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EVALUATION OF EFFICACY AND SAFETY OF BOTULINUM TOXIN-A IN MANAGEMENT OF POST STROKE SPASTICITY

Neurology

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ABSTRACT

Background: Spasticity is a major disabling complication of stroke. The use of botulinum toxin-A is becoming a common treatment due to its efficacy and favorable side effects profile but uncertainty exists; that whether intramuscular injections of botulinum toxin-A reduce disability in persons with spasticity.

Objective: This study of conducted with the objective to assess the efficacy and safety of botulinum toxin-A in post stroke spasticity.

Methods: A total of 107 patients with moderate to severe spasticity (based on the Modified Ashworth Spasticity Scale) 3-6 months after stroke or those with poor response to the conventional, physical and medical treatment were included in the study. Each patient was assessed by the stroke neurologist, experimental neuro-physiotherapist and a medical observer on the basis of Modified Ashworth Spasticity Scale, Disability Four Point Scale, Visual Pain Assessment Scale (VAS), Range of Movements (ROM) & Assessment of Daily Living (ADL). The botulinum toxin-A (BTX-A) injected into spastic muscles with the guide of electromyography (EMG). Keeping in view the safety of the patients, the dose was not injected at < 3month interval.

Results: A total of 107 patients were included in the study. The underlying cause was ischemic stroke in 77 (71.96%), hemorrhagic stroke in 24 (22.43%), cerebral embolism in 4 (3.74%) of the patients. The patients have shown improvement in the modified Ashworth scale score, range of movements and activities of daily living and improvement in disability with BTX-A at the end of the study. 30(62.5%) of upper limb spasticity and 41(69.5%) patients with lower limb spasticity, shown improvement in the range of movements. No serious adverse events were reported in the study period.

Conclusion: Our results showed that BTX-A treatment in post stroke spasticity safely and effectively decreases muscle tone and improves the range of motion, limb posture, function and pain.

KEYWORDS:

Spasticity, botulinum toxin, stroke, Modified Ashworth scale

INTRODUCTION:

Spasticity is a well-known motor dysfunction arising from upper motor neuron lesions due to stroke, spinal cord injury, multiple sclerosis and traumatic brain injury. Post stroke hemiparesis, along with the abnormal muscle tone, is a major cause of morbidity and disability. These patients often present a recognizable antigravity postures as shoulder adduction, elbow and wrist flexion in the upper limb, and hip adduction, knee extension and ankle plantar flexion in the lower limb. This hemiplegic posture is thought to result from the increased motor activity in the antigravity muscles (1).

Spasticity tend to occur in up to 38% of patients after stroke and often interferes with the activities of daily living, personal hygiene and ambulation, and can be associated with pain and significant discomfort (2-5). Spasticity was graded according to Modified Ashworth Scale (Grade 0: No increase in muscle tone, Grade 1: Slight increase in muscle tone reflected by catch and release or by minimal resistance at the end of range of movements, when the affected part is moved in flexion and extension, Grade 1+: Slight increase in muscle tone manifested by catch and release followed by minimal resistance throughout the remainder of the range of movements ROM, Grade 2: More marked increase in muscle tone through most of the ROM but affected part easily moved, Grade 3: Considerable increase in muscle tone , Grade 4: Affected part rigid in flexion and extension)(6).

Botulinum toxin being one of the most dangerous toxin to humans introduced by Scott acts by blocking the release of acetylcholine thus blocking neuromuscular transmission (7). Focal spasticity, resulting from cerebral disorders is currently being successfully treated with BTX-A injection in spastic muscles and now considered the pharmacologic treatment of choice in focal spasticity (8). BTX-A has been considered as a valuable tool in the management of focal adult spasticity by American Academy of Neurology and Publication of the European consensus (9,10). Botulinum toxin acts by chemodenervation thus preventing the release of acetylcholine at the neuromuscular junction. It is effective and safe to use on small localized areas or muscles. Keeping in mind the above findings, the present study was conducted to assess the efficacy and safety of Botulinum toxin-A in post stroke spasticity.

