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Effective Results With Botulinum Toxin in Cerebral Palsy

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This study evaluated the improvement in clinical measures and quality of life (QOL) among patients with cerebral palsy treated with botulinum toxin type A. Fifty-seven parents of cerebral palsy patients who used botulinum toxin during the time of the study were enrolled. The QOL questionnaires included the following: Child Caregiver Questionnaire, Pediatrics Outcomes Data Collection Instrument, and clinical evaluations. The questionnaires were administered before the first use of botulinum toxin and approximately 1 year later, a mean interval of 13.8 months. Treatment resulted in clinical improvement in tone, upper limb function, and Gross Motor Function Classification System score. Better outcomes were observed in patients younger than 6.5 years. QOL questionnaires revealed a tendency toward improvement in the comfort dimension of the Child Caregiver Questionnaire as well as in the upper extremities and physical functions, transfers and basic mobility, and global function and symptom of the Pediatrics Outcomes Data Collection Instrument. The QOL measures correlated with clinical evaluations. Patients with low cognitive ability and refractory epilepsy had the worst results. Children and adolescents have reduced spasticity and experience good results in the clinical measurements and in QOL after treatment with botulinum toxin.

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Introduction

Cerebral palsy (CP) "describes a group of permanent disorders of the development of movement and posture that cause activity limitation and are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain" [1]. Multidisciplinary treatment teams should be developed around the needs of each patient to provide continuously updated global care during the patient's lifetime; this would aid in reducing the constant stress in patients and their families that is often caused by this disease. Patients are typically subjected to multiple treatment options for prolonged periods; at present, botulinum toxin type A (BTXA) is an important modality for the treatment of patients with CP [2-5]. Several studies that used the Ashworth scale and goniometry demonstrated that BTXA is a useful tool for the management of spasticity in children and adults [6-16]. More recent studies have used functional outcomes, 3-dimensional gait analysis, and self-perception and pain scores [16-20]. The assessment of quality of life (QOL) may reflect the effect of clinical intervention [21-23]. Simões de Assis et al. [24] demonstrated that the Pediatric Outcomes Data Collection Instrument (PODCI) and the Child Caregiver Questionnaire (CCQ) could capture changes in outcome in children with CP who were treated with BTXA. Redman et al. [25], using health-related QOL measures, demonstrated no statistically significant differences between BTXA-treated children with hemiplegic CP and the control group. By means of an economic approach, 2 studies concluded that BTXA is an effective, safe, and acceptable treatment modality that is associated with only a modest increase in direct costs per child per year [26,27].

The goal of the current study was to verify whether QOL could detect differences in well-being in children and adolescents with CP treated with BTXA and whether the expectations of the patients' families and their perceptions of the happiness of their children correlated with medical evaluations.

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Patients and Methods

This was a prospective study of patients seen at the Pediatric Spasticity Outpatient Clinics (PSOC) at the Centro de Neuropediatria (CENEP) of the Hospital de Clínicas of the Federal University of Paraná, Curitiba, Paraná, Brazil, initiated at the beginning of 2001. It resulted from a partnership with the Health Department of the State of Paraná, which supplied the BTXA. The PSOC team consists of professionals and volunteers from the following areas: child neurology, pediatric orthopedics, physical therapy, occupational therapy, nursing, social work, anesthesia, psychology, neuropsychology, pedagogy, pediatrics, fellowships, and administration. All of the patients at the PSOC received community-based physiotherapy and occupational therapy, which consisted of 1 to 2 physical therapy sessions and 1 occupational therapy session per week. The caregivers received instructions from our team regarding daily stretching, positioning, and use of extending and polypropylene splints when appropriate to optimize the results of therapeutic management. Physiotherapists and occupational therapists of the CENEP also guided the professionals outside our team who were involved in the patients' rehabilitation.

During the consultation session, a treatment plan was formulated for each child before the BTXA treatment. This plan included realistic, prioritized goals, target muscle identification, calculation of the injection dosage, assessment of the need for casting, and the prescription of ankle-foot orthoses.

