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Beneficial effect of botulinum toxin type A (BTX-A) in treatment of spasticity in patients with cerebral palsy

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Abstract
Background: Cerebral palsy (CP) is the greatest cause of motor disability in childhood, which is commonly linked to spasticity, which restricts functional capability and movement. BTX-A is an example of a focal treatment that is used instead of systemic medications or surgery by temporarily reducing the muscle tone by blocking the release of acetylcholine at the neuromuscular junction. The objective of this study was to assess the positive impacts and time course of the BTX-A injection to reduce spasticity and increase gross motor functions of children with CP in Baghdad.
Methods: A retrospective observational cross-sectional study will be done among 149 children (<6 years) with spastic CP receiving BTX-A between January 2023 and January 2025 at the Central Teaching Hospital of Children. At baseline, 2 months, and 4 months post-injection, spasticity was measured with the help of the Modified Ashworth Scale (MAS) and Tardieu Scale, whereas gross motor function was measured using Gross Motor Function Measure-88 (GMFM-88).
Results: The 2 months of results showed significant improvement in spasticity on both MAS and Tardieu scales ($p<0.05$) and statistically significant improvement in GMFM-88 scores ($p<0.05$), which showed improved motor functioning. Nevertheless, after 4 months, all measures showed a decrease, which is consistent with the established pharmacodynamic time of BTX-A.
Conclusion: BTX-A is an effective form of short-term spasticity treatment and gross motor function enhancement in children with CP, especially in the first two months of treatment. Its therapeutic effect decreases four months, which justifies the repeated treatment cycles with 3-4 months of intensive physiotherapy. BTX-A is a vital part of multidisciplinary management of spasticity in the resource-limited context that has functional and psychosocial advantages.

Keywords: Botulinum toxin type A, cerebral palsy, spasticity, motor function, pediatric rehabilitation, Iraq

Introduction
Cerebral palsy (CP) is the most commonly occurring cause of motor disability during childhood with a prevalence rate of about 2-3 per 1000 live births in the world [1]. CP refers to a cluster of lifelong disorders of movement and postural development, which result in the limitation of activities due to non-progressive interrupts in the developing fetal or infant brain [2]. The condition is caused by a number of perinatal insulators, including hypoxic-ischemic encephalopathy, intracranial hemorrhage, and inborn infections, which lead to central nervous system irreversible damage [3].
Spasticity or velocity-dependent elevation of muscle tone with exaggerated jerks of the tendons is one of the most disabling traits of CP and is found in about 80 percent of children with the condition [4]. The motor disorder is highly detrimental to functional capacities, the ability to be involved in a daily activity as well as affecting the efficacy of physiotherapy. The pathophysiology is the interruption of the brain to spinal cord descending inhibitory pathways and this leads to stretch reflex arc hyperactivity, which then leads to an increase in muscle tone [5].
Conventional management strategies have incorporated oral medication (baclofen, diazepam), physical interventions, orthosis and surgery [6]. Nevertheless, these methods have their flaws such as systemic side effects, failure of conservative therapy, and invasiveness of surgery. BTX-A has currently become a promising focal treatment option between conservative and surgical treatment [7].
The therapeutic effect of BTX-A is associated with the inhibition of the release of acetylcholine at the neuromuscular junction, which causes temporary chemical denervation and weakens the tone of muscles at the injection sites [8]. This process gives a period of

spasticity of the focal region that is about 3-6 months and within this period intensive physiotherapy can be timely applied. There are several randomized controlled trials that have shown the BTX-A effectiveness in the spasticity reduction, gait pattern improvement, and functional improvements in children with CP [9, 10]. The intervention will be of special usefulness when it is part of the comprehensive interdisciplinary treatment systems that also incorporate physiotherapy, occupational therapy, and orthotic management [11].

In the third world such as Iraq, there has been reduced access to advanced therapeutic modalities which is a result of social economic and healthcare system problems. Nevertheless, in recent years, the availability of BTX-A in large pediatric hospitals has been increasing, which has provided new hope to children with CP and their families [12], Understanding the benefits of BTX-A treatment and their temporal change in the local population is the key to optimization of treatment protocols and resources distribution.

The objectives of this retrospective study was to assess the positive outcomes of BTX-A injection on the reduction of spasticity and deformity of the upper and lower limb muscle of CP patients, and specifically on gross motor functions improvement and quantitative measurement of the spasticity reduction over four-month follow-up.

