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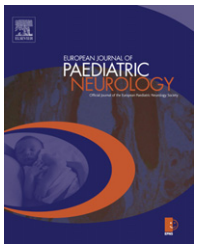
Official Journal of the European Paediatric Neurology Society



Original article

Botulinum toxin type A treatment in children with cerebral palsy: Evaluation of treatment success or failure by means of goal attainment scaling

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ARTICLE INFO

Article history:
Received 7 December 2009
Received in revised form
17 September 2010
Accepted 27 September 2010

Keywords:
Cerebral palsy
Botulinum toxin type A
Goal attainment scale

ABSTRACT

Background: There is considerable variability in the amount of response to BTX-A treatment between and within patients with cerebral palsy (CP).
Aims: The purpose of this retrospective cohort study was to evaluate the clinical responsiveness of Botulinum toxin type A (BTX-A) treatment in children with CP and specifically delineate features of treatment success and failure.
Methods: Four hundred and thirty-eight children (251 boys, 187 girls; mean age 8 years 2 months, SD 4 years) were included into the study. Goal Attainment Scaling (GAS) was used to classify and evaluate treatment efficacy. Two study groups were defined: one group with an excellent response (GAS $\geq$ 60.0) and one group with a lack of response (GAS $\leq$ 40.0) to BTX-A.
Results: Seventy-five patients (17.1%) had an excellent response and treatment was found to be unsuccessful for 31 patients (7.1%). Children with a lack of response to BTX-A were significantly older compared to children with a high responsiveness ($p = 0.0013$). In the latter group, more children received multi-level injections and fewer children had injections in proximal parts of the lower limb compared to the low responsiveness group ($p = 0.0024$). Moreover, there was a significant difference in the use of different types of casts between both study groups ($p = 0.0263$).
Conclusion: Age, level of treatment and casting seem to be crucial features of BTX-A treatment success or failure in children with CP.

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doi:10.1016/j.ejpn.2010.09.006

1. Introduction

Cerebral palsy (CP) is a non-progressive injury to the immature brain before, at or soon after birth, resulting in a changing disorder of movement and posture. The primary problems of CP may be spasticity, lack of selectivity, weakness/rigidity and balance problems.[1,2] These problems may, strengthened by growth, evolve to secondary orthopaedic problems (fixed contractures and bony deformities).[3] The majority of children with CP develop spasticity dominated movement disorders.[1,2] Botulinum toxin type A (BTX-A) is an intramuscular agent which has been established as a standard treatment option of spasticity in children with CP over the last few years. A variety of successful outcome parameters of BTX-A have been described in literature, such as reduced muscle tone,[4,5] increased range of joint motion,[4–8] improved gait pattern[7,8] and increased muscle length.[9] The influence of BTX-A injections on the function of children with CP is not entirely predictable so far.

From an overall view of the literature it can be concluded that, although BTX-A treatment can be considered as successful, there is still a large variability in outcome, both between as within studies. Different types of assessment tools have been used until now, which may explain the variety of treatment outcome parameters. The variability of outcome may also be related to crucial factors within the treatment strategy, such as dosage, antibody formation, aftercare and age. Various doses of BTX-A may cause a different number of responses.[5,10] With wider use of BTX-A for the long-term management of spasticity in children with CP, it also became apparent that a number of patients may develop neutralizing antibodies to this toxin, which has been linked to secondary non-response.[11] Attentive aftercare (physical therapy, serial casting, day and night orthoses) may provide more marked and enduring results of the BTX-A treatment.[12–15] Several studies recommend starting BTX-A treatment at an early age when muscle contractures are still dynamic.[3] The variability in the features mentioned above (dose, antibody formation, aftercare and age), and any other crucial factors, may explain the differences in the degree of response to BTX-A treatment in children with CP. So far, these potential crucial factors for success and failure have not been evaluated in a structured way for a large group of patients. The present study focuses on the outcome of BTX-A treatment administered according to a well-established integrated, high-dosage treatment strategy.[16] Despite the fact that children, who are treated with BTX-A at the University Hospital of Pellenberg (Leuven, Belgium), has a similar multidisciplinary policy, a variety in treatment outcomes can still be seen. The purpose of this study was to identify the characteristic features of success and failure of a standardised strategy for BTX-A treatment in children with CP.

