gouden standaard’ wordt vermeld in de literatuur (25; 26), blijkt uit een pilootstudie (De Blaeser, in press) dat dit in het kader van dit onderzoeksproject om verschillende redenen onmogelijk is. De pilootstudie toont namelijk aan dat het merendeel van de patiënten opgenomen op een palliatieve eenheid niet in staat is geheel zelfstandig deze vragenlijst in te vullen. De verpleegkundige moet dan ook, om toch een patiëntenscore te verkrijgen, de patiënt helpen bij het invullen van de vragenlijst. Gemiddeld neemt dit echter 15 à 20 minuten per patiënt in beslag. Wanneer een verpleegkundige dit voor elke patiënt moet doen, besteedt zij gedurende één shift 1.5 à 2 uur tijd aan het louter registreren van symptoomvoorkomen, -intensiteit en symptoomongemak. Gezien de verpleegkundige op die manier duidelijk minder tijd ter beschikking heeft voor de directe patiëntenzorg is dit praktisch niet haalbaar en ethisch niet te verantwoorden, temeer omdat het hier gaat om een longitudinale studie waarbij drie maal per week data dienen te worden geregistreerd. Bovendien is het risico groot dat er een grote uitval zal zijn op lange termijn gezien de patiënt op het einde van het leven niet meer in staat zal zijn zelfstandig te scoren. Daarom wordt ervoor geopteerd om symptoomvoorkomen en

symptoomongemak door de verpleegkundigen te laten scoren waarbij zij zich baseren op hun observaties.

De verpleegkundigen zullen bij opname en vervolgens telkens op maandag, woensdag en vrijdag gegevens verzamelen omtrent symptoomvoorkomen, symptoomongemak, bewustzijnsniveau en functionele status van de patiënt (cf. bijlage 1 en tabel 1). Van alle verpleegkundigen werkzaam op de afdeling worden een aantal demografische variabelen geregistreerd (geslacht, leeftijd, ervaring, ...). Iedere verpleegkundige krijgt bovendien een code die zij telkens op de registratieformulieren vermeld. OP die manier hoeft de verpleegkundige slechts éénmalig de demografische gegevens in te vullen en kan de onderzoeker, via deze code, de registratieformulieren linken aan de verpleegkundige die ze ingevuld heeft. De gemiddelde tijdsinvestering van de volledige dataregistratie wordt geschat op een achttal minuten per patiënt.

Tabel 1: Variabelen te registreren door de verpleegkundige bij opname en daarna telkens op maandag, woensdag en vrijdag

Naam variabele		**Meetinstrument**	**Frequentie dataverza-meling**	**Validiteit en Betrouw-baarheid**	**Tijd voor registratie**
Functionele status	Mobiliteit Activiteit en bewijs van ziekte Zelfzorg Voedsel- en vochtinname Bewustzijns-niveau	Palliative Performance Scale	Bij opname en vervolgens 3 maal per week	Getest in VS	1 min.
Symptomen	Symptoom Voorkomen, -intensiteit	Aangepaste Edmonton Symptom Assessment Scale	Bij opname en vervolgens 3 maal per week	Getest in Canada, UK, België	4 à 10 min.
	Symptoom ongemak	Aangepaste Edmonton Symptom Assessment Scale	Bij opname en vervolgens 3 maal per week	Getest in Canada, UK en België	
Bewustzijns-niveau	Openen ogen Verbale reactie Motorische reactie	Glasgow Coma Schaal	Bij opname en vervolgens 3 maal per week	Getest in VS	2 min.

* NVT = niet van toepassing

Naast de verpleegkundige zal ook de onderzoeker, op de verschillende palliatieve zorgeenheden zelf, een aantal variabelen scoren (cf. tabel 2 en bijlage 2). Het gaat hier voornamelijk omtrent informatie die terug te vinden is in het verpleegkundig of medisch dossier. Eénmaal per week komt de onderzoeker op iedere afdeling en verzamelt demografische gegevens van de patiënt en gegevens (inclusief eventuele wijzigingen) betreffende het medicatiegebruik en de parenterale toediening van

voeding en vocht. Hij zorgt ervoor dat er voldoende registratieformulieren beschikbaar zijn tot aan het volgend bezoek.

Tabel 2: Variabelen te registreren door de onderzoeker bij opname en daarna op maandag, woensdag en vrijdag

Naam variabele		**Meetinstrument**	**Frequentie dataverza-meling**	**Validiteit en Betrouwbaar-heid**	**Tijd voor registratie**
Patiënten kenmerken	Geslacht	VK dossier	Bij opname	NVT*	5 min.
	Leeftijd	VK dossier	Bij opname	NVT	
	Nationaliteit	VK dossier	Bij opname	NVT	
	Burgerlijke stand	VK dossier	Bij opname	NVT	
	Diagnose	VK dossier	Bij opname	NVT	
	Levensbeschou-wing	VK dossier	Bij opname	NVT	
	Opnamedatum	VK dossier	Bij opname	NVT	
	Datum ontslag	VK dossier	Bij ontslag	NVT	
	Datum overlijden	VK dossier	Bij overlijden	NVT	
Voedsel- en vochtinname	Per os	Registratieformulier opgesteld door onderzoeker	Bij opname en vervolgens drie maal per week	NVT	1 min.
	Parenteraal	Registratieformulier opgesteld door onderzoeker	Bij opname en vervolgens drie maal per week	NVT	5 min.
Medicatiegebruik	Soort medicatie	Verpleegkundig dossier	Bij opname en vervolgens drie maal per week	NVT	15 min.
	Dosis per 24 uur	Verpleegkundig dossier	Bij opname en vervolgens drie maal per week	NVT	
	Wijzigingen in medicatie	Verpleegkundig dossier	Bij opname en vervolgens drie maal per week	NVT	
	Reden van wijziging	Verpleegkundig dossier en bevraging arts en/of verpleegkundige	Bij opname en vervolgens drie maal per week	NVT	

*NVT = niet van toepassing

Wanneer zich op de afdeling een situatie voordoet waarbij een patiënt aangeeft dat hij ondraaglijk lijdt en hiervoor sedatie of euthanasie ontvangt, dan zal de verpleegkundige hieromtrent een aantal extra gegevens verzamelen (cf. tabel 3).