Possible target muscles for the BTXA injections included the following: adductor pollicis, flexor pollicis brevis and longus, flexor digitorum superficialis, pronators, flexor carpi ulnaris and radialis, brachioradialis and pectoralis major, iliopsoas, adductors, medial hamstrings, gastrocnemius, soleus, and tibialis posterior muscles. With the patient under general anesthesia, the injections were administered under electrostimulation guidance (model NS 252J; Fisher & Paykel Electronics, Auckland, New Zealand) to at least 2 sites per muscle belly and with a maximum dosage of 50 U per site. Selection of the muscles for blockade and BTXA injections were performed by the PSOC coordinator (L.H.C.S.). The toxin used was BTXA (Botox; Allergan, Irvine, CA), and the maximum dose was 15 U/kg per session up to 500 U, with a minimum interval of 3 months between sessions. A dilution of 100 U in 1 mL of 0.9% NaCl was used. Orthoses to support full knee-extension in the terminal stance, which were either stiff insoles or ankle-foot orthoses, were prescribed. Casting was performed if the passive ankle dorsiflexion with extended knee (measured during screening) was less than 0 degrees and after BTXA injection under anesthesia. If the foot was placed in a subtalar neutral position with the ankle at 10 degrees of dorsiflexion, the cast was maintained for 3 weeks and then removed; if this was not possible, serial casting was applied weekly, with each successive cast applying progressively greater dorsiflexion. The patients who received treatment between February 2003 and June 2005 were assessed for eligibility for inclusion in the study.

We evaluated 57 patients whose caregivers answered 2 QOL questionnaires, the first before the first use of BTXA and the second approximately 1 year after the use of BTXA. Patients were excluded if their parents refused to participate in the study, were illiterate, or did not answer the second questionnaire. This work was approved by the Scientific Committee of the Department of Pediatrics and the Human Research Ethics Committee of the Clinics Hospital of the Federal University of Paraná. Consent to participate in the study was obtained by signing the free and informed consent form.

Outcome Measures

The Ashworth scale [28] for spasticity, Physician's Rating Scale (PRS) of the dynamic gait pattern during active walking [29], upper limb Physician's Rating Scale (UPRS) [12], and Gross Motor Function Classification System (GMFCS) [30] were used to perform the clinical evaluations by L.H.C.S. The Ashworth scale provides scores for the adductor pollicis, finger flexors, pronators, wrist flexors, and elbow flexors, resulting in an upper limb score as suggested by Brown et al. [31]; the minimum score was 5 and the maximum was 25. For the lower limbs, the plantar flexors were considered, with a minimum score of 1 and a maximum score of 5.

Evaluation of QOL

Two instruments were used to evaluate QOL. They were based on self-reports from the guardians while the patients were waiting to be seen at the clinic. The questionnaires were translated into Portuguese (http://www.hc.ufpr.br/acad/pediatria/index.htm) and then back into English by a native speaker, and subsequently, both English versions were compared by an arbitrator. Explanations for how to answer the questionnaires were provided by T.R.S.A., who was unaware of the patients' clinical and therapeutic history and/or their classification. All questionnaires were checked after they were returned to verify that all of the fields were completed. The CCQ [23] comprises 4 domains: personal care (PEC), positioning/transferring (POSIC), comfort (COMF), and interaction/communication (INTER), and it provides a global score (G). The PODCI [32] was used in a format that was answered by the children's parents and/or tutors. It included the following dimensions: upper extremities and physical function (UEP), transfers and basic mobility (TBM), sports and physical function (SPF), pain and comfort (PC), expectations (EXP), happiness (HAPP), and global function and symptoms (GFS). GFS was obtained from the variables of the UEP, TBM, SPF, and PC scores. Outcome measures were obtained before blockade with BTXA and 1 year after the blockade. Data obtained from the charts included the following: age, sex, education, per-capita income, informant's relationship to the patient, caregiver's education level, date of the latest BTXA injection, follow-up at PSOC, and adverse events related to the BTXA injection. The presence of epilepsy and its control and cognition level were determined.

