

A Study of Effect of Botulinum Toxin a on Hand Functions in Patients with Spastic Disorders

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ABSTRACT

Introduction: Intramuscular botulinum toxin A offers the possibility of local treatment of spasticity without affecting sensation. It is an established treatment for squint, blepharospasm, hemifacial spasm, torticollis, and focal dystonias. More recently, it has been used to treat limb spasticity after stroke, traumatic brain injury, cerebral palsy and multiple sclerosis. Aims and objective: To prospectively evaluate the effect of Botulinum toxin type A on hand functions in patients with spastic disorders in terms of Improvement in range of motion, degree of reduction of spasticity, improvement in prehensile functions and improvement in grip and pinch strength.

Material and Methods: A total of 33 patients with upper limb spasticity were included in the study and received injection Botulinum Toxin A as per inclusion criteria. The analysis was done with SPSS for Windows version 17. Prior to analysis all the entries were double checked for any error.

Results: Significant decrease in tone was observed as per Modified Ashworth scale. Significant improvement in range of motion was observed after Botulinum Toxin A injection as measured by a universal goniometer.

Conclusion: Injection Botulinum Toxin A is an effective treatment modality for decreasing upper limb spasticity and improving range of motion resulting in better cosmesis and increased ease in many activities of daily living.

Keywords: Botulinum Toxin, Spastic Disorders

INTRODUCTION

Spasticity is a common symptom seen in many neurological conditions. Clinically, it is diagnosed with the velocity-dependent resistance felt by passive examination of joint motion. However, defining it is much more difficult.

The most commonly used definition of spasticity is that of Lance,¹ who in 1980 defined spasticity as: "a motor disorder characterized by 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 upper motor neuron syndrome."

A recent definition that is more clinically relevant is "disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles".² Spasticity may cause deformity, pain, reduced function and in the longer term, lead to the development of contracture. Patients with upper limb spasticity can develop abnormal limb posturing, such as the classic adducted internally rotated shoulder, flexed elbow, flexed wrist and clenched fist.² Decision to treat spasticity depends on patient's need, as along with disabling effects in many patients, it may also offer helpful effects in others. Hence, spasticity should be treated when it interferes with activities of daily living.

Intramuscular botulinum toxin A offers the possibility of local

treatment of spasticity without affecting sensation. It is an established treatment for squint,³ blepharospasm,⁴ hemifacial spasm,⁵ torticollis,⁶ and focal dystonias.⁷ More recently, it has been used to treat limb spasticity after stroke, traumatic brain injury, cerebral palsy and multiple sclerosis. Moreover, targeting specific muscle groups without affecting others has the theoretical potential to unmask selective voluntary movement in situations where this is over-ridden by mass patterns of spasticity in antagonistic muscle groups.

Botulinum toxin type A is one of the seven different serotypes of botulinum toxin (A to G) produced by the anaerobic bacterium *Clostridium botulinum*.⁸ Botulinum toxin type A selectively and reversibly blocks the release of acetylcholine at the cholinergic nerve terminal, ensuring a temporary reduction in muscular activity in the injected muscle. There are many studies which have consistently demonstrated that the treatment is safe and effective in reducing unwanted muscle spasticity and that the effect is maintained over repeated treatments. Functional benefits have also been demonstrated, in terms of reduction of disability and carer burden.

There is paucity of literature assessing the response of Botulinum toxin A for upper limb spasticity in Indian scenario. The present study was undertaken to assess the effectiveness of Botulinum toxin A in improving hand functions in patients with various spastic disorders.

Aims and objectives of the study were to prospectively evaluate the effect of Botulinum toxin type A on hand functions in patients with spastic disorders in terms of Improvement in range of motion, degree of reduction of spasticity, improvement in prehensile functions and improvement in grip and pinch strength.

MATERIAL AND METHODS

The study was a prospective follow up study. The study was conducted in Department of Physical Medicine and Rehabilitation, VMMC and Safdarjang Hospital, New Delhi. Patients visiting the department with spastic disorders of non-progressive etiology, having upper limb spasticity. The study was done from July 2011 to April 2013.

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Inclusion Criteria

- 1 Upper limb spasticity interfering with the activities of daily living, with Modified Ashworth Scale ≥ 2 .
- 2 Subjects more than 2 years of age.

Exclusion Criteria

- 1 Unwillingness to participate in the study.
- 2 Contracture in wrist or hand.
- 3 History of previous Botulinum toxin injection in the last 6 months.
- 4 History of surgical procedure performed on the upper limb.
- 5 Severe respiratory or cardiac disease.
- 6 History of allergy/ sensitivity to Botulinum toxin.
- 7 Progressive neurological disorder (e.g., multiple sclerosis).
- 8 Myasthenia Gravis, Eaton-Lambert Syndrome, Amyotrophic Lateral Sclerosis or any other disease that might interfere with neuromuscular function.