2. Methods

Between January 1996 and December 2006, a total of 2290 BTX-A treatments were performed at the University Hospital of Pellenberg (Leuven, Belgium). For the present study, the results of all patients between 1 and 23 years of age, who were treated between January 2004 and December 2006 ($N = 741$), were evaluated. The latter period was arbitrarily chosen, focussing on a high number of treatments and with full assurance of a stable Botox® preparation (Allergan Inc., Irvine, CA, USA) and treatment strategy.

The inclusion criteria in this study were a BTX-A treatment along with a gait or upper limb (UL) evaluation before and two months after the BTX-A injection in the laboratory for Clinical Motion Analysis at the University Hospital of Pellenberg (Leuven, Belgium). The gait evaluation included three-dimensional kinematics, kinetics and surface electromyography (EMG). For children younger than four years and for more involved children, a standardised video observation recording was performed. UL evaluation was based on functional evaluations using the Melbourne Assessment of Unilateral Upper Limb Function (Melbourne Assessment).[17] The gait or UL evaluation was always planned in combination with a standardised extended clinical examination focussing on spasticity, range of motion, strength and selectivity. All included children received close follow-up by the multidisciplinary team of the University Hospital of Pellenberg (Leuven, Belgium) and routinely received an integrated set of conservative treatment options including physical therapy and orthotic management. The final cohort of patients who fulfilled the inclusion criteria, comprised 438 children including 251 boys and 187 girls.

From the electronic patient files, a set of patient characteristics, injection characteristics and aftercare issues were defined. Patient characteristics included diagnoses (hemiplegia, diplegia, quadriplegia, other diagnosis), Gross Motor Function Classification System (GMFCS),[18] type of walking aids, age at the time of treatment and data concerning patients history (previous surgical and BTX-A treatments). Injection characteristics included number of injected muscles, total dosage, specification of treatment (treated levels – single- or multi-level, proximal or distal) and spontaneous reported side effects. Aftercare issues included use of day and night orthoses (type, frequency of use), physical therapy (frequency and duration) and serial casting (type and duration) combined with BTX-A injections.

For each selected muscle, BTX-A (Botox®, Allergan, Irvine, CA) was injected at multiple sites with dosages that did not exceed 50 U per treated site. The extent of dosage depended on the muscle size, patients body weight, gait analysis, clinical examination, evaluation under anaesthesia and individual treatment goals. The placement of the needle (usually 26 gauge × 23 mm) was controlled by stretching the target muscle and moving the above- or beyond-located joint and thereby examining the needle movement. Ultrasonography has also been used to confirm the correct needle placement for smaller muscle groups. A dilution of 100U Botox® in 1–2 ml saline was used.

Treatment success was defined by Goal Attainment Scaling (GAS).[19] GAS is an individualised, criterion-referenced measure that quantifies the achievement of treatment or intervention goals for different kinds of treatment issues.[19–22] For the present retrospective study, GAS scores were calculated by an independent assessor who was