Statistical Analysis

The mean, S.D., and range were used for descriptive purposes. The nonparametric Wilcoxon test was used to compare the 2 different time points; differences in the scores obtained for the time points before and after the intervention were compared (gain). The concordance between the QOL instruments and the clinical measures was determined by Spearman's correlation coefficients. To evaluate the association among quantitative variables, the Mann-Whitney test and Fisher's exact test for nominal dichotomous variables were performed. To estimate the proportions of cases of improvement in relation to the categorical variables, a 95% confidence interval was used. The correlation between age and improvement variables was performed by receiver operating characteristic curve analysis to determine the ideal cutoff for optimum specificity and sensitivity. For all tests, a P value of <0.05 was considered statistically significant.

Results

There were 57 patients (34 boys) with a mean age of 6 years and 2 $\pm$ 3.4 months S.D. (median 5 years and 5 months). The median interval between the 2 questionnaire administrations was 14 months and ranged from 11 to 18 months. The number of sessions of BTXA treatment between the 2 questionnaire administrations ranged from 1 to 4 and demonstrated a median of 2. Twenty patients underwent only 1 session of BTXA treatment. Thirty-seven patients underwent 2 to 4 sessions, with an interval between sessions of 3.5 to 8 months (median 6.5 months). The mean interval between time after the end of the last injection was 7 $\pm$ 4.4 months, with a range of 1 to 17 months. The GMFCS at the first evaluation consisted of the following levels: I—7, II—18, III—6, IV—13, and V—13. Spasticity was predominant in 45 patients, of whom 21 had hemiplegia, 14 had diplegia, and 10 had tetraplegia. Adequate cognition was observed in 31.5% of the patients, mild impairment in 33.5%, and mental retardation in 35%. Epilepsy was observed in 30% of the patients; 13 patients had no

seizures—9 were controlled with one medication and 4 with two. Four patients manifested refractory epilepsy.

The per-capita income ranged from 50 to 650 reais (mean 209 ± 134 reais). The minimum wage in Brazil is 465 reais. Twenty-four participants received a full disability pension. The education level of the caregivers was predominantly incomplete junior high school.

The outcomes measures are listed in Table 1. Weight gain during the study ranged from −1,500 g to 7,900 g, with a median of 2,200 g. Only one patient lost weight in association with depression. Increases in height ranged from 0 to 18 cm, with a median of 7 cm. The GMFCS ranged from I to V at the 2 questionnaire administrations; 25 patients increased one level, 1 patient increased two levels, 31 remained at the same level, and 7 were already at level I at the first evaluation (Table 2).

Comparison Between Outcome Measures and Influence of Patient Age, Number of BTXA Sessions, Sociocultural Factors, Cognition, and Epilepsy

Younger patients manifested a greater reduction in spasticity after intervention than older patients. The cutoff was optimized with the aid of receiver operating characteristic curve analysis, and the optimum specificity (60.0%, 95% confidence interval = 38.7-78.8) and sensitivity (81.3%, 95% confidence interval = 63.6-92.7) were obtained at a cutoff value off 78 months (area under the receiver operator curve = 0.68, $P = 0.015$). The age of the child was negatively correlated with TBM gain ($r = -0.36$, $P = 0.008$), SPF gain ($r = -0.28$, $P = 0.042$), HAPP after intervention ($r = -0.33$, $P = 0.018$), HAPP gain ($r = -0.35$, $P = 0.013$), GFS after intervention ($r = -0.27$, $P = 0.049$) and GFS gain ($r = -0.30$, $P = 0.03$). In the CCQ, the age of the child was negatively correlated with POSIC after intervention ($r = -0.31$, $P = 0.017$), INTER after intervention ($r = -0.33$, $P = 0.013$), and G after intervention ($r = -0.28$, $P = 0.036$).

The number of BTXA injections was positively correlated with the reduction in spasticity ($r = 0.27$, $P = 0.040$) and negatively correlated with SPF before intervention ($r = -0.31$, $P = 0.028$), POSIC after ($r = -0.29$, $P = 0.027$), and UPRS gain ($r = -0.63$, $P = 0.022$). The mean interval between injections demonstrated a statistically significant correlation only with UPRS gain ($r = 0.83$, $P = 0.021$).