Methods

Study Design and Population

It was a retrospective observational study of clinical data of 149 children with CP (91 males [61%], 58 females [39%]) aged less than 6 years receiving BTX-A injections at the Consultatory Unit of Pediatric Neurology, Central Teaching Hospital of Children, Baghdad, Iraq, between January 2023 and January 2025. Medical records and structured parent interviews at the follow-up visits were used to collect data. The age criterion was chosen because it was found that the best neuroplasticity and motor learning are possible at a young age [12].

Inclusion and Exclusion Criteria

The inclusion criteria were that children have to be confirmed to have CP and having clinically significant spasticity which impacted their functional abilities, and aged 6 years or below, and had parental consent to undergo the BTX-A injection. The exclusion criteria were known hypersensitivity to BTX-A, a comorbidity with neuromuscular conditions, acute at the injection sites, and contraindications to sedation.

Assessment Tools

Two validated scales, the Modified Ashworth Scale (MAS) 6-point ordinal scale (0-4) to assess the degree of resistance to passive stretching of muscle in the same direction [14] and the Tardieu Scale, which evaluates spasticity in the measure of the angle of muscle reaction to passive movement at varying velocities [15], were used to measure spasticity. They were selected as complementary scales to measure various aspects of spasticity as suggested in the existing clinical practice guidelines [16]. The analyses of motor functioning were performed with the Gross Motor Function Measure-88 (GMFM-88), a 88 item observational tool structured into five dimensions, including lying and rolling, sitting, crawling and kneeling, standing, and walking, running, and jumping. The assessment of each item is based on a 4-point scale (0-3), the better motor functioning is, the higher the score. The GMFM-88 has proved to be an excellent tool in terms of its reliability and validity in assessing the changes in gross motor functioning among children with CP [17].

BTX-A Injection Procedure

Injections were done by highly qualified pediatric neurologists using standard procedures. Ultrasound mode was applied due to the need to obtain precise localization of target muscles and adequate depth of injection, which had been found to enhance efficacy and minimize the risk of toxin dispersion to other muscles [18]. The most injected parts of the lower limb muscles were gastrocnemius, soleus, hamstrings and adductors, and on the upper limbs, they were biceps brachii, flexor carpi ulnar muscles, and flexor digitorum muscles, again depending on the individual presentation [19]. The doses were tailored according to patient weight, muscle size and severity of spasticity with a typical range of 4-8 units/kg body weight per session with no more than 400 units of maximum recommended dose of Botox (onabotulinumtoxinA) or equivalent dosages of other BTX-A preparations [20]. The injections were done under conscious sedation with the use of midazolam or chloral hydrate to reduce the pain and make the patient cooperate during the procedure.

Follow-up Assessment

The patients were evaluated in a systematic manner at two time-points which included 2 months (8-10 weeks) and 4 months (16-18 weeks) after injection. These were the time points that were chosen by the established BTX-A pharmacodynamics, where the peak effects were usually observed at 4-6 weeks and a slow but steady effect was noticed after 3-4 months [21]. Standardized tests of MAS, Tardieu Scale, and GMFM-88 were conducted by trained professionals who were aware of the baseline status of patients in case of each visit.

Statistical Analysis

Appropriate statistical programs were used to analyze the data. Demographic and clinical variables were provided in descriptive statistics. Paired t-tests or Wilcoxon signed-rank tests were used to compare scores in spasticity and motor functioning measures at baseline versus 2 months and 4 months, based on data distribution. The statistical significance was determined to be $P<0.05$.

Ethical Considerations

The researchers carried out the research based on the principles of the Declaration of Helsinki. The institutional ethics committee gave its approval to retrospective data collection and analysis. All patient confidentiality was observed in the course of the study and no identifying information was included in dataset.

Results

Patient Demographics

The cohort population consisted of 149 children with CP, the majority of whom were men (61% men, 39% women), and their age, at the time of the first BTX-A injection was under 6 years (Table 1).

Table 1: Demographic and Baseline Characteristics of Study Population

Characteristic	Value
Total number of patients	149
Male, n (%)	91 (61%)
Female, n (%)	58 (39%)
Age range	<6 years
Mean age (years)	3.8±1.4

Spasticity Outcomes

Modified Ashworth Scale

The MAS scores analysis revealed a substantial decrease in muscle spasticity at 2 months after the injection ($P<0.05$). The average decrease in scores of the spasticity depicted clinically significant improvement in muscle tone among both upper and lower limb muscle groups which were injected with BTX-A. Nevertheless, beyond 4 months of post-injection, MAS scores did not differ significantly with respect to baseline ($P > 0.05$), indicating that therapeutic effect of BTX-A had worn out by this period (Table 2).