neither involved in the treatment of the subjects nor in the evaluation procedure. At the time of treatment, the multidisciplinary team stipulated general goals based on all available evaluation data (kinematics, kinetics and EMG of gait analysis, observational gait and UL evaluation, clinical examination). These general goal settings were then retrospectively translated into three to six specific goals for treatment session. A list of 245 clinical relevant specific goals based on gait or UL evaluation, clinical examination and other parameters (such as hygiene, pain or measures on X-rays) was developed by the multidisciplinary team. The achievement of the individual goals was then assessed by the comparison of pre and post evaluations. An ordinal scale between −2 and 2 was used to rate each goal. The expected level of success was given score 0 when at least 30% of the pre-treatment gait or UL pathology was corrected. The amount of pre-treatment pathology was defined by comparing the pathological pattern with the normal mean, taking into account the normal standard deviation (standardised score calculated with normal mean and standard deviation). When the correction was more than 30%, a score of +1 was given. The most favourable outcome was a score of +2, when more than 50% of the pathology was corrected. Less than expected results (unchanged situation, <30% change) and the least favourable outcomes (increased pathology, >30% of the pre-treatment pathology) were scored −1 and −2 respectively. The scores of all individual goals were summed and converted into a standard *T*-score with an equal weight for each goal.[19,20] Converted GAS scores under 50.0 were considered non-successful treatments. Scores of 50.0 or more represented successful treatments. In this explorative study, we aimed for discriminating groups. Cut-off scores were introduced to define clear treatment success or failure (excluding treatments with minor success or failure). Scores below P25 (37.9) and above P75 (64.6) (Fig. 2) were taken into consideration as a first reference for clear failure and success. In a second step, the number of failure and success scores (scores −1, −2 and +1, +2 respectively) were defined in each group. In order to be sure of a clinically meaningful sample, it was decided to include all results which had a clear failure (scores −1, −2) or success (scores +1, +2) for at least half of the individually calculated goals. With this determination, cut-off scores of respectively 40.0 (LR-group = low response group) and 60.0 (HR-group = high response group) became evident and were used for final analysis. An accuracy study concerning intra- and interrater reliability has been performed on the GAS results of an independent group of 30 children. The patients specific goals were defined and scored twice by the same and another independent assessor with an interval period of 6 months. Excellent GAS intra- and interrater reliability was obtained for the converted total GAS score (Intraclass Correlation Coefficient (ICC) = 0.988 and Standard Error of Measurement (SEM) = 0.964 for intrarater reliability; Intraclass Correlation Coefficient (ICC) = 0.945 and Standard Error of Measurement (SEM) = 1.992 for interrater reliability).

For statistical analysis, differences of group characteristics for continuous and categorical data were analysed by an independent sample *t*-test and Chi-square respectively ($\alpha = 0.05$). All reported *p*-values are two-sided. A set of characterisctic variables (for which the *p*-value for the *t*-test or Chi-square test was less than 0.20) were subsequently combined in a multiple logistic regression model. All of the analyses were conducted by using SAS version 9.1 (SAS Institute Inc).

3. Results

Mean age at time of treatment of the 438 patients who met the inclusion criteria was 8 years 2 months (range 1 years 11 months to 22 years 11 months; SD 4 years). One-hundred and ten children (25.1%) had hemiplegia, 258 patients (58.9%) diplegia and 60 children (13.7%) quadriplegia. Ten patients (2.3%) suffered from other medical conditions such as chromosomal anomaly, spina bifida, meningitis and idiopathic tiptoeing.

Mean GAS score for the total group was 52.3 (SD 7.7, Median 52.5, P25 37.9, P75 64.3). Three-hundred and eight patients (70.3%) reached the expected GAS score of 50.0 and 130 patients (29.7%) had a converted GAS score of less than 50.0 (Fig. 1). Two extreme groups were defined: the group of children with a low GAS score who had a clear failure of response (GAS ≤ 40.0, *N* = 31/438) and the group with a high responsiveness (GAS ≥ 60.0, *N* = 75/438). Mean GAS scores of both groups are noted in Table 1.

3.1. *Patient characteristics*

There was no significant difference in diagnoses between both groups. The mean age at time of treatment of the LR-group (10 years 5 months, SD 3 years 4 months) was significantly higher compared to the HR-group (7 years 6 months, SD 4 years 4 months) ($p = 0.0013$, Table 1). In the LR-group, more patients had a functional classification of GMFCS I than in the HR-group. The LR-group did not include any children with a GMFCS V level. The other GMFCS levels (II, III, IV) were comparable between the two groups. Within the LR-group, the majority of patients had previously received BTX-A injections (70.9%). In the HR-group, 48.0% of the patients had received former BTX-A injections. Soft tissue lengthening and/or bony surgery was provided for approximately 10.0% of the patients

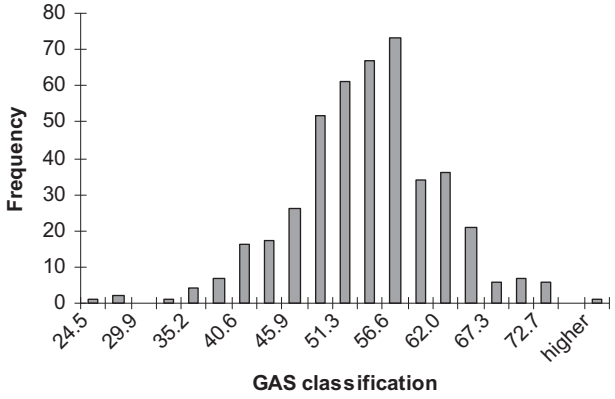

Fig. 1 – Histogram of GAS scores for the total patient group (N = 438). GAS = Goal Attainment Scaling.