Patients with refractory epilepsy had worse Ashworth scores at the 2 questionnaire administrations, and although they demonstrated a tone reduction during the study period, it was not statistically significant. Similar results have been observed for patients with mental retardation. Patients with refractory epilepsy demonstrated the worst GMFCS scores both before and after the intervention and did not improve with treatment. They also demonstrated lower scores for

Table 1. Outcomes of study participants

Characteristic	Before/After	Before	After	*P**
Ashworth score, mean	57/57	23.79	22.47	0.015
PRS right side, median	34/34	10	12	NS
PRS left side, median	34/34	11	12	NS
UPRS right side, median	6/6	10	19	0.03
UPRS left side, median	10/10	16.9	18.5	0.03
CCQ, PEC	57/57	71.54 (28.19)	71.94 (26.54)	0.78
CCQ, POSIC	57/57	78.80 (27.08)	80.92 (24.59)	0.68
CCQ, COMF	57/57	90.80 (15.23)	93.29 (11.30)	0.064
CCQ, INTER	57/57	78.72 (24.62)	82.01 (23.58)	0.109
CCQ, G	57/57	79.00 (19.19)	80.96 (18.37)	0.387
PODCI, UEP	55/55	52.72 (33.45)	60.97 (36.57)	<0.001
PODCI, TBM	53/54	55.98 (33.35)	63.39 (34.17)	0.02
PODCI, SPF	51/54	48.21 (27.97)	52.00 (31.23)	0.14
PODCI, PC	57/57	84.69 (17.01)	82.98 (23.15)	0.72
PODCI, HAPP	48/50	83.90 (16.73)	89.25 (14.43)	0.209
PODCI, GFS	50/52	60.43 (23.95)	75.95 (25.13)	0.034

*Wilcoxon test.

Abbreviations:
CCQ = Child Caregiver Questionnaire
COMF = Comfort
G = Global
GFS = Global function and symptoms
HAPP = Happiness
INTER = Interaction/communication
NS = Not statistically significant
PC = Pain and comfort
PEC = Personal care
PODCI = Pediatric Outcomes Data Collection Instrument
POSIC = Positioning/transferring
PRS = Physician Rating Scale
SPF = Sports and physical function
TBM = Transfers and basic mobility
UEP = Upper extremities and physical function
UPRS = Upper limb Physician's Rating Scale

Table 2. Gross Motor Function Classification System of study participants*

GMFCS Before	GMFCS After I	II	III	IV	V	GMFCS Before
I	7	0	0	0	0	7
II	10	8	0	0	0	18
III	1	2	3	0	0	6
IV	0	0	9	4	0	13
V	0	0	0	4	9	13
Total	18	10	12	8	9	57

*Comparison between time before and after, $P < 0.001$ (nonparametric Wilcoxon test, $P < 0.05$). The 95% confidence interval between cases with improvement in GMFCS is 32.70-58.5.

Abbreviation:
GMFCS = Gross Motor Function Classification System

PEC after invention ($P = 0.03$), POSIC after invention ($P = 0.03$), INTER before ($P = 0.007$) and after ($P = 0.001$) intervention, and global score before ($P = 0.02$) and after ($P = 0.002$) intervention of the CCQ and in the dimensions UEP after intervention ($P = 0.001$) and SPF after intervention ($P = 0.006$) and a decreased UEP gain ($P = 0.03$) of the PODCI. Patients with preserved cognition had better scores at the time after intervention for PEC ($P = 0.004$), POSIC ($P < 0.001$), COMF ($P = 0.02$), INTER ($P < 0.001$), and G ($P < 0.001$) of the CCQ and for the UEP ($P < 0.001$), TBM ($P < 0.001$), HAPP ($P = 0.03$), and GFS ($P < 0.001$), and for TBM gain ($P = 0.01$) and SPF gain ($P = 0.02$) of the PODCI.

