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Original Research Article

Clinical Study on Efficacy of Injection Botulinum Toxin in the Management of Spasticity in Cerebral Palsy

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Abstract:

Background: Cerebral palsy (CP), a group of disorders in movement and posture resulting from non-progressive injury of the immature brain is the most common cause of disability in the paediatric population. Among various subtypes grouped, spastic type is most common. Physiotherapy and occupational therapy remain the mainstays of treatment in spastic CP.

Objectives: To evaluate the effectiveness of injection botulinum toxin used in the management of spasticity in children with cerebral palsy.

Method: This is a prospective, longitudinal and interventional study which includes 25 cases of Botulinum toxin injection in the management of spasticity in cerebral palsy seen at Karnataka Institute of Medical Sciences (KIMS) Hospital, Hubballi for a period of one year from July 2022 to July 2023. Children between 2-12 years age diagnosed with spastic cerebral palsy with any level of Gross motor function classification system were included in study.

Results: Maximum number of patients 15(60%) had unilateral cerebral palsy and 10(40%) patients had bilateral cerebral palsy. About 15(60%) patients had hemiplegia and 10(40%) patients had diplegia. The GMFCS level frequency was same as that of 12 weeks among patients even at 6months. There is no statistically significant difference between before and after treatment at 6months in GMFCS level. There was no statistically significant difference in MAS grading for elbow flexors and forearm pronators before and after treatment at 12 weeks. Maximum number of patients 15(60%) were in MAS grading 1+ followed by 10(40%) patients in MAS grading 2. 10(40%) patients were in MAS grading 1 and 1+ each and 12(48%) patients were in MAS grading 1 and 1+ each at 12weeks and 6months respectively. This difference is statistically significant. There was a significant improvement on the MAS and R1 on the MTS for Calf muscles and Hip adductors at three follow-ups compared to before treatment. As for R2 on the MTS there was a significant improvement in tone in muscles of Hip adductors and Hamstring muscles.

Conclusion: It demonstrates that multilevel BTX-A injection as part of the integrated approach can be used for focal treatment of spasticity especially of hamstrings, hip abductors and calf muscles in non-ambulatory young children. Such a treatment affords the possibility of delaying/avoidingorthopaedic surgeries for children especially for those who are at high risk for general anaesthesia.

Keywords: Botulinum Toxin, Cerebral Palsy, Spasticity, Gross Motor Function Classification System, Modified Tardieu Scale, Modified Ashworth Scale.

Introduction

Cerebral palsy (CP), a group of disorders in movement and posture resulting from non-progressive injury of the immature brain is the most common cause of disability in the paediatric population. [1] Among various subtypes grouped according to neurologic dysfunction (spastic, hypotonic, dystonic, athetotic, or others), the spastic type is the most common. It can involve unilateral or bilateral sides and accounts for 70–80% of CP. Spasticity is defined as a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neuron syndrome. In CP, spasticity is known to increase up to 4 years of

age, after which it decreases up to 12 years of age [2].

Spasticity results in the shortening of myotendinous units, joint contracture, bony deformity, joint subluxation or dislocation, abnormal posture, and pathologic gait. Identifying the severity and distribution of spasticity is important in decisions about the options for managing spasticity [3]. Physiotherapy and occupational therapy remain the mainstays of treatment in spastic CP; botulinum toxin A (BoNT) is widely used for spasticity control and many studies support its safety and efficacy [5].

The most common types of CP are hemiplegia (one side of the body is affected), diplegia (both lower limbs are affected with fine motor problems restricted to the upper limbs) and quadriplegia, in which all four limbs are affected. Topographical classification is useful because it identifies the limb segments in which there may be hypertonia requiring intervention [5].

For the classification and prediction of motor function in children with CP, between the ages of 2 and 18 years, The Gross Motor Function Classification System (GMFCS) is a five-level ordinal grading system based on the assessment of self-initiated movement with emphasis on function during sitting, standing and walking [6]. The equivalent classification system to the GMFCS for classification of gross motor function in the upper limb is the Manual Ability Classification System (MACS) [6].

The Modified Ashworth Scale (MAS) is the most widely used scale to measure spasticity in the child with CP, despite problems with validity and reliability. The Modified Tardieu Scale (MTS) grades the quality of muscle reaction to passive stretch and measures the dynamic component of muscle spasticity [6].

The first publications reporting the use of BoNT-A in children with cerebral palsy (CP) were by Koman et al. in the United States in 1993 and by Graham et al. in the United Kingdom in 19945. Since then, the use of BoNT-A has become a ‘standard of care’ for children with CP in many countries, leading to widespread clinical use [6].