MATERIAL AND METHODS

This study was conducted in the department of neurology, Indraprastha Apollo Hospital, Sarita Vihar, New Delhi, approval of the Institutional Ethics Committee / Research Review Board and written Informed Consent was obtained from all the participants/ legal guardians before initiation of the study.

A total of 107 patients were included in the present study. 48 of the patients were of upper limb spasticity and 59 of lower limb spasticity. The inclusion criteria were: (i) Patients with moderate to severe spasticity 3 to 6 months of post stroke, (ii) Poor response to conventional, physical and medical treatment, (iii) Patients willing to participation in active rehabilitation and management programme. The exclusion criteria were: (i) Patients with history of previous injections, (ii) Weakness around the joints, (iii) Biomechanical shortening of muscles, (iv) Transient increase in tone only, (v) Responding well to conventional treatment, (vi) Pregnancy, (vii) Patients taking anticoagulants, (viii) Progressive neuromuscular disease. The injection sites and different dose range were set for the patients. The outcome was to monitor and assess the Modified Ashworth Scale, range of motion and pain. Pain dose of BTX-A has been well reviewed in literature (11,12). Pain was assessed using visual assessment scale (0-10) and the disability was assessed by using disability four-point scale (scale 0-no disability, scale 1-mild disability, scale 2-moderate disability and scale 3- severe disability) (5,6). Keeping in view the safety of the injected dose the dose was not injected at < 3month interval. Dose was not exceeded the recommended dose. It has been stated that Botulinum dose is adjusted according to the severity of spasticity, number of muscles involved, age, previous exposure to BTX therapy and adjunct therapy applications (6). Recommended

dose of BTX-A has been well reviewed in literature (11,12).

RESULTS

Total patients included in the study were 107. The mean age in the present study was a 64.1±20.2 year. The males were 83 (77.57%) and 24 (22.43%) were females and the male: female ratio is 3.46:1. The history of ischemic stroke were in 77 (71.96%), hemorrhagic stroke in 24 (22.43%), cerebral embolism in (4) 3.74%of the study patients. The cause of spasticity was unknown in 2(1.86%) of the patients (Table 1).

Age in years (Mean± SD)		64.1±20.2
Male		83(77.57%)
Female		24(22.43%)
Ischemic stroke (%)		77(71.96%)
Hemorrhagic stroke (%)		24(22.43%)
Cerebral embolism (%)		4(3.74%)
Unknown Cause(%)		2(1.86%)
Hemiparetic arm	Dominant	39
	Non dominant	68

Table 1: Demographic characteristics of the study population and details

Botulinum toxin A dose range varied for individual muscles. 48 (44.85%) patients were of upper limb spasticity and 59 (55.14%) were of lower limb spasticity, for upper limb 25units/ml and for lower limb 50units/ml was injected under EMG (Table 2).

No of patients	Dose	Result in upper limb
48	25 units /ml	Significant improvement in pain, ROM, Modified Ashworth scale and ADL
		Result in lower limb
59	50units/ml	Significant improvement in pain, ROM, Modified Ashworth scale and ADL

Table 2: Assessment in upper and lower limb

The Modified Ashworth Scale has shown improved in upper limb muscles as the score was reduced to 1-3 in biceps /brachialis and 2-4 in wrist flexors and finger flexors. The ROM improved in 30 (62.5%) of the patients as assessed by passive elbow flexion and extension, wrist palmer flexion and fingers flexion (Table 3).

Modified Ashworth scale	Muscles	Pre baseline	Post baseline
	Biceps/ Brachialis	3-4	1-3
	Wrist flexors	3-4	2-4
	Finger flexors	3-4	2-4
ROM	Passive elbow flexion and extension	-	Improvement in 30 patients 62.5%
	Wrist palmer flexion	-	
	Flexed fingers (Thumb in pain)	-	

Table 3: Clinical Assessment in upper limb (48 patients)

The modified Ashworth scale improved in lower limb as score was reduced to 1-2 in hamstring, plantar flexors and adductors. The range of movement was improved in 69.5% (41) of the patients (Table 4).