Tabel 3: Variabelen te registreren door de verpleegkundige wanneer de patiënt sedatie of euthanasie ontvangt

Naam variabele		**Meetinstrument**	**Frequentie dataverzameling**	**Validiteit en Betrouwbaar-heid**	**Tijd voor registratie**
Ondraaglijk lijden	Dag van vaststelling	Registratieformulier sedatie	Eénmalig	NVT*	2 min.
	Hulpverlener die de vraag te horen kreeg	Registratieformulier sedatie	Eénmalig	NVT	
	Persoon die de vraag stelde	Registratieformulier sedatie	Eénmalig	NVT	
Sedatie	Symptomen aanwezig vóór sedatie	Aangepaste ESAS	Eénmalig	NVT	5 min.
	Symptomen die sedatie noodzaken	Aangepaste ESAS	Eénmalig	NVT	
	Duur sedatie	Registratieformulier sedatie	Dagelijks	NVT	5 min.
	Soort sedatie	Registratieformulier sedatie	Dagelijks	NVT	
	Medicatie aangewend om sedatie te induceren	Verpleegkundig dossier	Dagelijks	NVT	
	Besluitvorming	Registratieformulier sedatie	Eénmalig	NVT	
Euthanasie	Symptomen aanwezig vóór de euthanasie	Registratieformulier sedatie	Eénmalig	NVT	5 min.
	Symptomen die euthanasie noodzaken	Registratieformulier sedatie	Eénmalig	NVT	

*NVT = niet van toepassing

Afhankelijk van het totaal aantal patiënten dat op jaarbasis opgenomen wordt op de palliatieve eenheden, zal de duur van de dataverzameling variëren van 4 (aantal opnames op jaarbasis = 180) tot 8 maanden (aantal opnames op jaarbasis = 75), dit op voorwaarde dat iedere patiënt, die in aanmerking komt voor inclusie en akkoord gaat met deelname aan het onderzoek, ook effectief geïncludeerd wordt.

INSTRUMENTARIUM

Doorheen de studie zal gebruik gemaakt worden van 3 reeds bestaande meetinstrumenten namelijk, de **Aangepaste Edmonton Symptom Assessment Scale** (symptoomvoorkomen en symptoomongemak) (26) (De Blaeser, in press), de **Palliative Performance Scale** (functionele status) (27) en de **Glasgow Coma Scale** (bewustzijnsniveau) (28).

De **Edmonton Symptom Assessment Scale** (ESAS) is een vragenlijst die ontwikkeld werd door Bruera et al. (1991). Deze vragenlijst bestaat uit negen Visueel Analoge Schalen (VAS) voor pijn,

misselijkheid, depressie, angst, slaperigheid, eetlust, kortademigheid en een gevoel van welzijn. Daar bovenop is er nog een tiende VAS-schaal die niet benoemd is en zo de kans geeft een bepaald symptoom, dat minder frequent voorkomt maar toch belangrijk is voor deze specifieke patiënt, eveneens in kaart te brengen. Deze schaal is specifiek ontwikkeld voor het in kaart brengen van symptoomvoorkomen en symptoomintensiteit bij patiënten die terminaal ziek zijn en palliatief verzorgd worden .

In eerste instante is de ESAS een zelfrapportage instrument dat dagelijks door de patiënt ingevuld wordt. De gezondheidstoestand van de patiënten op een palliatieve eenheid laat dit echter niet altijd toe. Dit instrument kan dan ook door of met behulp van een familielid of een hulpverlener ingevuld worden. Validatie van de ESAS werd uitgevoerd door Chang et al. (2000). Cronbach alpha bereikte 0.79 in de onderzochte populatie. Er bestond bovendien een statistisch significante correlatie tussen de ESAS en de Karnofsky Performance status ($p<0.001$) en de concurrent en criterium validiteit werden voor verschillende items aangetoond (29).

In het kader van dit onderzoek wordt de ESAS vertaald naar het Nederlands. Een back to back translation, evenals een validatiestudie van de Nederlandse vragenlijst werden uitgevoerd. Op basis van deze validatiestudie werd een **Aangepaste Edmonton Symptom Assessment Scale** ontwikkeld (De Blaeser, in press). Deze bestaat uit de 13 Visueel Analoge Schalen (VAS) waarvan er 12 een specifiek symptoom (pijn, vermoeidheid, misselijkheid, neerslachtige stemming, angst, slaperigheid, eetlust, algemeen ongelukkig gevoel, kortademigheid, constipatie, droge mond, gestoorde slaap) bevragen naar symptoomvoorkomen en intensiteit en 1 VAS de mogelijkheid laat een niet vernoemd maar wel aanwezig symptoom te scoren (cf. bijlage 1). Naast 13 Visueel Analoge Schalen voor symptoomvoorkomen en –intensiteit werden er nog 13 VAS toegevoegd om ook het symptoomongemak van de patiënt in kaart te brengen (cf. infra). Deze schaal zal ingevuld worden door de verpleegkundige bij opname en nadien telkens op maandag, woensdag en vrijdag.

Een tweede vragenlijst die voor dit onderzoek wordt aangewend, is de **Palliative Performance Scale** (PPS) (27). Ook dit instrument is specifiek ontwikkeld voor de palliatieve zorg en heeft als doel een zicht te krijgen op de functionele status van de patiënt. Deze vragenlijst is afgeleid van de Karnofsky Performance Scale (30). De functionele status is onderverdeeld in 11 niveaus die per 10% afnemen (0% - 100%). Om te bepalen tot welk niveau de patiënt behoort, wordt gebruik gemaakt van vijf observeerbare parameters: mobiliteit, mogelijkheid om activiteiten uit te voeren/de graad van de ziekte, mogelijkheid tot zelfzorg, voedsel- en vochtinname en de mate van bewustzijn. De status van

een specifieke patiënt wordt bepaald door horizontaal door de tabel te lezen, waarbij de linkse kolommen zwaarder doorwegen dan de zich meer rechts bevindende kolommen.

Deze vragenlijst zal afgenomen worden bij opname en daarna op maandag, woensdag en vrijdag. Dit laat toe een onderscheid te maken tussen de patiënten op basis van hun functionele status en geeft een beeld van de evolutie van deze functionele status. Het instrument wordt gescoord door de verpleegkundige.

Gegevens omtrent de validiteit en betrouwbaarheid zijn slechts in beperkte mate beschikbaar (31;32). Morita et al. (1999) vond in zijn studie een significante correlatie tussen de PPS en de Karnofsky Performance Scale (Spearman's $\rho = 0.94$). Bovendien blijkt de PPS goed in overeenstemming met overlevingsprofielen van de patiënten (31;32). Ook deze vragenlijst is vertaald naar het Nederlands en heeft een back to back translation ondergaan.

Een derde instrument dat aangewend wordt, is de **Glasgow Coma Scale (GCS)** (28). Dit instrument is in 1974 ontwikkeld door Teasdale & Jennett (1974) en heeft als doel het in kaart brengen van een verminderd bewustzijn. De auteurs streefden naar het ontwikkelen van een instrument dat eenvoudig in gebruik is voor verschillende ziekenhuizen, diensten en dat bovendien geen extra opleiding vraagt (28). Aangezien de mate van bewustzijn fluctueert over een continuüm (volledig bewustzijn versus coma), lijkt het de auteurs dan ook niet opportuun om deze twee begrippen te definiëren als twee compleet van elkaar gescheiden concepten. Zij kiezen er voor om de verschillende wijzen waarop een verminderd bewustzijn zich manifesteert in de praktijk te beschrijven en maken hierbij gebruik van drie gedragsmatige reacties, namelijk motorische reactie, verbale reactie en het al of niet openen van de ogen (28). Ieder onderdeel wordt hierbij onafhankelijk van de andere gescoord. De scores zijn gebaseerd op duidelijk gedefinieerde responsen die individueel gescoord worden aan de hand van een rangorde die de mate van dysfunctioneren aangeeft. Eens de drie verschillende reacties in kaart zijn gebracht kan er een totaalscore opgemaakt worden. Naargelang de score wordt de patiënt toegekend aan één van de drie groepen: niveau 1 (score 3-8), niveau 2 (score 9-12) en niveau 3 (score 13-15). Hoe lager de score, hoe lager het bewustzijn van de patiënt is.