Children with caregivers who had more education demonstrated the highest gains in GMFCS ($P = 0.004$). Patients with families that had a larger per-capita income had better scores in the comfort dimension and for the global score of the CCQ after intervention ($r = 0.38$, $P = 0.008$ and $r = 0.29$, $P = 0.05$) and for TBM gain ($r = 0.35$, $P = 0.020$) in the PODCI. Patients with better GMFCS scores had larger weight gains. An inverse relationship was observed between weight gain ($r = -0.38$, $P = 0.004$) and stature ($r = -0.27$, $P = 0.04$) in the comfort dimension of the CCQ. Weight gain was positively correlated with the highest scores after intervention for the UEP ($P = 0.001$), TBM ($P < 0.001$), SPF ($P < 0.001$), PC ($P = 0.02$), and GFS ($P < 0.001$), and stature gain correlated positively with SPF after intervention ($P = 0.05$).

Relationships Between Clinical Measures and QOL Instruments

The Ashworth score before treatment correlated negatively with GMFCS before treatment ($r = -0.52$, $P < 0.001$), and the right PRS ($P = 0.009$) demonstrated no correlation with UPRS before treatment. The Ashworth score before treatment correlated negatively with all dimensions of the PODCI, excluding pain and comfort, UEP ($r = -0.49$, $P < 0.001$), TBM ($r = -0.45$, $P = 0.001$), SPF ($r = -0.50$, $P < 0.001$), HAPP ($r = -0.44$, $P = 0.002$), and GFS ($r = -0.52$, $P < 0.001$). The same was observed for the CCQ dimensions before treatment: PEC ($r = -0.42$, $P = 0.001$), POSIC ($r = -0.31$, $P = 0.02$), COMF ($r = -0.40$, $P = 0.002$), INTER ($r = -0.45$, $P < 0.001$), and G ($r = -0.48$, $P < 0.001$).

The Ashworth score after treatment correlated negatively with GMFCS after intervention ($P < 0.001$) and tended toward a negative correlation with the left UPRS ($r = -0.54$, $P = 0.07$), but not with PRS after treatment. The Ashworth score after treatment correlated negatively with all dimensions of the PODCI after treatment, excluding pain and comfort, UEP ($P < 0.001$), TBM ($P < 0.001$), SPF ($P < 0.001$), HAPP ($P = 0.03$), and GFS ($P < 0.001$). The same was observed for the CCQ dimensions after intervention, PEC ($P = 0.005$), POSIC ($P < 0.001$), COMF ($P = 0.05$), INTER ($P < 0.001$), and G ($P < 0.001$). The gain observed in the Ashworth scale correlated with the gain in the TBM ($P = 0.05$) and GFS ($P = 0.03$) of the PODCI. Patients who demonstrated a larger reduction in spasticity had a greater gain in the POSIC dimension ($P = 0.04$) of the CCQ.

The PRS scale (right and left side) before treatment correlated positively with GMFCS before treatment ($P < 0.001$). The left PRS scale demonstrated an association with TBM ($P = 0.02$), SPF ($P < 0.001$), and GFS ($P = 0.01$) of the PODCI before treatment. The PRS scale (right and left) after correlated negatively with GMFCS after treatment ($r = -0.83$, $P < 0.001$). The right PRS after correlated positively with UEP ($P = 0.05$), TBM ($P < 0.001$), SPF ($P < 0.001$), and GFS ($P = 0.001$) after treatment. The left PRS after correlated positively with TBM ($P < 0.001$), SPF ($P < 0.001$), and GFS ($P = 0.001$) after treatment.

The UPRS scale before and after treatment correlated positively with the POSIC dimension of the CCQ after treatment ($r = 0.90$, $P = 0.005$ and $r = 0.77$, $P = 0.02$, respectively).

The GMFCS score before treatment correlated positively with Ashworth values before treatment ($P < 0.001$) and negatively with the left and right PRS before-treatment values ($r = -0.68$, $P < 0.001$ and $r = -0.62$, $P < 0.0001$, respectively), UEP ($P = 0.02$), TBM ($P < 0.001$), SPF ($P < 0.001$), and GFS ($P < 0.001$) of the PODCI before treatment and with PEC ($P = 0.005$), POSIC ($P = 0.02$), INTER (P = 0.02), and G (P = 0.002) of the CCQ before treatment. The GMFCS values after treatment correlated positively with the Ashworth scale after treatment ($P < 0.001$) and negatively with the left and right PRS ($r = -0.81$, $P < 0.0001$ and $r = -0.77$, $P < 0.0001$, respectively), UEP ($P < 0.001$), TBM ($P < 0.001$), SPF ($P < 0.001$), HAPP ($P = 0.001$), and GFS ($P < 0.001$) of the PODCI after treatment, and with PEC ($P < 0.001$), POSIC ($P < 0.001$), COMF ($P < 0.001$), INTER ($P = 0.035$), and G ($P < 0.001$) of the CCQ after treatment.