Modified Ashworth scale	Muscles	Pre baseline	Post baseline
	Plantar flexor	2-3	1-2
	Hamstring		
	Adductors		
Rangeof movements	In 69.5%(41) of the patients improved		

Table 4: Clinical Assessment in Lower Limb (59 patients)

The four-point disability scale showed improvement in cleaning the palm (40%), cutting the finger nails (30%), putting the arms through sleeves (60%), putting on gloves (40%), rolling in bed (60%), walking balance (70%) and speed of walking (70%) of the patients (Table 5).

Cleaning the palm	40%
Cutting the finger nails	30%
Putting the arm through sleeves	60%
Putting on gloves	40%
Rolling in bed	60%
Walking balance	70%
Speed of walking	70%

Table 5: Functional disability Improvement Assessed by Four-point scale

The visual pain assessment scale has shown improvement in pain in both upper and lower limbs at the end of the study. The safety was assessed throughout the study but no anaphylactic reactions or other side effects were reported.

Discussion:

Severe hypertonia of muscles is a frequent complication in patients with stroke. Spasticity may interfere with voluntary motor function in patients with residual muscle power. The current methods of treatment are unsatisfactory; furthermore, the value of oral antispasticity drugs diminish with prolonged use or tolerance develops. In recent years the BTX-A has been shown to be an effective antispasticity agent (13,14). The procedure is simple and the toxin does not cause skin sensory loss or dysthesia.

The mean age in the present study was 64.1±20.2 years, which is in relation to the study by Bakheit et al (15). In the present study, post stroke spasticity was found in 77.57% males and 22.43% females, which is consistent with previous study, where male predominance was observed (16). While in an another study the disease was found to be more prevalent among females 56% (16).

In the present study the underlying cause was ischemic stroke in 77 (69.5%), followed by hemorrhagic stroke in 24 (22.43%), cerebral embolism in (4)3.74%, which is similar to other study where the majority of cases of ischemic stroke have developed spasticity (15). Botulinum toxin A is an efficacious treatment for the spasticity after stroke. In the present study the upper limb spasticity was improved with the BTX injection in affected muscles as assessed by Modified Ashworth scale and the range of movements was also improved, this is in relation to the earlier studies which also suggested safe and effective use of BTX in upper limb spasticity (17-20). Several spastic upper limb muscles of chronic hemiparetic patients were injected in these studies and tone reduction assessed by Modified Ashworth scale (6). The results are consistent with a study by Bakheit AM et al that suggested the sustained antispastic effects of botulinum after repeated injections for upto at least three treatment cycles (15).

Lower limb in the context of hemiplegic posture tends to be in position of adducted hip, extended knee, plantar flexed and inverted ankles. Compared to the upper limb spasticity the studies of lower limbs spasticity are relatively insufficient. In the present study the BTX injection has shown improvement in spasticity and in range of motion which is in context to the previous study by Dengler et al who have reported improvement in 8 of 10 patients considering spasticity (21). Another study by Hesse et al has reported injection of 400 U of botulinum toxin into spastic calf muscles has shown significant improvement in gait parameters (10,18,19,22).

The functional disability was assessed using four point disability scale and the improvement in parameters as cleaning the palm in 40%, cutting the finger nails in 30%, putting the arm through sleeves in 60%, putting on gloves in 40%, rolling in bed in 60%, walking balance in 70% and speed of walking in 70% of the patients which is in relation to the study by Bakheit et al where also the improvement in cleaning the hands was in 81.3%, cutting fingernails in 50%, putting arm through sleeves in 62.5%(15).

In conclusion, the present study the improvement in range of motion, limb posture, function and reduction in pain has been observed. The results of our study of BTX-A treatment in post stroke upper and lower limb spasticity suggest that the BTX-A injections safely and effectively decrease muscle tone and increase the range of motion.

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