De GCS is een veel gebruikt instrument bij het in kaart brengen van het bewustzijn van patiënten. Verschillende onderzoekers hebben dan ook het instrument getest op betrouwbaarheid en validiteit (33;34;35). De interbeoordelaarsbetrouwbaarheid (Pearson's $r = 0.95$, Cohen's Kappa varieert tussen 0.54 en 0.82), de stabiliteit (Spearman's rho = 0.85, $p<0.001$) evenals de Cronbach's alpha (0.69, 0.83-0.87) worden goed bevonden. Wat betreft de validiteit wordt een Pearson's $r = 0.68$ gevonden ($p<0.001$), wat wijst op een goede constructvaliditeit.

De GCS wordt gescoord door de verpleegkundige bij opname en nadien op maandag, woensdag en vrijdag. Dit laat toe de evolutie van het bewustzijn van de patiënt te volgen. Eventuele gelijkenissen of verschillen tussen patiënten die niet gesedeerd en patiënten die wel gesedeerd worden, kunnen aan de hand van dit profiel in kaart gebracht worden.

ANALYSE

Na het controleren van de verdeling van alle data (normaal verdeeld of niet) wordt descriptieve statistiek uitgevoerd. De evoluties van de verschillende parameters zullen in kaart gebracht worden. Afhankelijk van het type meting, zal voornamelijk gewerkt worden met betrouwbaarheidsintervallen. Vergelijkingen tussen normaal verdeelde data, niet-normaal verdeelde continue of ordinale variabelen en nominale en dichotome variabelen gebeuren aan de hand van de daarvoor ontwikkelde testen. Bovendien zullen vergelijkingen gemaakt worden tussen verschillende groepen binnen de populatie. Dit zal toelaten eventuele significante verschillen op te sporen en aan te tonen. Het statistisch significantieniveau wordt gezet op $p<0.05$.

PROCEDURE

De onderzoeker zal alle hoofdverpleegkundigen en hun directie verpleegkunde van de palliatieve eenheden in Vlaanderen aanschrijven. Naast een begeleidende brief zal ook het onderzoeksprotocol aan de desbetreffende personen bezorgd worden. De palliatieve eenheden kunnen aan de hand van een antwoordformulier, dat teruggestuurd wordt aan de onderzoeker, laten weten of zij al dan niet geïnteresseerd zijn om deel te nemen aan de studie. Wanneer bepaalde eenheden niet wensen deel te nemen, zal de onderzoeker trachten te achterhalen waarom dit zo is, zodanig dat deze gegevens kunnen meegenomen worden in de latere analyse en bespreking. Eens de antwoordformulieren in het bezit van de onderzoeker zijn, zal een informatievergadering gepland worden, waar alle geïnteresseerden worden voor uitgenodigd. Hier zal verdere informatie verstrekt worden over het onderzoek en zal de ruimte gelaten worden aan de aanwezigen om kritisch te reflecteren omtrent het voorstel. Bemerkingen worden bestudeerd en waar mogelijk mee opgenomen in het onderzoeksvoorstel. Het herwerkte document wordt opnieuw naar de geïnteresseerde ziekenhuizen gestuurd. De ziekenhuizen kunnen dan hun definitieve beslissing via mail meedelen aan de onderzoekers. Eens geweten is welke palliatieve eenheden deelnemen aan de studie, kan de opleiding voor de verpleegkundigen van start gaan. De onderzoekers nemen hiervoor contact op met de afdeling en bepalen twee momenten waarop dit zal plaats vinden. Alle verpleegkundigen (in twee groepen) zullen gedurende 1.5 à 2 uur informatie krijgen omtrent het afnemen van de vragenlijsten en het verzamelen van de gegevens. Extra aandacht wordt besteed aan het afnemen van het informed consent. Een aantal verpleegkundigen wordt, op vrijwillige basis, aangesteld als referentieverpleegkundige en

vormt de contactpersoon tussen de afdeling en de onderzoekers. Eens deze opleiding achter de rug is, kan gestart worden met de eigenlijke dataverzameling.

Telkens een patiënt zich aanmeldt op de eenheid, zal de verpleegkundige nagaan of de patiënt voldoet aan de inclusiecriteria (cf. infra). Wanneer dit het geval is, zal de verpleegkundige tijdens het opnamegesprek een informed consent aan de patiënt en/of zijn familie vragen (cf. bijlage 4). Wanneer de patiënt en/of zijn familie bereid zijn deel te nemen aan de studie, zal de verpleegkundige bij opname en nadien telkens op maandag woensdag en vrijdag gegevens verzamelen op basis van haar observaties (cf. tabel 1). Deze worden geregistreerd in het daartoe bestemde registratieformulier (cf. bijlage 1) op de wijze die reeds eerder werd beschreven (cf. infra). De dataverzameling loopt door tot de patiënt ontslagen wordt of overlijdt. Patiënten die weigeren deel te nemen aan de studie zullen gevraagd worden naar hun beweegredenen, teneinde de uitval te kunnen beschrijven. Van die patiënten die ontslagen worden, zal genoteerd worden naar waar deze ontslagen worden. Wanneer mogelijk zal ook de datum en plaats van overlijden geregistreerd worden. Eens het aantal patiënten per afdeling bereikt is, zal de dataverzameling stopgezet worden. Alle afdelingen zullen naast de geanonimiseerde algemene resultaten ook de volledige gegevens ontvangen m.b.t. hun eigen afdeling.

ETHISCHE AANDACHTSPUNTEN

INFORMED CONSENT

Alle patiënten zullen, afhankelijk van de fysieke en psychische toestand, bij opname een informed consent formulier ontvangen. Dit document zal de patiënt inlichtingen verschaffen omtrent zijn status in het onderzoek, de doelstelling van de studie, het soort data dat verzameld wordt, het soort engagement dat van de patiënt en zijn familie verwacht wordt, de procedures, de eventuele risico's en voordelen die aan het onderzoek verbonden zijn, en informatie omtrent de privacy, het recht om zich ten allen tijde terug te trekken en het recht op vrijwillige toestemming. De verpleegkundige zal dit document mondeling met de patiënt en zijn familie overlopen en de nodige toelichtingen geven bij de verschillende onderdelen van het consent formulier. Enkel wanneer de patiënt en/of zijn familie toestemmen in deelname, zal de dataverzameling starten.

ANONIMITEIT

Alle registratieformulieren worden voorzien van een code, die enkel door de onderzoeker zelf kan gelinkt worden aan de desbetreffende patiënt. Elke verwijzing die mogelijkerwijs de identiteit van de patiënt kan vrijgeven, zal uit de resultatenbeschrijving worden weggelaten. Ook de verwijzingen naar ziekenhuizen zal gebeuren aan de hand van een code. Enkel de ziekenhuizen zelf zullen in staat zijn

zich in de gerapporteerde data te herkennen. Het onderzoek zal, zoals de nieuwe privacywetgeving vereist, gerapporteerd worden aan de Commissie voor de Bescherming van de Persoonlijke Levenssfeer.