Table 2: Modified Ashworth Scale Scores at Baseline, 2 Months, and 4 Months Post-Injection

Time Point	Mean MAS Score±SD	P-value (vs Baseline)
Baseline	3.2±0.6	-
2 months post-injection	1.8±0.5	<0.05*
4 months post-injection	2.9±0.7	>0.05

*Statistically significant

Tardieu Scale

The results of Tardieu Scale evaluation were similar to those of MAS. Two-month post-injection showed a great enhancement in the angles of catch and the quality of muscle response to passive stretch ($P<0.05$). This was an enhancement in significant decrease in velocity-related spasticity that would support functional activities and physiotherapy actions. At 4 months, Tardieu Scale was not significantly different than the baseline values ($P > 0.05$), which demonstrates the temporal limitation of BTX-A antispastic effect (Table 3).

Table 3: Tardieu Scale Measurements at Different Time Points

Time Point	Mean Angle of Catch (degrees)±SD	P-value (vs Baseline)
Baseline	42.5±8.3	-
2 months post-injection	68.4±9.2	<0.05*
4 months post-injection	45.8±8.9	>0.05

*Statistically significant

Motor Function Outcomes

Gross Motor Function Measure-88

At 2 months post- injection of BTX-A, GMF was significantly improved using GMFM-88 assessment ($P<0.05$). This was improved in the various dimensions of GMFM-88 and showed improved functional capabilities in terms of sitting, standing, and ambulatory functions of children with proper baseline motor capabilities. The fact that the motor functioning improved in a time of maximum spasticity amelioration offered testimonies of functional advantages in BTX-A use in combination with physiotherapy. Interestingly, the results of the GMFM-88 at 4 months exhibited quite high reduction in comparison to 2 months ($P<0.05$). Although this did not always restore the baseline levels, there is a time-based correlation between this decrease in motor functioning scores and the decline in antispastic effect found in MAS and Tardieu tests, which provide evidence of a correlation between the control of spasticity and functional motor activity (Table 4).

Table 4: GMFM-88 Scores at Different Time Points

Time Point	Mean GMFM-88 Score (%)±SD	P-value (vs Baseline)	P-value (vs 2 months)
Baseline	54.3±12.6	-	-
2 months post-injection	68.7±11.4	<0.05*	-
4 months post-injection	58.9±13.1	>0.05	<0.05*

*Statistically significant

Temporal Pattern of Treatment Response

The findings showed that there was evident temporal pattern in the therapeutic response to BTX-A injection. The best benefit time was observed during the first 2 months after injection during which both of them (spasticity reduction and improvement in motor functions) were at their optimum point. Following this time interval, positive changes started to diminish, and statistical significance in the measures of spasticity and deterioration in the motor function scores at the 4-month follow-up (Table 5).

Table 5: Summary of Treatment Response at Different Time Points

Outcome Measure	2 Months Post-Injection	4 Months Post-Injection
MAS score change	Significant decrease ($P<0.05$)	Non-significant (P>0.05)
Tardieu scale change	Significant improvement ($P<0.05$)	Non-significant (P>0.05)
GMFM-88 score change	Significant increase ($P<0.05$)	Significant decrease from 2 months ($P<0.05$)
Overall therapeutic effect	Optimal	Diminished

Discussion

This retrospective study is useful in terms of positive outcomes and time trends of BTX-A-based spasticity management in children with CP within a Middle Eastern clinical context. The results reveal comparative benefits in the reduction of spasticity and motor functioning in the initial 2 months of injection followed by a subsequent loss of treatment effect in 4 months after the treatment which is consistent with other current systematic reviews that report efficacy of BTX-A in the management of pediatric spasticity [22].

The remarkable reduction in spasticity of the present study at 2 months after the injection is in line with the current evidence. A systematic review and meta-analysis conducted by Albavera-Hernandez *et al*. (2020) indicated that BTX-A was effective in reducing lower limb spasticity in children with CP with a maximum effect at 4-8 weeks after the injection [23]. The working process of temporary chemical denervation offers the benefit of reducing focal spasticity, and without systemic side effects caused by oral medications which is especially beneficial in pediatric population [8].

Both MAS and Tardieu Scale were used in this study, which made it possible to assess spasticity in a comprehensive way. Recent studies have stressed on the significance of applying more than one assessment tool in order to describe various aspects of spasticity [15, 16]. The agreement of these two measures in showing substantial improvement at 2 months enhances the self-belief in observed treatment effect. A similar study within the same year by Park *et al*. also found that combined MAS and Tardieu Scale are able to more effectively measure the changes in spasticity in response to BTX-A treatment [24].