Table 1 – Patient characteristics.

	LR-group $n = 31$	HR-group $n = 75$
Diagnosis		
Diplegia	20 (64.5%)	38 (50.7%)
Hemiplegia	7 (22.6%)	27 (36.0%)
Quadriplegia	3 (9.7%)	7 (9.3%)
Other Diagnoses	1 (3.2%)	3 (4.0%)
Age at treatment	10Y5M (3Y4M)	7Y6M (4Y4M)
GMFCS (for lower limb treatment) and upper limb treatment		
GMFCS I	15 (48.4%)	23 (30.7%)
GMFCS II	6 (19.4%)	19 (25.3%)
GMFCS III	7 (22.6%)	17 (22.7%)
GMFCS IV	1 (3.2%)	3 (4.0%)
GMFCS V	0 (0.0%)	6 (8.0%)
Upper limb	2 (6.5%)	7 (9.3%)
History		
Previous BTX-A treatment	22 (70.9%)	36 (48.0%)
Previous surgery	4 (12.9%)	6 (8.0%)
Mean number treated muscles	5.3 (SD 2.0)	5.1 (SD 2.1)
Mean dosage in U/kg bw	15.4 (SD 5.1)	15.2 (SD 7.2)
GAS mean score	36.6 (SD 4.1)	63.4 (SD 3.9)

Y = Years, M = Months; GMFCS = Gross Motor Function Classification System; U/kg bw = Units per kilo body weight; GAS = Goal Attainment Scaling; LR = Low responder; HR = High responder.

in each group before the screened BTX-A treatment (Table 1). No significant difference between the two groups was found regarding the number of former treatments and type of surgery in the past. Most of the patients in both groups did not use walking aids. This situation remained stable after the BTX-A treatment (Table 2).

3.2. *Injection characteristics*

Fig. 2 shows that in the LR-group 45.2% of the children ($N = 14/31$) received multi-level injections and another 45.2% received injections in the proximal parts of the lower limb (LL). This differed significantly from the HR-group, where 10.7% of the children ($N = 8/75$) were injected in the proximal parts of the LL and 69.3% of the children ($N = 52/75$) received multi-level injections ($p = 0.0024$). The mean of five injected muscle groups did not differ significantly between groups. The mean injected dosage for the total group was 16.78 U/kg BW (SD 6.46).

The mean total dosage was located around 15 U/kg bw in both study groups. No adverse events were reported.

Most popular treatment goals in the LR-group were goals related to the proximal parts of the LL. In the HR-group, goals concerning the distal parts of the LL were more frequently selected (Table 3).

3.3. *Aftercare*

The use and frequency of day and night orthoses, as well as frequency and duration of physical therapy sessions slightly increased in both study groups after treatment (Table 2), however no significant difference between groups were found. The fixed or hinged ankle foot orthoses (AFOs) and posterior leafsprings were the most popular day orthoses in both groups. Other types of orthoses (twister, swatch orthoses, UL orthoses) were used occasionally. Children in the LR-group used the standing table more frequently than children with a high responsiveness. The most frequently used night orthoses in the LR-group were a combination of AFO and knee extension brace, whereas children in the HR-group most frequently received a combination of AFO, knee extension brace and an abduction bar. There was a significant difference in the use of different types of casts between the two groups ($p = 0.0263$). Children in the HR-group received serial casts more frequently, particularly below the knee casts and combinations of knee extension and below the knee casts (Table 2). Mean duration for cast application within the LR-group was 14.4 days (SD 7.0). This did not differ significantly from the HR-group (mean 15.0 days, SD 5.9).

3.4. *Multiple logistic regression*

The combination of characteristic variables significantly discriminated between the LR- and HR-group ($p = 0.0110$, area under the curve from the ROC was 0.860). Table 4 gives more details of the multiple logistic regression analysis. According to the Wald criterion, three predictors (types of casts combined with BTX-A, distribution of treatment levels and age at the time of treatment) made a statistically significant contribution to the prediction of the outcome.