RAPPORTAGE VAN DE RESULTATEN EN PUBLICATIEREGELS

De resultaten van het onderzoek zullen beschikbaar worden gesteld aan iedere afdeling die deelgenomen heeft aan het onderzoek. Bovendien zal iedere afdeling de gedetailleerde gegevens van zijn eigen afdeling ontvangen zodanig dat zij hun gegevens kunnen situeren ten opzichte van deze van de andere (geanonimiseerde) afdelingen.

Bij de publicatie van de onderzoeksresultaten wordt de auteursgroep steeds als volgt vastgelegd:

namen onderzoekers + namen promotoren + “on behalf of the Palsed Consortium*”. Onderaan de eerste bladzijde wordt aangegeven wie tot het Palsed Consortium behoort. Worden telkens vermeld: naam arts & naam hoofdverpleegkundige, naam instituut (namen vermeld per instituut; instituten in alfabetische volgorde).

REFERENCE LIST

(1) World Health Organization. Palliative Care. 2003. Ref Type: Internet Communication

(2) Cannaerts N, Dierckx de Casterlé B, Grypdonck M. Palliatieve zorg: zorg voor het leven. Een onderzoek naar de specifieke bijdrage van residentiële palliatieve zorg. First ed. Leuven: Academia Press, 2000.

(3) Chater S, Viola R, Paterson J, Jarvis V. Sedation for Intractable Distress in the Dying-a Survey of Experts. Palliat Med 1998; 12(4):255-269.

(4) Vainio A, Auvinen A, Members of the Symptom Prevalence Group. Prevalence of Symptoms among Patients with Advanced Cancer: an International Collaborative Study. J Pain Symptom Manage 1996; 12(1):3-10.

(5) Zech DFJ, Grond S, Lynch J, Hertel D, Lehman KA. Validation of World Health Organization Guidelines for Cancer Pain Relief: a 10-year prospective study. Pain 1995; 63:65-76.

(6) Ahmedzai S. New Approaches to Pain Control in Patients with Cancer. European Journal of Cancer 1997; 33(Suppl 6):S8-S14.

(7) Cherny NI, Portenoy RK. Sedation in the Management of Refractory Symptoms: Guidelines for Evaluation and Treatment. J Palliat Care 1994; 10(2):31-38.

(8) Menten J. Cancer pain: Interdisciplinary and Comprehensive Management. Katholieke Universiteit Leuven, 2003.

(9) Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of Terminal Illness in the Advanced Cancer Patient: Pain and Other Symptoms During the Last Four Weeks of Life. J Pain Symptom Manage 1990; 5(2):83-93.

(10) Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom Prevalence and Control During Cancer Patients' Last Days of Life. J Palliat Care 1990; 6(3):7-11.

(11) Schotsmans P. Een discussie-advies omtrent gecontroleerde sedatie. Ethische perspectieven 1999; 9(1):29-34.

(12) Fainsinger R, Miller MJ, Bruera E, Hanson J, Maceachern T. Symptom Control During the Last Week of Life on a Palliative Care Unit. J Palliat Care 1991; 7(1):5-11.

(13) Fainsinger RL, Landman W, Hoskings M, Bruera E. Sedation for Uncontrolled Symptoms in a South African Hospice. J Pain Symptom Manage 1998; 16(3):145-152.

(14) Fainsinger RL. Use of Sedation by a Hospital Palliative Care Support Team. J Palliat Care 1998; 14(1):51-54.

(15) Fainsinger RL, Waller A, Bercovici M, Bengtson K, Landman W, Hosking M et al. A Multicentre International Study of Sedation for Uncontrolled Symptoms in Terminally Ill Patients. Palliat Med 2000; 14(4):257-265.

(16) Fainsinger RL, De Moissac D, Mancini I, Oneschuk D. Sedation for Delirium and Other Symptoms in Terminally Ill Patients in Edmonton. J Palliat Care 2000; 16(2):5-10.

(17) Peruselli C, Di Giulio P, Toscani F, Gallucci M, Brunelli C, Costantini M et al. Home Palliative Care for Terminal Cancer Patients: a Survey on the Final Week of Life. Palliat Med 1999; 13(3):233-241.

(18) Morita T, Tsunoda J, Inoue S, Chihara S. Do Hospice Clinicians Sedate Patients Intending to Hasten Death? J Palliat Care 1999; 15(3):20-23.

(19) Stone P, Phillips C, Spruyt O, Waight C. A Comparison of the Use of Sedatives in a Hospital Support Team and in a Hospice. Palliat Med 1997; 11(2):140-144.

(20) McDaniel RW, Rhodes VA. Symptom Experience. Seminars in Oncology Nursing 1995; 11(4):232-234.

(21) Rhodes VA, Watson PM. Symptom Distress - The Concept: Past and Present. Seminars in Oncology Nursing 1987; 3(4):242-247.

(22) Vermylen J, Schotsmans P. Adviezen in verband met het handelen van artsen bij het eindigende leven. Ethiek in de kliniek. Leuven: Universitaire pers, 2002: 87-114.

(23) Broeckaert B. Palliatieve sedatie. Palliatieve Zorg 2001; 2:3-5.

(24) Broeckaert B, Nunez-Olarte JM. Sedation in Palliative Care: Facts and Concepts. In: ten Have HAMJ, Clark D, editors. Ethics in palliative care. 2002.

(25) Nekolaichuk CL, Maguire TO, Suarez-Almazor M, Rogers T, Bruera E. Assessing the Reliability of Patient, Nurse and Family Caregiver Symptom Ratings in Hospitalized Advanced Cancer Patients. Journal of Clinical 0ncology 1999; 17(11):3621-3630.

(26) Bruera E, Kuehn N, Miller MJ, Selmser P, Mcmillan K. The Edmonton Symptom Assessment Scale. J Palliat Care 1991; 7(2):6-9.

(27) Anderson F, Downing GM, Hill J, Casorso L, Lerch N. Palliative Performance Scale: a New Tool. J Palliat Care 1996; 12(1):5-11.

(28) Teasdale G, Jennett B. Assessment of Coma and Impaired Consciousness. A Practical Scale. Lancet 1974; 2:81-84.

(29) Chang VT, Hwang SS, Fuerman M. Validation of the Edmonton Symptom Assessment Scale. Cancer 2000; 88(9):2164-2171.

(30) Karnofsky DA, Albelman WH, Craver LF, Burchenal JH. The Use of Nitrogen Mustards in the Palliative Treatment of Carcinoma. Cancer 1948; 1:634-656.

(31) Virik K, Glare P. Validation of the Palliative Performance Scale for Inpatients Admitted to a Palliative Care unit in Sydney, Australia. J Pain Symptom Manage 2002; 23(6):455-457.

(32) Morita T, Tsunoda J, Inoue S, CHihara S. Validity of the Palliative Performance Scale from a Survival Perspective. J Pain Symptom Manage 1999; 18(1):2-3.

(33) Braakman R, Avezaat CJJ, Mais AIR, Roel M, Schouten HJA. Inter-observer Agreement in the Assessment of the Motor Response of the Glasgow Coma Scale. Clin Neurol Neurosurg 1977; 80:100-106.