A total of 33 patients with upper limb spasticity were included in the study and received injection Botulinum Toxin A as per inclusion criteria. Out of 33 patients, 30 patients completed the study and were followed for three months. A total number of thirty-three (33) subjects satisfying the inclusion criteria were enrolled in the study. Out of these only thirty patients completed three month follow-up period. There were three drop outs in the study. One case did not come for the first follow-up while two other cases did not attend the second follow-up.

Various profiles assessed were

Demographic profile

- a. Age
- b. Gender
- c. Socio-economic status

Etiological profile

- a. Underlying etiology

Outcome measures

- a. Modified Ashworth Scale
- b. Range of motion

STATISTICAL ANALYSIS

Demographic and clinical information of the subjects were recorded in the proforma and then maintained on the excel software. The analysis was done with SPSS for Windows version 17. Prior to analysis all the entries were double checked for any error. Descriptive statistics including mean and standard deviation (SD) were found for each quantitative variable. For nonparametric data, the mean change from baseline was estimated and mean changes at different follow-ups was analyzed using Friedman test followed by Wilcoxon signed ranks test. The results were considered significant at 5% level of significance, i.e. $p < 0.05$.

RESULTS

Assessment was done at 0 week (pre-injection), 4 weeks and 12 weeks post-injection.

Tools of measurement used in the study were:

- 1 Modified Ashworth Scale - The Modified Ashworth scale (MAS) is used as a simple measure of spasticity.
- 2 Range of motion

I. Modified ashworth scale

In table-1 MAS improved by a mean of 2.0 ± 0.086 at four weeks

follow up which was statistically significant ($p = 0.001$). When compared to baseline, there was also statistically significant improvement at 12 weeks follow up by mean of 0.45 ± 0.94 ($p = 0.001$). Significant increase in MAS was also noted from 4 weeks follow up to 12 weeks with mean difference being 1.55 ± 0.94 ($p = 0.001$).

As shown in table-2, significant improvement in MAS was seen from baseline to 4 weeks and 12 weeks. Difference in the mean MAS score from baseline to 4 weeks and 12 weeks was 1.83 ± 0.14 and 0.58 ± 0.12 respectively. Mean MAS increased from 4 weeks to 12 weeks with the difference being 1.24 ± 0.13 .

As shown in table-3, MAS improved by a mean of 1.414 ± 0.14 at four weeks follow up which was statistically significant ($p = 0.001$). When compared to baseline, there was also statistically significant improvement at 12 weeks follow up by mean of 0.37 ± 0.09 ($p = 0.001$). There was no decrease in MAS from 4 weeks to 12 weeks follow up.

As shown in table-4, there was a statistically significant improvement in Range of Motion from baseline to 4 weeks follow up (-2.133 ± 0.42 , $p = 0.0001$). Changes in mean Range of Motion from baseline to 12 weeks and 4 weeks to 12 weeks were (-1.667 ± 0.813 , $p = 0.148$) and (0.467 ± 0.74 , $p = 1.00$) which were not significant.

MAS Mean Difference at different time intervals (n=30)

Time interval	MAS Mean difference	p value
Between baseline and 4 weeks	2.0 ± 0.086	0.0001
Between 4 weeks and 12 weeks	1.55 ± 0.94	0.0001
Between baseline and 12 weeks	0.45 ± 0.94	0.0001

Table-1: MAS for Wrist Flexors

MAS Mean Difference at different time intervals (n=30)

Time interval	MAS Mean difference	P value
Between baseline and 4 weeks	1.83 ± 0.14	0.0001
Between 4 weeks and 12 weeks	1.24 ± 0.13	0.0001
Between baseline and 12 weeks	0.58 ± 0.12	0.0001

Table-2: MAS for thumb flexors

MAS Mean Difference at different time intervals (n=30)

Time interval	MAS Mean Difference	P value
Between baseline and 4 weeks	1.414 ± 0.14	0.0001
Between 4 weeks and 12 weeks	1.034 ± 0.12	0.0001
Between baseline and 12 weeks	0.37 ± 0.09	0.0001

Table-3: MAS for Finger Flexors

Range of Motion mean difference at different time intervals (n=30)

Time Interval	ROM Mean Difference	P value
Between baseline and 4 weeks	-2.133 ± 0.42	0.0001
Between 4 weeks and 12 weeks	0.467 ± 0.74	1.00
Between baseline and 12 weeks	-1.667 ± 0.813	0.148

Table-4: Range of motion

DISCUSSION

This study was conducted to examine the effectiveness of Botulinum Toxin A Injection on hand functions in patients 2 years and above with spastic upper limb due to any non-progressive etiology.

Demographic factors

Average age of patients in our study was 23.17 years \pm 3.576 ranging from 3 to 62 years. Number of males (73%) outnumbered females (27%) in our study. Majority of patients in our study belonged to lower middle (56.67%), upper middle (23.23%) and upper lower (13.33%) socio-economic strata with very few patients in the upper socio-economic strata (6.67%) and no patient from the lower class (0%).