4. Discussion

Between and within children with CP, the variability in the degree of outcome of BTX-A injections is considerable. Some children have a lack of response, while others have a high responsiveness. The purpose of this study was to identify the crucial factors for a successful outcome after a standardised strategy for BTX-A treatment in children with CP. Therefore we sorted the total group into the low responders (GAS < 40) and the high responders (GAS > 60) and different features between both groups were evaluated.

Results show that more children in the LR-group had already received former BTX-A treatments when compared with the HR-group. According to the study by Herrmann et al.[23] repeated BTX-A treatments may be a possible risk factor for antibody formation. In some studies, the presence of antibodies was considered as an important cause of treatment failure.[11,23] However, it is unlikely that antibody formation is the reason why within our study group more children with former BTX-A injections showed a failure of treatment. In the HR-group, 48% of the children also received repeated BTX-A injections. Moreover, in an earlier study we found that dosages and treatment intervals between repeated multi-level BTX-A injections remained stable, thereby excluding the development of antibodies.[15] Koman et al.[24] also showed that bad responsiveness is unlikely to be due to the development of antibodies to BTX-A.

The age at injection may be an important factor of treatment success or failure.[25] In our study group, the age at time of treatment was significantly lower in the HR-group (7.5 years) compared to the LR-group (10.4 years). Wissel et al.[5] also found

Table 2 – Development of additional conservative therapy and aftercare.

	LR-group $n = 31$		HR-group $n = 75$	
	Pre BTX-A	Post BTX-A	Pre BTX-A	Post BTX-A
Day orthoses				
Not used	5 (16.1%)	3 (9.7%)	18 (24.0%)	6 (8.0%)
AFO, LSP	24 (77.4%)	27 (87.1%)	53 (70.7%)	65 (86.7%)
Others	2 (6.4%)	1 (3.2%)	8 (10.7%)	10 (13.3%)
<50% of the day	7 (22.6%)	9 (29.0%)	20 (26.7%)	12 (16.0%)
>50% of the day	19 (61.3%)	19 (61.3%)	37 (49.3%)	57 (76.0%)
Standing table	14 (45.2)	15 (48.4%)	25 (33.3%)	26 (34.7%)
Night orthoses				
Not used	10 (32.3%)	4 (12.9%)	40 (53.3%)	13 (17.3%)
AFO	3 (9.7%)	2 (6.4%)	8 (10.7%)	8 (10.7%)
AFO, KE	12 (38.7%)	13 (41.9%)	7 (9.3%)	22 (29.3%)
AFO, KE, Abd bar	6 (19.4%)	10 (32.3%)	15 (20.0%)	24 (32.0%)
Others	0 (0.0%)	2 (6.4%)	5 (6.7%)	8 (10.7%)
<50% of the day	11 (35.4%)	12 (38.7%)	17 (22.7%)	21 (28.0%)
>50% of the day	10 (32.3%)	15 (48.4%)	18 (24.0%)	41 (54.7%)
Physiotherapy				
Frequency/week	3.6 (SD 1.5)	4.4 (SD 1.9)	3.3 (SD 1.5)	4.2 (SD 1.9)
Duration (min)	42.4 (SD 16.0)	45.3 (SD 14.9)	42.1 (SD 14.0)	43.5 (SD 12.3)
Walking aids				
Not used	23 (74.2%)	23 (74.2%)	47 (62.7%)	47 (62.7%)
Kayewalker	7 (22.6%)	7 (22.6%)	17 (22.7%)	19 (25.3%)
Wheelchair/buggy	1 (3.2%)	1 (3.2%)	11 (14.7%)	9 (12.0%)
Serial casting				
Not used	–	4 (12.9%)	–	5 (6.7%)
Below knee	–	0 (0.0%)	–	9 (12.0%)
Knee extension	–	9 (29.0%)	–	9 (12.0%)
Combination	–	16 (51.6%)	–	47 (62.3%)
Others	–	2 (6.4%)	–	5 (6.7%)

BTX-A = Botulinum toxin type A; AFO = ankle foot orthoses; LSP = leafsprings; KE = knee extensors; Abd = abduction; LR = Low responder; HR = High responder.

