Use of Tramadol Drip in Controlling Renal Colic Pain

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ABSTRACT

Background and Purpose: Although the continuous perfusion of antispasmodic drugs has been the traditional mainstay in the treatment of renal colic, the results more often than not are unsatisfactory. Our hypothesis was that a continuous intravenous (IV) drip of tramadol would be an effective and safe alternative.

Patients and Methods: In this prospective study, 300 patients with renal colic were randomized into four treatment groups, single blind for the patients. At the start, all received an anti-inflammatory drug intramuscularly and an antiemetic and antispasmodic IV. Group A was given the classical IV antispasmodic perfusion combined with a sham drip. Group B received the classical antispasmodic perfusion in combination with a tramadol drip. Group C had a sham perfusion and drip. Group D received a sham perfusion and tramadol drip. There was no significant difference in the degree of pain between the groups on a visual analog scale (VAS) at the start. The pain was scored again on the VAS at 30 minutes, 1 hour, and 4 hours after the start of the treatment and at IV urography. Side effects, as well as the need for rescue medication, were registered.

Results: Both tramadol groups scored significantly better after 60 and 240 minutes and during IV urography ($P < 0.005$). There was a significant decrease in VAS in group B after 30 minutes. The tramadol groups needed significantly less rescue medication ($P = 0.001$). There was no significant difference in the reported side effects. The combination spasmolytic-tramadol drip scored the best, although the difference was not statistically significant.

Conclusion: We consider our hypothesis proved that a continuous tramadol drip is a safe and valuable analgesic regimen in renal colic.

INTRODUCTION

ANALGESIA IN RENAL COLIC is a therapeutic challenge. As this excruciating pain often is difficult to control. Increased fluid intake was erroneously credited with supplying a "vis a tergo" that would expel a concrement out of the ureter.¹ However, diuresis reduces peristalsis in the ureteral wall and increases the accumulation of urine proximal to the obstruction, leading to greater pain and more hydronephrosis with a higher risk of urine extravasation without having the slightest impact on stone passage. Therefore, fluid restriction will be more advantageous to the patient.^{2,3}

Dating back to the 1800s, anticholinergic spasmolytic agents have been used. The rationale is that they induce smooth-muscle relaxation in the wall of the ureter. The ureter receives a

parasympathetic motor supply, which is cholinergic and acts on the muscarinic receptors in the smooth muscle.⁴ Although antispasmodics still are widely used, their therapeutic value is more and more being challenged.⁴⁻⁷ Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used, as they decrease afferent vasodilatation and inhibit ureteral smooth-muscle tone.^{1,8,9} For long-lasting pain relief, intravenous (IV) opioids titrated to effect are recommended.¹⁰ However, on-demand IV titration of drugs is difficult to organize in a busy emergency department, especially if patients have to leave for the medical imaging department for IV urography (IVU). Notably, the contrast bolus of IVU increases diuresis, creating a higher demand for analgesics.

Therefore, we looked for an efficient and ergonomic alternative. Tramadol has proven to be effective in SW^{11,13} and in

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FIG. 1. Triage scheme. All patients had same start medication.

an animal ureteral-calculus model.¹³ Experimental studies also proved an anti-inflammatory effect besides the central analgesia.^{14,15} As single-dose therapy seemed to be insufficient,^{16,17} we chose a continuous tramadol drip such as we use for trauma patients. Our hypothesis was that a tramadol drip could be a safe and valuable therapeutic alternative in controlling colic pain.

PATIENTS AND METHODS

From February 4, 2003, until August 6, 2004, 300 consecutive patients aged 18 years or older referred for, or presenting with renal colic-like symptoms were randomized into four treatment groups (Fig. 1), assignment being single blinded for the patients. Exclusion criteria were pregnancy or lactation, use of monoamine oxidase inhibitors, Parkinsonism, known allergy to any of the products used, chronic tramadol use, use of oral anticoagulants, prehospital administration of morphine mimetics, and a diagnosis other than renal colic. The diagnosis of urolithiasis had to be confirmed on ultrasonography, IVU, or CT scan. A total of 43 patients had to be excluded because of technical problems with the perfusion pump ($N = 1$), transfer to another hospital ($N = 2$), adverse reaction to a drug ($N = 1$), insufficient or lost data ($N = 9$), or diagnosis other than renal colic ($N = 30$) (Table 1).