(34) Fielding K, Rowley G. Reliability of Assessments by Skilled Observers Using the Glasgow Coma Scale. Australian Journal of Advanced Nursing 1990; 7(4):13-17.

(35) Rowley G, Fielding K. Reliability and Accuracy of the Glasgow Coma Scale with Experienced and Inexperienced users. Lancet 1991; 337:535-538.

APPENDIX 2: MEASUREMENT INSTRUMENTS

Katholieke Universiteit Leuven

Departement Maatschappelijke Gezondheidszorg

Centrum voor Biomedische Ethiek & Recht

Symptoomprevalentie en symptoombehandeling bij patiënten die verblijven op een palliatieve eenheid. Wat is de rol van palliatieve sedatie?

Dataverzamelingsformulier

Onderzoekers: Patricia Claessens, MSN, RN, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Kristel Marquet, MSN, RN, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Promotor: Prof. P. Schotsmans, Centrum voor Biomedische Ethiek en Recht, K.U.Leuven

Co-promotoren: Prof. B. Broeckaert, Interdisciplinair Centrum voor Religiestudie, K.U.Leuven

Prof. J. Menten, Oncologie-Radiotherapie en Palliatieve Zorg, Universitaire Ziekenhuizen Leuven

DEEL 1: REGISTRATIEFORMULIER VERPLEEGKUNDIGEN

Volgende gegevens worden bij iedere patiënt door de verpleegkundige geregistreerd en dit **3 maal per week** namelijk op **maandag, woensdag** en **vrijdag**.

- Voedsel- en vochtinname
- Functionele toestand aan de hand van de Palliative Performance Scale (PPS)
- Bewustzijnstoestand aan de hand van de Glasgow Coma Scale (GCS)
- Symptoomvoorkomen en -ongemak aan de hand van de Aangepaste Edmonton Symptom Assessment Scale (A-ESAS)

Aandachtspunten bij de registratie:

- Zorg er voor dat ieder dossier voorzien is van uw **eigen code** (een V-code wordt u toegekend door de onderzoekers waarvan een lijst terug te vinden is op uw eenheid).
- Zorg ervoor dat **datum en tijdstip** van registratie altijd zorgvuldig ingevuld zijn.
- Baseer u voor de registratie ten allen tijde op de extra informatie aanwezig in de **handleiding** (bv. betekenis van symptomen, wijze van registratie, ...).
- Verifieer of het dossier voorzien is van een **patiëntencode** (P-code vooraf ingevuld door de onderzoeker). Wanneer dit niet het geval blijkt te zijn, gelieve de onderzoeker hiervan op de hoogte te brengen.
- Gelieve de **ingevulde dossiers** te deponeren in het **daarvoor voorziene recipiënt** dat op de afdeling aanwezig is. Vooraleer dit te doen, verifieer of het dossier voorzien is van een **P-code**. Zoniet, laat het formulier dan in het verpleegkundig dossier zitten en maak de onderzoeker hier attent op.
- Zorg ervoor dat alle **registraties onafhankelijk** van elkaar gebeuren. Probeer zo objectief mogelijk te scoren. Dit verhoogt de waarde van de resultaten. Baseer u nooit op scores van de vorige dagen!
- Bij onduidelijkheden of vragen kan u ons steeds contacteren!

VEEL SUCCES EN HARTELIJK DANK VOOR DE MOEITE!

Patricia en Kristel

Code van de verpleegkundige die registreert: V- .....

Dag en datum van de registratie: .....

Tijdstip van registreren: ❑ **morgen**
❑ **middag**
❑ **avond**

VOEDSEL EN VOCHTTOEDIENING PER OS

Kruis de beschrijving aan die het meest in overeenstemming is met de situatie van de patiënt.

- ❑ Eet en drinkt normaal (> 1 liter/dag)
- ❑ Slaat maaltijden over, drinkt nog voldoende (> 1 liter/dag)
- ❑ Eet geen maaltijden meer, drinkt kleine hoeveelheden (< 1 liter/dag)
- ❑ Nipt enkel nog aan een glas of spuit
- ❑ Niks meer per os

PALLIATIVE PERFORMANCE SCALE

Omcirkel het percentage, waarvan de beschrijving het best overeenstemt met de situatie.

PPS Level	Mobiliteit, ambulant	Activiteit en bewijs van de ziekte	Zelfzorg	Voedsel & vocht inname	Bewustzijnsniveau
100%	Volledig	Normale activiteit & werk Geen bewijs van de ziekte	Volledig	Normaal	Volledig
90%	Volledig	Normale activiteit en werk Enig bewijs van de ziekte	Volledig	Normaal	Volledig
80%	Volledig	Normale activiteit met moeite Enig bewijs van de ziekte	Volledig	Normaal of beperkt	Volledig
70%	Beperkt	Ongeschikt voor normale job/werk Belangrijke ziekte	Volledig	Normaal of beperkt	Volledig
60%	Beperkt	Ongeschikt voor uitvoeren van hobby's, huishoudelijke activiteiten Belangrijke ziekte	Af en toe nood aan assistentie	Normaal of beperkt	Volledig of verward
50%	Voornamelijk zitten/liggen	Ongeschikt om gelijk welk werk uit te voeren Uitgebreide ziekte	Behoorlijk veel assistentie noodzakelijk	Normaal of beperkt	Volledig of verward
40%	Voornamelijk in bed	Ongeschikt om de meeste activiteiten uit te voeren Uitgebreide ziekte	Voornamelijk assistentie	Normaal of beperkt	Volledig of suf +/- verward
30%	Volledig bedlegerig	Ongeschikt om gelijk welke activiteit uit te voeren Uitgebreide ziekte	Volledige hulp	Normaal of beperkt	Volledig of suf +/- verward
20%	Volledig bedlegerig	Ongeschikt om gelijk welke activiteit uit te voeren Uitgebreide ziekte	Volledige hulp	Minimaal tot slokjes	Volledig of suf +/- verward
10%	Volledig bedlegerig	Ongeschikt om gelijk welke activiteit uit te voeren Uitgebreide ziekte	Volledige hulp	Enkel mondzorg	Suf of coma +/- verward
0%	Dood				

GLASGOW COMA SCHAAL

Kruis de reële reactie van de patiënt aan.

Te beoordelen reactie	Score
Ogen openen	❑ Spontaan (4) ❑ Op aanspreken (3) ❑ Op pijnprikkels (2) ❑ Geen reactie (1)
Beste verbale reactie	❑ Georiënteerd (5) ❑ Verward (4) ❑ Onsamenhangende woorden (3) ❑ Onverstaanbare klanken (2) ❑ Geen reactie (1)
Beste motorische reactie	❑ Gehoorzamend (6) ❑ Lokaliseren (5) ❑ Flexie op pijn (4) ❑ Abnormale flexie (3) ❑ Extensie (2) ❑ Geen reactie (1)

TOTAALSCORE (in te vullen door de onderzoeker): .....