The most frequent indication for BoNT-A therapy in CP is to treat focal muscle over-activity to improve gait and function in children who can walk [5]. Injection of the upper limb to improve posture and function is the second most frequent indication for BoNT-A therapy in children with CP. Injections of BoNT-A may also be used as an analgesic agent, particularly when pain is related to muscle spasm [5].

Materials and Methods

This study includes 25 cases of Botulinum toxin injection in the management of spasticity in cerebral palsy seen at Karnataka Institute of Medical Sciences (KIMS) Hospital, Hubballi.

Study Design: It is a prospective, longitudinal and interventional study.

Study Period:1 year(July 2022 to July 2023)

Place of study: Karnataka Institute of Medical Sciences, Hubballi.

Sample size: 25 patients

Inclusion Criteria:

- Age between 2-12 years.
- Diagnosis of spastic cerebral palsy.
- Any level of Gross Motor Function Classification System (GMFCS)

Exclusion criteria:

- Concomitant neuromuscular disorders other than cerebral palsy.
- Fixed deformity and contractures.
- Known history of allergy to Botulinum toxin injection.

Method

Patients of Karnataka Institute of Medical Sciences who had been diagnosed with spastic cerebral palsy were taken in to study after obtaining written informed consent. Demographic data, History, Clinical examination and details of investigations were recorded in the study proforma.

Types of interventions:

All the patients included in the study were injected with injection botulinum toxin depending the spasticity, muscle bulk and body weight. After injection of botulinum toxin all patients underwent standardized rehabilitation program as per guidelines.

Types of outcome measures:

Standardized measurement of an individual's overall functional status can help guide treatment selection and allows for monitoring of change over time. The GMFCS is the most widely used for assessing and monitoring overall functional status. The manual Ability classification System used asses handling objects in daily activities of upper limbs.

The clinical measurement of muscle spasticity was done by the modified Ashworth scale and Tardieu scale. Tardieu is a scale for measuring spasticity that takes into account resistance to passive movement at both slow and fast speed.

The angle of full ROM(R2) is taken at a very show speed(V_1). The angle of muscle reaction (R1) is defined as the angle in which a catch or clonus is found during a quick stretch(V3) R1 is then subtracted from R2 and this represents the dynamic tone component of the muscle.

Modified Ashworth classification (MAS)

- 0: No increase in tone
- 1: Slight increase in muscle tone, manifested by a catch and release or minimal resistance at the end of the ROM when the affected part(s) is moved in flexion or extension
- 1+: Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
- 2: More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
- 3: Considerable increase in muscle tone, passive movement difficult
- 4: Affected part(s) rigid in flexion or extension

Gross motor functional classification system (GMFCS)

- TYPE I - Walks without Limitations
- TYPE II - Walks with Limitations
- TYPE III - Walks Using a Hand-Held Mobility Device
- TYPE IV - Self-Mobility with Limitations; May Use Powered Mobility
- TYPE V - Transported in a Manual Wheel chair

Manual ability classification system (MACS)

1. Objects are handled easily and successfully
2. Handled most objects but with some reduced quality and speed
3. Handled objects with difficulty
4. Handled objects with some help
5. Not able to handle objects

Results: Majority of patients 15(60%) were in the age group 5-8 years followed by 07(28%) patients in the age group 2-5 years&03(12%) patients were in the age group 8-12 years. Maximum number of patients 16(64%) were males and 09(36%) patients were females.

Maximum number of patients 15(60%) had unilateral cerebral palsy and 10(40%) patients had bilateral cerebral palsy.15 (60%) patients had hemiplegia and 10(40%) patients had diplegia.

Maximum number of patients 11(44%) and 10(40%) were in GMFCS level III before treatment and after treatment respectively. None of the patients were in GMFCS level IV and V after treatment. However, this difference is statistically not significant.

Table 1: Comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 4 weeks

GMFCS level	Before treatment (N=25) No. (%)	After treatment at 4 weeks (N=25) No. (%)	p value
I	06(24.0)	06(24.0)	0.99*
II	07(28.0)	09(36.0)	
III	11(44.0)	10(40.0)	
IV	01(4.0)	00(0.0)	
V	00(0.0)	00(0.0)	

*Chi-square test; p value<0.05 is significant.

11(44%) patients were in GMFCS level III before treatment compared to maximum number of patients 10(40%) in GMFCS level II after treatment. 01(4%) patient was in GMFCS level IV before treatment whereas, none of the patients were in level IV after treatment. However, this difference is statistically not significant.

Table 2: Comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 12 weeks

GMFCS level	Before treatment (N=25)	After treatment at 12 weeks (N=25)	p value
I	06(24.0)	09(36.0)	0.46*
II	07(28.0)	10(40.0)	
III	11(44.0)	06(24.0)	
IV	01(4.0)	00(0.0)	
V	00(0.0)	00(0.0)	

*Chi-square test; p value<0.05 is significant.