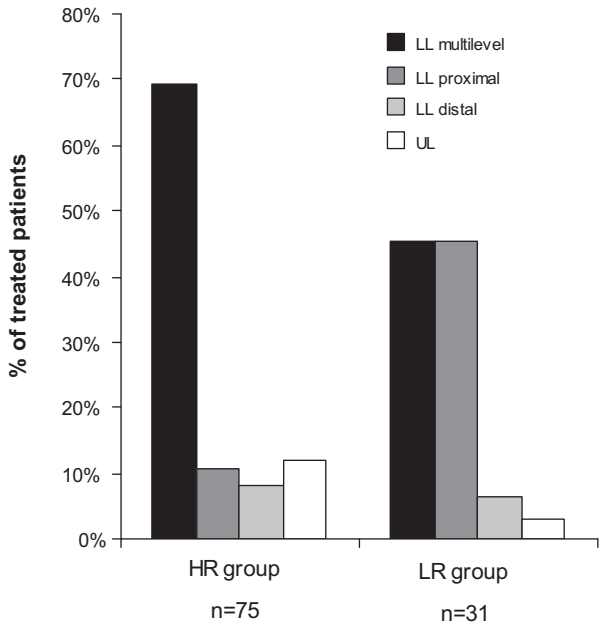

Fig. 2 – Distribution of treatment levels. LL = lower limb. UL = upper limb. HR = High responders. LR = Low responders.

that children aged 7 years or less scored significantly better on the Ashworth scale than older children ($p < 0.01$). When our two study groups were compared, it became clear that the children with a treatment failure had a slightly higher functional level (expressed by a lower GMFCS level). This high functional level can have a ceiling effect and therefore it may have been more difficult for these children to improve. For future GAS calculations, it might therefore be necessary to specify more sensitive goals for children with functionally high levels in order to verify minimal improvements as well (with more focus and weight on prevention than on correction). Linder et al.[25] evaluated functional outcome in 25 children with CP after 1 year of repeated BTX-A injections. Their study showed a tendency for moderately impaired children (GMFCS level III) to attain higher gains in GMFM scores. In our study, both subgroups had an equal amount of children with a GMFCS level of III. These children did not seem to be better responders than the others.

Some studies showed that treatments with high BTX-A dosages were more successful than treatments with low dosages. Wissel et al.[5] performed a randomized, double-blind study to assess dose–response relationships of local BTX-A treatment in the management of CP. They defined a high-dose (200U of Botox® per leg) and a low-dose group (100 U of Botox® per leg). Gait analysis revealed a significant difference

Table 3 – Most frequently used parameters to define treatment goals.

Gait and clinical parameters defining treatment goals (number of calculated goals)	Total group ($n = 2453$)	LR-group ($n = 174$)	HR-group ($n = 426$)
Knee angle at IC	10.1%	14.4%	8.7%
Max. knee extension in stance	8.6%	11.5%	8.5%
Max. hip extension in stance	7.6%	12.1%	7.3%
Hip extension deficit (Thomas test)	6.3%	9.2%	3.1%
2nd ankle rocker	5.7%	5.8%	7.0%
Ankle angle at IC	4.4%	4.0%	8.2%
Ankle ROM during push-off	3.8%	3.5%	3.1%
Spasticity of M. Gastrocnemius (Tardieu scale)	3.6%	1.7%	4.2%
Spasticity of Hamstrings (Tardieu scale)	3.6%	6.3%	2.1%
Hip adduction in stance	3.6%	3.5%	3.3%

IC = Initial contact; ROM = Range of motion; LR = Low responder; HR = High responder; Numbers are percentages of the total calculated goals per group.

in functional parameters such as gait velocity and stride length after the BTX-A treatment for the patients in the high-dose group when compared with the low-dose group ($p < 0.01$). Our study reports no significant difference of the injected BTX-A dosages between the LR- and HR-group. As all of our children received high total dosages, final conclusions about dosage dependency cannot be made. Within the high-dosage treatment strategy, however, dosage fluctuations seem not to have any further major impact.