A-ESAS: Symptoomvoorkomen

Gelieve, d.m.v. een verticale lijn aan te kruisen hoe sterk ieder symptoom *aanwezig is bij de patiënt.*

GEEN **ERGST MOGELIJK**

PIJN _____

VERMOEIDHEID _____

MISSELIJKHEID _____

NEERSLACHTIGE STEMMING _____

ANGST _____

SLAPERIGHEID _____

VERMINDERDE EETLUST _____

ALGEMEEN ONGELUKKIG GEVOEL _____

KORTADEMIGHEID _____

CONSTIPATIE _____

DROGE MOND _____

GESTOORDE SLAAP _____

ANDER PROBLEEM _____

A-ESAS: Symptoomongemak

Gelieve, d.m.v. een verticale lijn aan te kruisen in welke mate de patiënt dit symptoom *als storend ervaart.*

	GEEN	**ERGST MOGELIJK**
PIJN		
VERMOEIDHEID		
MISSELIJKHEID		
NEERSLACHTIGE STEMMING		
ANGST		
SLAPERIGHEID		
VERMINDERDE EETLUST		
ALGEMEEN ONGELUKKIG GEVOEL		
KORTADEMIGHEID		
CONSTIPATIE		
DROGE MOND		
GESTOORDE SLAAP		
ANDER PROBLEEM		

DEEL 3: REGISTRATIEFORMULIER VAN DE ONDERZOEKER

Volgende gegevens worden bij iedere patiënt door de onderzoeker geregistreerd en dit op basis van het verpleegkundig dossier. De onderzoeker zal 1 maal per week langskomen om volgende gegevens te registreren:

- Demografische gegevens van de patiënt (eenmalig in te vullen bij opname, aan te vullen bij overlijden)
- Demografische gegevens van de verpleegkundigen
- Gegevens over parenterale vocht- en voedseltoediening en medicatie

De registratie zal betrekking hebben op de dagen waarop de verpleegkundige eveneens heeft geregistreerd namelijk, maandag, woensdag en vrijdag.

DEMOGRAFISCHE GEGEVENS VAN DE PATIENT

GESLACHT: ❑ Man
❑ Vrouw

LEEFTIJD (in jaren): ..... jaar

NATIONALITEIT: .....

BURGERLIJKE STAND:
❑ Gehuwd
❑ Samenwonend
❑ Alleenstaand
❑ Weduwe/weduwnaar
❑ Gescheiden

PRIMAIRE DIAGNOSE: .....

METASTASERING:
❑ Bot
❑ Long-, buikholte
❑ Lever
❑ Hersenen
❑ Klieren
❑ Huid

LEVENSBESCHOUWING:
❑ Vrijzinnig
❑ Christelijk
❑ Islamiet
❑ Boeddhist
❑ Hindoe
❑ Joods

OPLEIDING:
❑ Buitengewoon onderwijs
❑ Lager onderwijs
❑ Secundair onderwijs
❑ Hoger onderwijs
❑ Universiteit

OPNAMEDATUM: .....

ONTSLAGDATUM / DATUM VAN OVERLIJDEN*: .....
* Schrap wat niet van toepassing is

Indien ontslag:
❑ Thuis
❑ Thuis met ondersteuning van Palliatieve Thuiszorg
❑ Rusthuis
❑ Ander (psychiatrisch verzorgingstehuis, beschut wonen, andere PE)

Eventuele datum en plaats van overlijden na ontslag: .....

DEMOGRAFISCHE GEGEVENS VAN DE VERPLEEGKUNDIGEN[3]

- **Naam verpleegkundige:.....**
- **Code toegekend aan de verpleegkundige: V.....**
- **Leeftijd (in jaren) : .....**
- **Geslacht :** ❑ **Man**
  ❑ **Vrouw**
- **Opleidingsniveau** ❑ **Verzorgenden, 2A2, bejaardenhelpster**
  ❑ **Gebrevetteerde verpleegkundige**
  ❑ **Gegradueerde verpleegkundige**
  ❑ **Universitair onderwijs**
- **Hoelang werkzaam op palliatieve eenheid (in jaren):.....**

[3] Deze demografische gegevens worden voor iedere verpleegkundige, werkzaam op de afdeling, geregistreerd. Iedere verpleegkundige ontvangt een code die hij/zij telkens op het registratieformulier van de patiënt vermeldt.

KUNSTMATIGE VOEDSEL- EN VOCHTTOEDIENING

Datum	**Soort kunstmatige voedsel- en/of vochttoediening**	**Toegediende dosis per 24 uur**	**Indien wijzigingen, welke?**	**Reden van wijziging**

MEDICATIEGEBRUIK

Datum	**Naam geneesmiddel en toedieningswijze**	**Toegediende dosis per 24 uur**	**Indien wijzigingen, welke?**	**Reden van wijziging**

DEEL 2: BIJKOMENDE GEGEVENSVERZAMELING BIJ SEDATIE OF EUTHANASIE

Indien de patiënt, zijn familie en/of de hulpverlener aangeven dat de patiënt ondraaglijk lijdt en daarom sedatie of levensbeëindigend handelen noodzakelijk is om een menswaardig levenseinde te garanderen of indien de patiënt sedatie ontvangt ten gevolge van een beslissing van de arts, gelieve **volgende gegevens te registreren en één van de onderzoekers te contacteren.**

Contactgegevens

Patricia Claessens
Tel.:
GSM:

Kristel Marquet
Tel.:
GSM:

Volgende definities worden hierbij gehanteerd:

Sedatie = toestand van tijdelijke of continue bewustzijnsverlaging ter behandeling van refractair, ondraaglijk lijden

Euthanasie = het opzettelijk levensbeëindigend handelen door een ander dan de betrokkene, op diens verzoek

Aandachtspunten bij de registratie:

- Volgende onderdelen dienen slechts **eenmalig** ingevuld te worden: datum, wie, welke hulpverlener, reden van sedatie of reden van euthanasie.
- In geval van **sedatie** dient, **elke dag** dat de patiënt gesedeerd is, geregistreerd te worden om welke soort sedatie het gaat.
- Indien de soort sedatie gewijzigd wordt (cf. handleiding voor de definities), dan dient de **reden van wijziging** op het registratieformulier vermeld te worden!

IN GEVAL VAN SEDATIE

Datum van deze vaststelling: .....

Wie heeft aangegeven dat de patiënt ondraaglijk lijdt?

- ❑ patiënt
- ❑ familie
- ❑ hulpverlener (ga verder naar punt 2 op de volgende pagina)
  - ❑ verpleegkundige
  - ❑ arts
  - ❑ vrijwilliger
  - ❑ sociaal asistente
  - ❑ pastor
  - ❑ psycholoog
  - ❑ kinesitherapeut
  - ❑ andere, zoja, specifieer: .....
- ❑ andere, zoja, specifieer: ..... (ga verder naar punt 2 op de volgende pagina)

Indien de patiënt of zijn familie het ondraaglijk lijden aangeven, aan **welke hulpverlener** werd deze boodschap dan gegeven?

- ❑ verpleegkundige
- ❑ arts
- ❑ vrijwilliger
- ❑ sociaal asistente
- ❑ pastor
- ❑ psycholoog
- ❑ kinesitherapeut
- ❑ andere, zoja, specifieer: .....