Table 3: Comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 6 months

GMFCS level	Before treatment (N=25)	After treatment at 6months (N=25)	p value
I	06(24.0)	09(36.0)	0.46
II	07(28.0)	10(40.0)	
III	11(44.0)	06(24.0)	
IV	01(4.0)	00(0.0)	
V	00(0.0)	00(0.0)	

The GMFCS level frequency was same as that of 12 weeks among patients even at 6months. There is no statistically significant difference between before and after treatment at 6months in GMFCS level.

Table 4: Comparison of MAS grading for Upper limb according to modified Ashworth scale after application of injection Botulinum at 4weeks

MAS grading	Elbow flexors (N=04)		Forearm pronators (N=04)	
	Before treatment No. (%)	After treatment at 4weeks No.(%)	Before treatment No. (%)	After treatment at 4weeks No. (%)
0	00(0.0)	00(0.0)	00(0.0)	01(25.0)
1	00(0.0)	02(50.0)	01(25.0)	02(50.0)
1+	03(75.0)	02(50.0)	02(50.0)	02(50.0)
2	02(50.0)	01(25.0)	02(50.0)	00(0.0)
3	00(0.0)	00(0.0)	00(0.0)	00(0.0)
4	00(0.0)	00(0.0)	00(0.0)	00(0.0)
p value*	0.85		0.88	

*Chi-square test; p value<0.05 is significant.

Upper limb weakness was present among 05 patients. For elbow flexors maximum patients 03(75%) were having MAS grading 1+ before treatment compared to 02(50%) patients in MAS grading 1 and 1+ each after treatment. This difference is statistically not significant. For forearm pronators, maximum patients 02(50%) were in MAS grading 1+ and 2 each before treatment compared to 02(50%) patients in MAS grading 1 and 1+ each after treatment. This difference is also statistically not significant.

Table 5: Comparison of MAS grading for Upper limb according to modified Ashworth scale after application of injection Botulinum at 12 weeks

MAS grading	Elbow flexors (N=04)		Forearm pronators (N=04)	
	Before treatment No. (%)	After treatment at 12 weeks No. (%)	Before treatment No. (%)	After treatment at 12 weeks No.(%)
0	00(0.0)	00(0.0)	00(0.0)	01(25.0)
1	00(0.0)	03(75.0)	01(25.0)	02(50.0)
1+	03(75.0)	02(50.0)	02(50.0)	02(50.0)
2	02(40.0)	00(0.0)	02(50.0)	00(0.0)
3	00(0.0)	00(0.0)	00(0.0)	00(0.0)
4	00(0.0)	00(0.0)	00(0.0)	00(0.0)
p value	0.67		0.88	

There was no statistically significant difference in MAS grading for elbow flexors and forearm pronators before and after treatment at 12 weeks.

Table 6: Comparison of MAS grading for Upper limb according to modified Ashworth scale after application of injection Botulinum at 6 months

MAS grading	Elbow flexors (N=04)		Forearm pronators (N=04)	
	Before treatment No. (%)	After treatment at 6 months No. (%)	Before treatment No. (%)	After treatment at 6 months No. (%)
0	00(0.0)	03(75.0)	00(0.0)	02(50.0)
1	00(0.0)	02(40.0)	01(25.0)	02(50.0)
1+	03(75.0)	00(0.0)	02(50.0)	01(25.0)
2	02(50.0)	00(0.0)	02(50.0)	00(0.0)
3	00(0.0)	00(0.0)	00(0.0)	00(0.0)
4	00(0.0)	00(0.0)	00(0.0)	00(0.0)
p value	0.44		0.72	

For elbow flexors maximum number of patients 03(75%) were in MAS grading 1+ before treatment compared to 03(75%) patients in MAS grading 0 after treatment and this difference is statistically not significant. For forearm pronators maximum patients were in MAS grading 1+ and 2 before treatment compared to MAS grading 0 after treatment. This difference is also statistically not significant.

Discussion

Majority of the patients 15(60%) were in the age group 5-8 years followed by 07(28%) patients in the age group 2-5 years. 03(12%) patients were in the age group 8-12 year. Maximum number of patients 16(64%) were males and 09(36%) patients were females.

Previous studies suggest that superior treatment outcomes were obtained with a treatment at earlier ages. Linder et al [7]. Reported that higher functional outcomes were seen for younger (age < 5 years) and moderately impaired children with GMFCS III level. Boyd et al [8]. Emphasized that BTX-A treatment should be done within the age range of 1–5 years in order to gain optimal outcomes.