At the start all patients received an NSAID (meloxicam 15 mg) intramuscularly and an antiemetic (droperidol 1.25 mg) with an anticholinergic antispasmodic (butylhyoscine bromide 20 mg) as an IV bolus. Patients who had received an NSAID before admission were not given meloxicam. Group A was given the routinely used classical antispasmodic perfusion (80

mg of butylhyoscine bromide) combined with a saline sham drip. Group B received the classical antispasmodic perfusion in combination with a tramadol drip IV (100-mg loading dose in 20 minutes and 400 mg over the following 24 hours). Group C (placebo group) had a glucose perfusion and the sham saline drip. Group D received a glucose perfusion and the tramadol drip. (See Table 2 for all products used and their pharmacological mechanisms of action.) There was no significant difference in age (mean 44.5 years), visual analog scale (VAS) score prior to treatment (mean 7), or sex distribution (70% males) in the four groups.

Patients again scored their pain according to the VAS at 30 minutes, 1 hour, and 4 hours after starting the therapy (Fig. 2)

TABLE 1. PATIENTS EXCLUDED BECAUSE OF DIAGNOSIS OTHER THAN RENAL COLIC

Diagnosis	No.
Intestinal colic/fecal impaction	7
Pyelonephritis	6
Orthopedic cause/back pain	5
Hemorrhagic cystitis	2
Appendicitis	2
Gynecologic problem/extruterine pregnancy	2
Abdominal aortic dissection	1
Diverticulitis/sigmoiditis	1
Biliary colic	1
Herpes zoster of the flank	1
Pleuritis	1
Influenza	1

FIG. 2. Evolution of VAS scores.

and at IVU (the maximal pain score during the examination: 50 mL of sodium ioxitalamate as an IV bolus followed by a 200-mL sodium ioxitalamate infusion in 5 minutes). The decline in VAS relative to the start value was calculated for every time interval. Side effects, as well as the need for rescue medication (paracetamol 1 g in step 1 and piritramide 10 mg in step 2), were also registered. Every patient, irrespective of assigned group, received this rescue medication immediately on demand, as agreed on inclusion. Satisfaction with the pain control on the part of both the patient and the treating physician was noted.

All data were recorded in a Microsoft Excel database, and the different groups were compared statistically by means of SPSS for Windows V. 11.0.1. A $P < 0.05$ was considered to be significant. Parametric statistics were calculated with one-way analysis of variance. Multiple comparisons used the Tukey method and the nonparametric statistics were calculated with the Kruskal-Wallis test.

RESULTS

There was no significant difference in the VAS at 30 minutes (mean 3.8), but considering the decline in VAS after 30 minutes, group B scored significantly better than group A or C (4.0 v 2.8 and 2.4, respectively). Group B had a significant lower VAS than groups A and C after 1 hour (1.5 v 2.7 and 2.9, respectively) (Fig. 3A), while the decline in VAS over 1 hour in groups B and D (5.7 and 5.1) was significantly greater than in group C (3.6) (Fig. 3B). After 4 hours, there was a significantly lower VAS in groups B and D (0.6 and 0.7) relative to group A (2.1) (Fig. 4A). Groups B and D also had a significantly greater decline (both 6.7) than group A (5.6) after 4 hours (Fig. 4B). At the time of IVU, groups B and D scored significantly better than groups A and C, both for the VAS (0.9 and 1.2 v 3.3 and 3.2) and for the decline (6.3 and 5.9 v 3.9 and 3.3) (Fig. 5). Both tramadol groups had a significantly lower need for rescue medication (0.3 and 0.4 units v 0.9 and 1.0 units) than the others did (Fig. 6). There was no significant difference in most of the reported side effects between the four groups (dry mouth in 30.7%, vomiting in 6.3%, disturbed

vision in 1%, and constipation in 0.7%). Although the ward nurses had the subjective feeling that the tramadol groups had more nausea, the incidence was significantly lower in these groups: group A 20%, B 5.3% ($P = 0.002$), C 25.3%, and D 10.6% ($P = 0.003$). As for the reported patient (96% and 95% v 76% and 69%) and observer (95% and 92% v 60%) satisfaction, both tramadol groups scored significantly better than the others.

DISCUSSION

Tramadol is a synthetic cyclohexanol derivative used since the late 1970s. It is a centrally acting analgesic with weak mu-opioid receptor agonism and inhibition of serotonin and norepinephrine reuptake. These modes of action appear to be syn-

A

B

FIG. 3. Effects at 1 hour after start of treatment. (A) Mean VAS. Group B has significantly better result than group A ($P = 0.009$) and group C ($P = 0.001$). (B) Decline of mean VAS. Groups B ($P < 0.001$) and D ($P = 0.011$) score significantly better than group C.