Reden van sedatie:

1. Indien de patiënt of zijn familie de vraag naar sedatie ten gevolge van ondraaglijk lijden aangeeft

Welke **symptomen** zijn volgens de patiënt of familie aanwezig op het moment dat de sedatie gestart wordt (cf. A-ESAS)?

❑ pijn	❑ verminderde eetlust
❑ vermoeidheid	❑ algemeen ongelukkig gevoel
❑ misselijkheid	❑ kortademigheid
❑ neerslachtige stemming	❑ constipatie
❑ angst	❑ droge mond
❑ slaperigheid	❑ gestoorde slaap

❑ ander probleem: ..... (specifieer)

Welke van deze **symptomen wegen volgens** de patiënt of de familie **het zwaarst door** bij de beslissing over te gaan tot sedatie (cf. A-ESAS)?

❑ pijn	❑ verminderde eetlust
❑ vermoeidheid	❑ algemeen ongelukkig gevoel
❑ misselijkheid	❑ kortademigheid
❑ neerslachtige stemming	❑ constipatie
❑ angst	❑ droge mond
❑ slaperigheid	❑ gestoorde slaap

❑ ander probleem: ..... (specifieer)

2. Indien de patiënt niet in het beslissingsproces omtrent sedatie betrokken is, wat was dan de reden van sedatie?

.....
.....
.....

KRUIS <u>DAGELIJKS</u> AAN WELKE SOORT SEDATIE DE PATIËNT ONTVANGT.

	Code verpleegkundige	Mild-Intermittent	Diep-Intermittent	Mild-Continu	Diep-Continu	Reden van wijziging van de sedatie
Dag 1 Datum:	V-					
Dag 2	V-					
Dag 3	V-					
Dag 4	V-					
Dag 5	V-					

IN GEVAL VAN EUTHANASIE

Reden van euthanasie:

Welke **symptomen** zijn aanwezig op het moment dat de beslissing tot euthanasie wordt genomen (cf. A-ESAS)?

- ❑ pijn
- ❑ vermoeidheid
- ❑ misselijkheid
- ❑ neerslachtige stemming
- ❑ angst
- ❑ slaperigheid
- ❑ verminderde eetlust
- ❑ algemeen ongelukkig gevoel
- ❑ kortademigheid
- ❑ constipatie
- ❑ droge mond
- ❑ gestoorde slaap
- ❑ ander probleem: ..... (specifieer)

Welke van deze **symptomen wegen het zwaarst** door bij de beslissing over te gaan tot euthanasie (cf. A-ESAS)?

- ❑ pijn
- ❑ vermoeidheid
- ❑ misselijkheid
- ❑ neerslachtige stemming
- ❑ angst
- ❑ slaperigheid
- ❑ verminderde eetlust
- ❑ algemeen ongelukkig gevoel
- ❑ kortademigheid
- ❑ constipatie
- ❑ droge mond
- ❑ gestoorde slaap
- ❑ ander probleem: ..... (specifieer)

GEINFORMEERDE TOESTEMMING

Geachte mevrouw, mijnheer,

Op de eenheid waar u bent opgenomen loopt er momenteel een onderzoek rond symptoomvoorkomen en symptoombehandeling met als doelstelling het optimaliseren van de symptoomcontrole in de palliatieve zorg. In het kader van dit project is het belangrijk dat wij inzicht krijgen in het voorkomen en het ongemak van uw symptomen, de diverse behandelingen (bijv. pijnstillers en rustgevende medicatie) en in de factoren die de symptoomcontrole beïnvloeden (bijv. functionele toestand, medicatie, eetgewoontes, enz.). Omdat deze gegevens voor het onderzoek zeer belangrijk zijn, en omdat alleen u ons deze essentiële informatie kan verschaffen, zouden wij graag op uw medewerking een beroep willen doen.

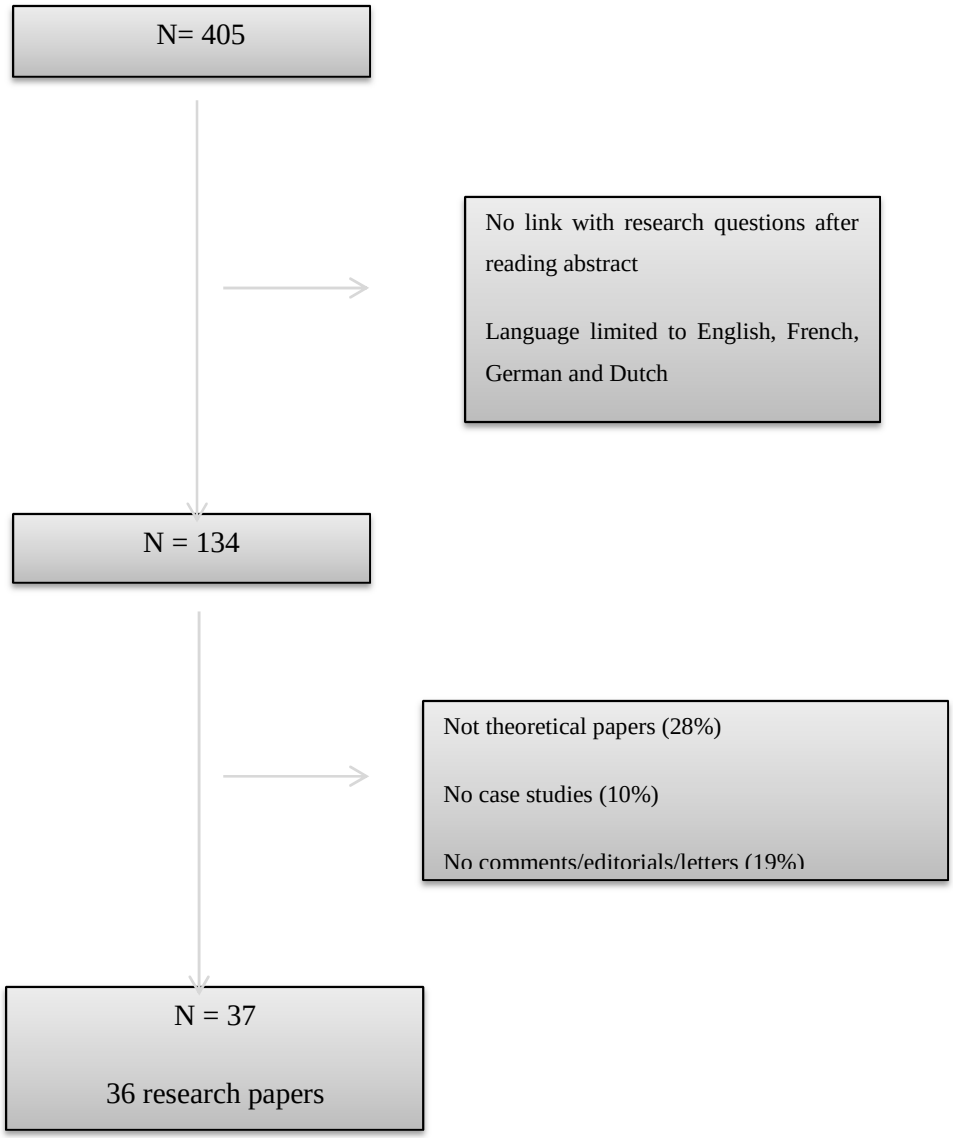
Indien u bereid bent mee te werken aan dit onderzoek, zal de verpleegkundige drie maal per week, haar/zijn observaties omtrent uw symptoomvoorkomen en het ongemak dat daarmee gepaard gaat, registreren en doorgeven aan de onderzoeker. Verder zal de onderzoeker uw dossier inkijken om zo een zicht te krijgen op uw medicatiegebruik en uw eetgewoontes. In uitzonderlijke gevallen zal de verpleegkundige ook bij u langs komen en vragen welke symptomen het sterkst aanwezig zijn op dat moment.
U heeft het recht uw deelname aan het onderzoek op eender welk moment stop te zetten, zonder dat u hiervoor een reden hoeft te geven. Uw beslissing om niet deel te nemen aan het onderzoek zal geen enkele ongunstige invloed hebben op de verzorging.
De informatie die u ons geeft, zal op een strikt vertrouwelijke wijze behandeld worden en blijft volledig anoniem. Uw gegevens zullen enkel gebruikt worden in functie van dit onderzoek. Hiertoe zal ieder registratieformulier voorzien worden van een code. Enkel de onderzoeker zal in staat zijn het verband te leggen tussen deze code en de naam van de patiënt.