As long as the relation between topography and age groups are concerned it is important to observe that the hypotonic group is found among children under the age of 2 and the dyskinetic group is identified later in life. There are few studies (Hanson et al., 1970) [9] trying to establish the moment when the child moves from hypotonia to spastic hypertonia or dyskinesia. According to those authors spasticity occurs during the three first months and dyskinesia occurs in up to three years in most of the cases. Just few children stay hypotonic and there were no children over 2 classified as hypotonic CP in their study.

Maximum number of patients 15(60%) had unilateral cerebral palsy and 10(40%) patients had bilateral cerebral palsy. 15(60%) patients had hemiplegia and 10(40%) patients had diplegia.

Other studies (Voorman et al., 2006) [10] also report that diplegic children are the majority. Diplegia affects principally, or especially the lower limbs because of the serious injury in periventricular areas and subcortical white matter; its main causes are cerebral ischemic and haemorrhagic phenomena and natal or post-natal hydrocephaly especially in preterm newborn children [11].

The most common types of CP are hemiplegia (one side of the body is affected), diplegia (both lower limbs are affected with fine motor problems restricted to the upper limbs) and quadriplegia, in which all four limbs are affected [12]. Topographical classification is useful because it identifies the limb segments in which there may be spasticity requiring intervention. It is not very reliable and precise classification is not always possible. This has led colleagues in Europe to simplify the topographical distribution into ‘unilateral’ and ‘bilateral’ [13].

When comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 4 weeks done, maximum number of patients 11(44%) and 10(40%) were in GMFCS level III before treatment and after treatment respectively. None of the patients were in GMFCS level IV and V after treatment. However, this difference is statistically not significant.

When comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 12 weeks, 11(44%) patients were in GMFCS level III before treatment compared to maximum number of patients 10(40%) in GMFCS level II after treatment. 01(4%) patient was in GMFCS level IV before treatment whereas, none of the patients were in level IV after treatment. However, this difference is statistically not significant.

When comparison of GMFCS level frequency before and after application of injection Botulinum toxin at 6 months. The GMFCS level frequency was same as that of 12 weeks among patients even at 6months. There is no statistically significant difference between before and after treatment at 6 months in GMFCS level.

Whereas another study (Aydil et al., 2019) showed that there was a statistically significant improvement on mean R1 angles of gastrocnemius and hamstring muscles at 1st and 3rd months after BTX-A injection in non-ambulatory young children with CP GMFCS level IV. Statistically significant improvement was found in the MAS, R1, and R2 angles of the knee and ankle joints after the 1st month of BTX-A injection and study reveals that multilevel BTX-A injection is effective in the treatment of spasticity in non-ambulatory young children with CP GMFCS level IV, and might help delay the need for orthopaedic surgeries [14].

Despite a generalized pattern and severity of spasticity, BTX-A injections can be used in non-ambulatory young children with CP GMFCS level IV to improve posture and positioning, to ease the use of orthoses and wheel chair, to facilitate personal care and to enhance compliance to physical therapy [15]. Early treatment of spasticity might decrease the need for orthopaedic surgeries especially in young children, while reserving single-event, multi-level surgery for fixed musculotendinous contractures and bony deformities in older children16. In the present study, regarding comparison of MAS grading for upper limb according to modified Ashworth scale

after application of injection Botulinum at 4weeks, upper limb spasticity was present among 05 patients. For elbow flexors maximum patients 03(75%) were having MAS grading 1+ before treatment compared to 02(50%) patients in MAS grading 1 and 1+ each after treatment. This difference is statistically not significant.

For forearm pronators, maximum patients 02(50%) were in MAS grading 1+ and 2 each before treatment compared to 02(50%) patients in MAS grading 1 and 1+ each after treatment. This difference is also statistically not significant.

There was no statistically significant difference in MAS grading for elbow flexors and forearm pronators before and after treatment at 12 weeks. Regarding comparison of MAS grading for upper limb according to modified Ashworth scale after application of injection Botulinum at 6 months, For elbow flexors maximum number of patients 03(75%) were in MAS grading 1+ before treatment compared to 03(75%) patients in MAS grading 0 after treatment and this difference is statistically not significant. For forearm pronators maximum patients were in MAS grading 1+ and 2 before treatment compared to MAS grading 0 after treatment. This difference is also statistically not significant.

Conclusion

Compared to GMFCS level before treatment there was slight improvement in GMFCS level after treatment however statistically not significant. The GMFCS level frequency was same as that of 12 weeks among patients even at 6months. The present study shows the effectiveness of BTX-A injection in non-ambulatory CP patient by assessments done at 3 different times after treatment. It demonstrates that multilevel BTX-A injection as part of the integrated approach can be used for focal treatment of spasticity especially of hamstring, hip abductors and calf muscles in non-ambulatory young children. Such a treatment affords the possibility of delaying/ avoiding orthopaedic surgeries children especially for those who are at high risk for general anaesthesia.

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