Children with a low responsiveness received more BTX-A injections in the proximal parts of the LL and less multi-level injections compared to children with a high responsiveness. Proximal injections are linked to treatment goals of the proximal part of the LL. These goals may be more difficult to achieve than goals for the distal part. Recently, a higher number of muscle groups in multiple levels instead of single-level treatments has been promoted to achieve optimal results.[26,27] In the present study, children with a good response more frequently received multi-level treatments than children with a lack of response.

The patients within the HR-group were also most frequently casted with a combination of knee extension and ankle casts which has been associated with superior treatment outcomes earlier.[12,13]

In both groups, distal day orthoses were more popular than the proximal orthoses (twister, swatch), which seemed to be less tolerated. This may be one of the reasons why the proximal goals, which were scored more often in the LR-group, were less often achieved. The present study population consisted of children who where treated and evaluated according to a standardised strategy at the University Hospital of Pellenberg (Leuven, Belgium). This explains why all the additional conservative treatments (physical therapy, day and night orthoses) increased after BTX-A treatment.

To evaluate functional improvement, the GMFM, which was developed specifically for use in children with CP, is widely used and is now the standard outcome assessment tool for clinical intervention in children with CP.

But with the GMFM as the primary outcome measure in BTX-A studies, conflicting results have been reported. Failure

Table 4 – Multiple logistic regression results for the best-fitting model.

Variable	Wald chi-square	P	Estimated OR	95% CI
Number treated muscles	0.185	0.667	1.080	0.760–1.535
Serial casting	13.583	0.001		
'Not used' versus 'Below the knee casts'			0.192	0.015–2.395
'Not used' versus 'Knee extension or combination'			2.304	0.150–35.350
'Below the knee casts' versus 'Knee extension or combination'			12.018	3.078–46.921
Treatment specification	7.958	0.019		
'Lower limb multi-level' versus 'Lower limb proximal or distal'			4.733	1.349–16.607
'Lower limb multi-level' versus 'Upper limb'			0.379	0.026–5.431
'Lower limb proximal or distal' versus 'Upper limb'			0.080	0.006–1.091
Age (years) at treatment	7.192	0.007	0.808	0.692–0.944
Patient history	2.295	0.317		
'No treatments' versus 'Former BTX-A treatments'			2.818	0.637–12.474
'No treatments' versus 'Former surgical procedures'			3.854	0.488–30.450
'Former BTX-A treatments' versus 'Former surgical procedures'			1.367	0.227–8.253
Use of night orthoses post BoNT-A	3.582	0.167		
'Not used' versus '>50% of night'			1.471	0.321–6.743
'Not used' versus '< 50% of night'			0.454	0.106–1.948
'>50% of night' versus '<50% of night'			0.308	0.089–1.072

OR = Odds Ratio for high response; CI = Confidence Interval.

to detect improvement with a general quantitative measurement instrument could be caused by lack of sensitivity to a change at individual level. Therefore, Goal Attainment Scaling was used to evaluate the effects of the BTX-A treatment in the present study. The GAS was found to be useful to evaluate the effect of an intervention at individual level. The GMFM or other functional measurements are not standard included in the evaluation of children with CP in the Hospital of Pellenberg (Leuven, Belgium), therefore no results on functional gains have been included in this study.

The validity and reliability of GAS have been evaluated by several studies in different clinical areas.[21,22] The validity of GAS as a measure of motor change was determined by Palisano et al.[20] They report a satisfactory interrater reliability before ($\kappa = 0.89$) and during their trial ($\kappa = 0.75$). Our own accuracy study indicated excellent intra- and interrater reliability for GAS.

The results of this study may provide important information concerning the identification of crucial features for favourable response to BTX-A injections in children with CP. The key factors seemed to be age, functional level, specification of treatment goals, levels of treatment and casting. More future scientific research should be performed to define the factors mentioned above more specifically. In this way, it may be possible to get a more focused patient selection for future BTX-A treatments and a better prognosis of the outcome.

Acknowledgements

The authors wish to thank Mr. Jozef Nijs for performing statistical analysis. We also want to acknowledge the multidisciplinary CP team of Pellenberg University Hospital. This research project was supported by an unrestricted educational grant from Allergan, Inc. (USA).

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