De onderzoekers geven u en uw familie de garantie deze richtlijnen in acht te zullen nemen doorheen het volledige onderzoek. Ze zullen u ook een antwoord geven op eventuele bijkomende vragen, bemerkingen of opmerkingen. Wij danken u alvast op voorhand voor uw bereidwillige medewerking. Wanneer u instemt om aan dit onderzoek deel te nemen en dus toegang verleent aan de onderzoekers tot uw dossiers, vragen wij u dit document te ondertekenen.

Datum, naam & handtekening patiënt en/of familie

Datum, naam & handtekening onderzoeker en/of hoofdverpleegkundige

APPENDIX 3: SEARCH STRATEGY


N= 405
No link with research questions after reading abstract
Language limited to English, French, German and Dutch
N = 134
Not theoretical papers (28%)
No case studies (10%)
No comments/editorials/letters (19%)
N = 37
36 research papers

PROFESSIONAL CAREER

Patricia Claessens was born on January 25, 1974 in Eeklo, Belgium. At the KaHog she obtained her bachelor degree in nursing (1996). In 1999 she graduated, at the Catholic University of Leuven, as a Master in Nursing Science. In the same year she started working as a nurse in a psychiatric hospital, Broeders Alexianen, Tienen. In February 2000, she started working as a research associate at the Centre for Health Services and Nursing Research, Catholic University Leuven. At that time she was working on a research project focusing on the implementation of clinical leadership. In 2002, after finishing the project on clinical leadership, she started working at the Centre for Biomedical Ethics and Law, Catholic University of Leuven, where she conducted the work described in this study. In December 2006 she was in charge of the paramedics in a nursing home, VZW St. Anna Wingene. Since December 2008, she is working at the University College Artevelde, Ghent, where she is coordinator at the degree programme bachelor in nursing. She is also member of the board of directors of a nursing home.

LIST OF PUBLICATIONS

ARTICLES IN PEER REVIEWED JOURNALS

De Geest S, **Claessens P,** Longerich H, Schubert M, & the International Clinical Leadership Group (2003). Transformational Leadership: Worthwhile the investment! European Journal of Cardiovascular Nursing, 2, 3-5.

Claessens P, Dierckx de Casterlé B (2003). Skilled companionship: Verpleegkundige zorg vanuit een zorgethisch perspectief. Tijdschrift voor Gezondheidszorg en Ethiek, 13, 3, 76-80.

Claessens P, Menten J (2003). Zorg voor terminale patiënten. Een overzicht van een aantal studies omtrent de belangrijkste problemen van palliatieve patiënten. Acta Hospitalia, 4, 21-35.

Claessens P, De Blaeser L & Broeckaert B (2003). Palliatieve sedatie. Acta Hospitalia, 4, 37-47.

Broeckaert B & **Claessens P** (2003). Medisch begeleid sterven: van euthanasie tot het stopzetten van een levensverlengende behandeling. Acta Hospitalia, 4, 9-20.

Claessens P, Moons P, Dierckx de Casterlé B, Cannaerts N, Budts W, Gewillig M. What does it mean to live with a congenital heart disease? A study on the lived experiences of adult patients. European Journal of Cardiovascular Nursing, 4, 3-10.

Claessens P, Genbrugge E, Vanuffelen R, Broeckaert B, Schotsmans P, Menten J. Palliative sedation and nursing: The place of palliative sedation within palliative nursing care. Journal of Hospice and Palliative Nursing, 9, 100-106.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation: a review of the research literature. Journal of Pain and Symptom Management, 36:310-333.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation, not slow euthanasia: a prospective, longitudinal study of sedation in Flemish palliative care units. Journal of Pain and Symptom Management. 2011;41:14-24.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Development and Validation of the Modified Edmonton Symptom Assessment Scale in a Flemish Palliative Care Population. American Journal of Hospice and Palliative Medicine. 2011;28:475-482.

Claessens P, Menten J, Schotsmans P, Broeckaert B. Starving them to death? Food and fluid intake and palliative sedation in palliative care units: a longitudinal prospective study (submitted for publication).

Claessens P, Menten J, Schotsmans P, Broeckaert B. Level of consciousness in dying patients. The role of palliative sedation, a longitudinal prospective study. American Journal of Hospice and Palliative Medicine 2012;29:195-200.

OTHER ARTICLES

Siebens, K., Moons, P., **Claessens, P.**, Budts, W., Gewillig, M. (1999). Verzekering, Arbeid en Congenitale Hartaandoeningen. Cordiaal, 3, 88-90.

Moons P, **Claessens P**, Dierckx de Casterlé B, Cannaerts N, Budts W, Gewillig M (2000). Lived experiences in adult patients with congenital heart disease. Link: The communication bulletin in psychosocial research in congenital heart disease; special issue June:38-42.

Claessens P, Genbrugge E, Vannuffelen R, Broeckaert B, Schotsmans P, Menten J (2005). Hoe past palliatieve sedatie binnen goede verpleegkundige zorg en wat is de rol van de verpleegkundige? Pijninfo, 8, 45-54.

Claessens P & Menten J (2006). Palliatieve sedatie: een stand van zaken. Bijblijven.

Beeckman D, Foulon M, Vermeulen M, **Claessens P**, Duprez V, Beyls L, Leys J, Robbeers R, Dereymaeker L, Nuyttens C. (2009). De student verpleegkunde in Vlaanderen: vandaag … en morgen? Nursing, juni, 1-2.

De Coninck l, Beyls L, De Schepper J, **Claessens P**. Ergotherapie als actor binnen een multidisciplinaire aanpak van valpreventie in de WZC in Vlaanderen. Jaarboek Ergotherapie 2012;141-154.

BOOKS

De Visschere Luc & Claessens P. Mondzorg. Jong geleerd is oud gedaan. Acco, Leuven, in press (October 2012).