The important increase in GMFM-88 entitled to be at 2 months indicates valuable functional outcome, rather than just a reduction in spasticity. This observation confirms idea that BTX-A combined with intensive physiotherapy helps to learn and acquire functions and make motor progress during a low muscle tone phase. According to a recent randomized controlled trial by Franki *et al*. (2020), BTX-A injection plus goal-directed training showed a better effect on GMFM scores in comparison to BTX-A in children with spastic CP [25]. The process that could have caused motor functioning enhancement probably includes several components: the spasticity decreased its tendency to cause more ease of movement, the lowered spasticity enhanced more useful physiotherapy activities, and the better movement patterns that encouraged motor learning and neuroplastic processes.

The clinical implication that the positive effects decline 4 months after injection is significant in terms of planning and scheduling of the treatment. This temporal profile is in line with established BTX-A pharmacodynamics and the recent longitudinal time-series. Similar patterns were observed in a 2021 prospective study tracking functional outcomes over the 6 months where the greatest benefits were observed at 8-12 weeks and then gradually declined [9]. The substantial reduction in GMFM-88 at 4 months indicates the relevance of strategic time of treatment and the possible necessity of repeat injections at about 3-4 months to sustain functional advantages.

Recent results have indicated that cumulative functional gains can be achieved over time with repeated cycles of BTX-A treatment which is complemented by intensive physiotherapy [10]. A 2022 longitudinal study by Molenaers *et al*. found that children who underwent regular BTX-A over a 2-year span had enduring better gait parameters and functional mobility than baseline although individual cycles of treatment showed temporal deterioration [19]. This implies that repeat injection cycles should be strategically planned to enable optimization of long term outcomes.

Facilitation of physiotherapy interventions is one of the main benefits that were witnessed in clinical practice. BTX-A helps to generate optimal rehabilitation time by decreasing spasticity and painful movements. In a 2023 qualitative study by Ryll *et al*., it was described that therapists individually found that they could perform stretching and strengthening exercises more effectively during the post-BTX-A treatment period [11]. Throughout this window, a therapist is able to more easily apply functional training which would have been restrained by severe cases of spasticity.

On top of the quantifiable physical results, BTX-A therapy adds to psychological health and quality of life of CP children and their families. According to recent studies, patient-reported outcomes become important in analyzing the intervention of spasticity [4]. Enhanced motor activity and less spasticity may increase independence on daily activities, increase engagement in age-associated activities and raise self-esteem. When a child undergoes functional recovery with the use of BTX-A, parents tend to report a decrease in burden of caregiving and better family relations.

The BTX-A therapy can minimize the necessity of more surgical invasive operations as it could prevent or delay the formation of fixed contractures. In a 2021 retrospective cohort study, Wang *et al*. discovered that children with CP who underwent regular treatments with BTX-A had much lower orthopedic surgery in which tendon lengthening is required, compared to match controls who did not receive treatments with toxin [7]. BTX-A has the potential to reduce the need to undergo surgical procedures and this is a significant factor to consider the allocation of health care resources in developing nations because of the ability of BTX-A to maintain muscle length by reducing focal spasticity during critical growth stages.

Some of the study limitations are that the study is retrospective and hence cannot be used to make causal conclusions, that there is no control group, which cannot conduct a direct comparison with other types of treatments, that there is variability in dosing across patients which might affect the study, and that the follow up period is relatively short and thus cannot give the long-term effect of repeated treatment cycles. Prospective studies with longer follow-up, standardized treatment regimens, and measurement of other outcomes such as adverse effects, quality of life measures, and cost-effort are needed to give more comprehensive evidence on how to practice clinical studies in resource-limited countries [12].

Conclusions

This study demonstrates that BTX-A injection produces significant beneficial effects in children with CP, including meaningful spasticity reduction and gross motor function improvement within 2 months of treatment, though these benefits diminish by 4 months post-injection, necessitating repeat treatment cycles at 3-4 month intervals to maintain therapeutic effects. The findings confirm BTX-A as a valuable component of comprehensive spasticity management when integrated with physiotherapy, with key

clinical implications including maximizing rehabilitation interventions during the optimal 2-month post-injection window, utilizing combined assessment tools (MAS, Tardieu Scale, GMFM-88) for comprehensive evaluation, and implementing interdisciplinary approaches to prevent secondary complications and potentially reduce surgical intervention needs. The observed facilitation of physiotherapy, psychological benefits, and functional improvements support BTX-A's continued use as a cornerstone of pediatric spasticity management, while future research should focus on optimizing injection protocols, identifying treatment response predictors, evaluating long-term outcomes of repeated treatment cycles, and assessing cost-effectiveness in resource-limited settings to further refine clinical practice and improve outcomes for children with CP.

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Conflicts of Interest
The authors declare no conflicts of interest.

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