Relationships Between QOL Instruments

All of the scores for the dimensions of the PODCI before treatment correlated with the scores of the CCQ

before treatment, excluding PC with PEC, HAPP with PEC, and HAPP with POSIC. At the time after treatment, all dimensions of the PODCI and CCQ were correlated, excluding PC with PEC and POSIC and HAPP with COMF. The gain obtained in the SPF dimension of the PODCI correlated with the gain in the INTER dimension of the CCQ (P = 0.04). The HAPP gain of the PODCI correlated with the POSIC gain of the CCQ (P = 0.04) (Table 3).

Discussion

This consecutive study demonstrated that multilevel BTXA injections provided a reduction in spasticity and an improvement in UPRS and QOL at the 1-year follow-up. The mean interval between the moment after treatment in the study and the last injection was 7 months, with some patients having an interval of up 17 months; this provided the first opportunity to observe a long follow-up of patients treated with BTXA. Improvement in the level of GMFCS was observed in 44% of the patients. Ten patients at level II reached level I, 9 patients at level IV reached level III, and 1 patient at level III reached level I. Although this system is a standardized method to classify gross motor function in children with CP and Palisano et al. [33] provided evidence of GMFCS stability, this system can help clinicians determine realistic goals for patients. For example, when a doctor examines a child at level IV, he or she should consider how to help the child improve to level III. To achieve this goal, BTXA injection in the upper extremities and proximally in the lower limbs with the aid of ankle-foot orthoses could be an efficient therapeutic plan. Better upper extremity function correlated with improvement in the scores of the QOL, especially in positioning and transferring. In patients at level II in the present study, BTXA was used mainly in the gastrocnemius and the soleus muscles.

How can the use of BTXA to reduce spasticity improve a child's ability to reach the next level? Alterations of the GMFCS level demand time, and they occur in a consecutive way, with the patients demonstrating gradual improvements from level to level. In the present study, the follow-up period of 1 year was only sufficient for a patient to change 1 level. Therefore, there is a need for longer study periods to assess the systematic consolidation and acquisition of new abilities. The improvement in GMFCS was corroborated by the improvement in the UPRS and PODCI (UEP, TBM, and GFS) in the moment after therapy. At present, the possibility of modifying the progress of a child with CP and the good prognostic factors of youth, preserved cognition, and absence of refractory epilepsy should be considered by all professionals involved to enable them to provide better patient care. Caregivers with a higher education level can provide training situations at home with better understanding and frequency, which would help the child acquire new motor skills. Physiotherapists should to help families understand the treatment goals and to be aware of the importance of specific replicable tasks.

In the present study, children younger than 6 demonstrated a larger reduction in spasticity. Further, daily practice revealed that children who received earlier BTXA treatment had a better chance of acquiring new abilities,

Table 3. Correlations between dimensions of the PODCI and the CCQ

		PEC		POSIC		COMF		INTER		G	
		Before	After	Before	After	Before	After	Before	After	Before	After
UEP	Before	<0.001		<0.001		0.004		<0.001		<0.001	
	After		<0.001		<0.001		0.05		<0.001		<0.001
TBM	Before	<0.001		<0.001		0.02		<0.001		<0.001	
	After		<0.001		<0.001		0.004		<0.001		<0.001
SPF	Before	<0.001		<0.001		0.01		0.05		0.05	
	After		<0.001		<0.001		0.004		<0.001		<0.001
PC	Before	0.31		0.03		0.01		0.05		0.05	
	After		0.19		0.09		0.03		0.05		0.04
HAPP	Before	0.15		0.26		<0.001		0.004		0.019	
	After		<0.001		0.004		0.11		<0.001		<0.001
GFS	Before	<0.001		<0.001		<0.001		<0.001		<0.001	
	After		<0.001		<0.001		0.004		<0.001		<0.001