A

B

FIG. 4. Effects at 4 hours after start of treatment. (A) Mean VAS. Groups B and D score significantly ($P < 0.001$) better than group A. (B) Decline of mean VAS. Groups B ($P = 0.034$) and D ($P = 0.019$) score significantly better than group C.

ergistic. Negligible cardiac and respiratory depression has been shown, and reported side effects are minor: mainly nausea and emesis, usually preventable by slow injection of the drug and prophylactic administration of an antiemetic.¹⁸⁻²¹ The safe and efficient use as a continuous perfusion²² as well as anti-inflammatory effects in an experimental situation^{14,15} are interesting features in the management of renal colic.

In our patients, we found a significantly greater decline in VAS after 30 minutes in the tramadol-butylyscine bromide group than in the patients not receiving tramadol. Both tramadol groups scored better after 1 and 4 hours of treatment and with the contrast bolus at the time of the IVU. This is expressed not only in the pain scores but also in the consumption of rescue

Decline VAS at IVU time

FIG. 5. Decline of mean VAS between start of treatment and IVU. Groups B ($P = 0.001$) and D ($P = 0.005$) score significantly better than groups A and C ($P < 0.001$).

medication. Although we could not prove any significant difference between the two tramadol groups, there is a higher score in all the tests for the tramadol-butylyscine bromide group. This group also had the fastest decline in VAS (after 30 minutes). One could therefore be more inclined toward this regimen, although there is no statistical evidence of its superiority. However, tramadol alone is less expensive and easier for the nursing staff. On the other hand, there proved to be no statistical difference between the placebo (group C) and butylyscine bromide only (group A), strongly challenging the efficacy of

Total need for rescue medication

FIG. 6. Total need for rescue medication. Group B has significantly less need than groups A ($P = 0.004$) and C ($P = 0.001$). Also, group D has significantly less need than groups A ($P = 0.017$) and C ($P = 0.004$).

TABLE 2. AGENTS USED WITH PHARMACOLOGIC MECHANISMS OF ACTION

Generic name	Trade name	Mechanism of action	Use
Butylhyoscine bromide	Buscopan	Anti-muscarinic anticholinergic	Anti-spasmodic
Droperidol	Dehydrobenzperidol	Dopamine blockade and α 1 adrenolytic	Anti-emetic
Meloxicam	Mobic	Nonselective NSAID	Analgesic
Paracetamol (acetaminophen)	Perfusalgan	Inhibiting pain threshold	Rescue analgesic
Piritramide	Dipidolor	Opioid	Rescue analgesic
Tramadol	Contramal	Opioid, serotonin and norepinephrine reuptake inhibition	Analgesic

perfusion of antispasmodic drugs alone in the management of renal colic.

We did not observe a significantly higher incidence of complications or adverse effects when using tramadol. Although the ward nurses had the subjective impression that the patients treated with tramadol had more nausea, this could not be proved statistically. As both renal colic and the administration of tramadol are prone to inducing nausea, we strongly advocate administering a powerful antiemetic.

Last but not least, there proved to be a significant difference in the satisfaction score of both the patients and the treating physicians favoring the use of a tramadol drip.

Remarkable in this series is the relatively high incidence (10%) of non-renal colic-associated diagnoses. Confusion with gastrointestinal colic ($N = 8$) was to be expected, but life-threatening pathology, such as acute dissection of an abdominal aortic aneurysm, should also be included in the differential diagnosis. Therefore, in clear-cut cases of renal colic, we still prefer an IVU as initial diagnostic tool, whereas in cases where there is clinical doubt, we advocate the performance of an unenhanced spiral CT scan.

The protocol not being double blinded could be considered a flaw in the study design. However, double blinding would have complicated the therapeutic monitoring of patients in an emergency department, where treatments often are followed by different physicians as shifts change. Furthermore, a single-blinded set-up could influence only the physician's satisfaction scores, not the patient's VAS scores.

CONCLUSION

Although the perfusion of an antispasmodic alone has been the traditional mainstay of the management of renal colic, this prospective study proves its value in pain control to be not statistically different from the administration of a placebo. A continuous IV tramadol drip, on the other hand, proved to offer superior analgesia and greater patient satisfaction without an increase in reported side effects. Therefore, we consider the continuous IV administration of tramadol a safe, efficient, and elegant measure for the management of renal colic.

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ABBREVIATIONS USED

CT = computed tomography; IV = intravenous; IVU = intravenous urography; NSAID = nonsteroidal anti-inflammatory drug; VAS = visual analog scale.