Modified Ashworth Scale

In the study population, MAS score observed at pretreatment was 3.34 (\pm 0.55) in wrist flexors, 3.14 (\pm 0.78) in thumb flexors and 3.07 (\pm 0.99) in finger flexors. Statistically significant improvement was seen in the MAS score at 1 month and 3 months after intervention.

In Wrist flexors, MAS score decreased to 1.34 (\pm 0.48) at first month and then marginally increased to 1.79 (\pm 0.41) at 3 months. In thumb flexors, MAS score decreased to 1.31 (\pm 0.47) at first month and then marginally increased to 1.89 (\pm 0.77) at 3 months. Similarly, in finger flexors, MAS score decreased to 1.65 (\pm 0.61) at first month and then marginally increased to 2.03 (\pm 0.62) at 3 months.

Similar improvements were found by Bakheit et al.⁹ (2001) in which Botulinum Toxin A was compared with placebo in 59 patients. He reported significant reduction in the summed MAS score at 4 weeks in the Botulinum Toxin A group as compared with the placebo group ($p = 0.004$). The magnitude of benefit over 16 week follow-up period was significantly reduced for the Botulinum Toxin A group in wrist ($p=0.004$) and the finger joints ($p = 0.001$) when compared with placebo.

Simpson et al.¹⁰ (1996) also reported significant tone reduction in Botulinum Toxin A group as compared to placebo. Peak effect was at 2 to 6 weeks post injection that returned to baseline by 10 weeks.

Corry et al. (1997)¹¹ compared the effects of intramuscular Botulinum toxin A with placebo (normal saline) in the hemiplegic upper limb of 14 children with cerebral palsy (5 male, 9 female; mean age 9 years). The study showed significant improvement in Modified Ashworth scale in wrist and elbow at follow up period of 2 weeks and 12 weeks. Similar improvement in MAS was also noted by Reiter et al.¹² (1996), Pierson et al.¹³ (1997), Sampaio et al.¹⁴ (1997), Rodriguez et al.¹⁵ (2000) and Smith et al.¹⁶ (2000).

The results of our study do not match with the study by Fehling et al.¹⁷ (2000), a single blind trial on 30 patients with cerebral palsy with spastic hemiplegia which found no statistically significant differences in MAS between treatment and control group at 4 weeks, 12 weeks and 24 weeks post injection.

Range of motion

In the present study, there is marginal but significant improvement in range of motion at 4 weeks post-injection (13.63 \pm 4.86 degrees at pretreatment to 15.76 \pm 5.33 degrees after 4 weeks which did not persist till 12 week post intervention (14.1 \pm 5.6 degrees which was statistically insignificant when

compared to baseline).

Similar results were shown by Pierson et al.¹³ (1996) who reported significant improvement in range of motion in 39 patients with acquired spasticity. Reiter et al.¹² (1996) also observed significant improvement in range of motion at wrist and fingers, the effect apparent after 1 week, peak effect observed within 30 days.

Similar improvements in range of motion were also noted by Smith et al.¹⁶ (2000) who studied the efficacy of Botulinum toxin A in upper limb spasticity after stroke or head injury. Mean increase of 14 degrees in range of motion at wrist was seen which lasted by 12 weeks.

Corry et al.¹¹ (1997) also observed increase in range of motion at 2 weeks which failed to persist till 12 weeks post-injection in their study of the effect of Botulinum Toxin in hemiplegic upper limb of 14 patients with cerebral palsy. Bakheit et al.⁹ (2001) observed no statistically significant difference in range of motion between Botulinum Toxin A group and placebo group at 4 weeks of study. At week 16, significantly greater improvement in ROM was noted in the study group.

Our result differed with Fehling et al.¹⁷ (2000) who reported no significant improvement in range of motion while evaluating the effects of Botulinum Toxin A injection in improving upper extremity function in 30 patients with hemiplegic cerebral palsy.

Adverse Effects

Majority of the patients (25 out of 30 i.e. 83.33%) did not have any complications. Only five out of thirty patients reported side effects after receiving Botulinum Toxin A injection. No major systemic adverse effects were noted in this study.

Soreness at injection site in two patients (6.67%) and transient nausea in one patient (3.33%) was observed in our study. Weakness of previously functionally helpful hook grasp was reported by two patients (6.67%) in our study. Overall, Botulinum Toxin A was found to have no serious adverse effects and was well tolerated.

CONCLUSION

Injection Botulinum Toxin A is an effective treatment modality for decreasing upper limb spasticity and improving range of motion resulting in better cosmesis and increased ease in many activities of daily living. Effect of Injection Botulinum toxin on functional improvement of spastic hand is inconclusive and needs further research. Botulinum Toxin A injection is a useful and safe treatment modality when used judiciously in focal spasticity of upper limbs.

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