Abbreviations:
CCQ = Child's Caregiver's Questionnaire
COMF = Comfort
G = Global
GFS = Global function and symptoms
HAPP = Happiness
INTER = Interaction/communication
PC = Pain and comfort
PEC = Personal care
PODCI = Pediatric Outcomes Data Collection Instrument
POSIC = Positioning/transferring
SPF = Sports and physical function
TBM = Transfers and basic mobility
UEP = Upper extremities and physical function

especially those related to the use of the upper extremities. Children with CP almost always acquire gait through the use of a walker, and therefore, regular use of the upper extremities is a prerequisite to walk. The number of BTXA injections was positively correlated with the reduction of spasticity but negatively with SPF before therapy and UPRS gain; this result highlights that patients with a decreased requirement for BTXA have a better prognosis for acquiring more advanced abilities, such as those involved in participation in sports and the use of the upper extremities. Patients with large intervals between injections demonstrated greater gain in the UPRS, which underscores the finding that patients with an increased requirement for BTXA are more compromised and therefore have worse prognoses for good outcomes.

The relationships between intelligence and simple and complex motor proficiency have been documented by Groden [34], and in our study, children with generalized adaptive deficiency demonstrated the worst motor prognosis. Although patients with upper motor neuron syndrome display compromised strength, sensitivity, and perception, the clear relationship observed in the present study among the reduction in spasticity and improvement in functional measurements and QOL demonstrated that the degree in spasticity is an important factor in the acquisition of motor functions. The doctor's impression of a good response to treatment correlated well with that of the caregiver. Although the perception of the caregiver as well as the health of the child are influenced by many variables, which include but are not limited to economic restrictions, the caregiver's mood, and the child's participation in the school and community, these findings highlight the value of the perspective of the caregiver. However, caution should be used when interpreting some of the data as indicative of a good prognosis. For instance, if the caregiver finds that taller, heavier children experienced increased difficulty in manipulations that produce intense pain, this perspective is comprehensible for those responsible for the daily care and transport of the children.

The questionnaires we used were developed for children: one was general (PODCI), designed for children with musculoskeletal changes, and the other was specific (CCQ), created for children with CP. CCQ was the easiest to administer and represents a good general QOL measure, but patients with better functional levels (I and II GMFCS) exhibited a ceiling effect. However, the PODCI provided more reliable information concerning more specific functional activities. Vitale et al. [22] demonstrated that PODCI was more sensitive to differences in diplegic and hemiplegic patients, but quadriplegic patients exhibited a ceiling effect in 2 of the 12 domains of that questionnaire; CCQ in our study was more effective is this group of patients (more compromised patients). Barnes et al. [32] conducted a study in ambulatory patients with CP and with GMFCS levels I through III and concluded that PODCI is effective regardless of the clinical classification. Similar findings were obtained in the present study, and mean gain was 3% in the global score of the PODCI. McMulkin et al. [35] demonstrated a mean gain of 5% after orthopedic surgery. The use of PODCI to evaluate QOL in children with several orthopedic conditions has demonstrated that its indicators, particularly those related to motor function, may be used to monitor stabilization, deterioration, or clinical improvement and are valid for evaluating the benefits of various orthopedic interventions. The same authors used the PODCI in 84 healthy children and adolescents and obtained high scores (close to or equal to 100); a score of $\leq$80 meant that the child or adolescent had a lower than expected functional capacity [36]. In the present study, the CCQ and PODCI dimensions demonstrated a good correlation.

From the present results, we can conclude the following: (1) BTXA injections promoted improvements in clinical evaluations and in QOL instruments; (2) the clinical measures and instruments used to assess QOL (PODCI and CCQ) were sensitive enough to detect changes over time in children with CP, were easy to administer, and were inexpensive; (3) the QOL measures were consistent with the clinical evaluations; and (4) children younger than 6 with preserved cognition and without refractory epilepsy had a better functional prognosis after BTXA injection. Additional studies with a larger number of patients in each of the GMFCS levels may be necessary to confirm these findings and to investigate whether the improvements in the clinical evaluation and QOL are maintained with a longer follow-up, especially during adolescence.

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