Original Article

Botulinum Toxin A in Blepharospasm and Hemifacial Spasm and Meige's Syndrome: An 8 Year of Experience in Northeast India

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Abstract

Aim of study: This study was done to examine the usefulness of botulinum toxin A injections in treating various neurological disorders such as Hemifacial spasm, Blepharospasm and Meige's Syndrome, in patients of the resource limited communities from Northeastern parts of India, who attended neurology movement disorder clinic of NEIGRIHMS. **Material and methods:** This was a prospective, interventional trial of patients seen in a movement disorder clinic of NEIGRIHMS a tertiary care institute in Northeast India over a period of 8 years from August 2008 to September 2016, with diskinesias potentially treatable with botulinum toxin. All the patients were assessed before and after injections using Jankovic spasm grading and improvement in functional impairment scale. Relevant findings were noted. **Results:** There were 29 patients with Hemifacial spasm, 5 with Blepharospasm and 1 with Meige's Syndrome. The mean Jankovic disability rating score in cases of hemifacial spasm and blepharospasm was 2.86 (± Standard deviation 0.54, range 2 to 4), 2.51(± Standard deviation 0.58, range 2 to 4) respectively and Meige's Syndrome 4. The mean improvement in function score was 3.4 ± 0.7 SD in hemifacial spasm and 3.9 ± 0.3 in blepharospasm. The clinical benefits induced by botulinum toxin lasted for a mean of 4.5(± Standard deviation 2.8, range 2.5 to 6.5), 4.3(± Standard deviation 1.6, range 3 to 7.5) of hemifacial spasm and blepharospasm respectively. While 1 with Meige's Syndrome received substantial benefit. Blepharoptosis was the commonest complication accounting for 55.7%. HFS seems more prevalent in northeastern Indian compared with western populations. **Conclusions:** Our findings have shown that Injections of botulinum toxin are useful in treating various neurological disorders studied in Northeast part of India. This is advancement in the treatment of these diskinesias which responds poorly to oral medications.

Keywords: Hemifacialspasm; Jankovic spasm grading; Meige'syndrome; Blepharospasm

Introduction

Hemifacial spasm, Blepharospasm and Meige's Syndrome are the three chronic distressing and embarrassing movement disorder of face. HFS is a disorder characterized by episodic and intermittent twitching; tonic spasm and synkinesis of the muscles of one side of the face innervated by the facial nerve. [1] In contrast BFS causes incapacitating closure of the eyelids. The cause of BFS is multifactorial. [2] Henri Meige described in 1904 what is now commonly called oral facial dystonia.There is some variations in what has been described since in what has been called Meige's syndrome (MS), but in all descriptions there is blink and chin thrusting. Some patients have lip pursing or tongue movements and for a few, the movement spread into the shoulders. [3] The cause remains obscure, a treatment less than ideal, and frustration is a major factor. Many physicians, even regarding the more common BFS, may have had no experience with MS and the patients may be told the process is psychological. [4] Dystonia is difficult to treat medically. The injection of botulinum toxin has now become an accepted treatment modality for BFS, HFS and MS. [5]

Botulinum toxin (BTX) is a potent neuroparalysing agent.[3] The bacterium clostridium botulinum produces seven serologically distant toxins nominated as A,B,C,D,E,F and G. [3,5] Since the introduction of BTX in to therapeutics in 1978 for squint, botulinum toxin type A, one the most lethal biologic toxins, has been found to be of therapeutic value in the treatment of a variety of neurological disorders and hence has been used for movement disorders frequently, once BTX A got food and drug administration (FDA) approval. [3]

Several publications have addressed the role of BTX A in treatment of BF, HFS and MS. [6-15] Hence, this study was undertaken in an attempt to see the role of BTX A in treatment of these movement disorders in northeastern Indian population. Movement disorders are treated by different modalities, including surgery. [6-16] However, in northeastern India surgical treatment for such movement disorders are either in its primitive stages or has not begun in many centers. The aim of this study was to examine the usefulness of botulinum toxin A injections in treating various neurological disorders such as Hemifacial spasm, Blepharospasm and Meige's Syndrome. This study is expected to provide a new dimension in treatment of BF, HFS and MS in northeastern Indian populations.

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Material and Methods

This was a hospital based, prospective, interventional study, which was carried out in NEIGRIHMS from August 2008 to September 2016.Thirty-five patients of BS, HFS and MS were selected from the outpatient department of the movement disorder clinic of neurology department of NEIGRIHMS to undergo BTX A therapy, after obtaining their informed consent. All patients underwent full clinical evaluation, including neurological as well as ophthalmic examination. None of the patients had been treated with botulinum toxin before. All patients refrained from taking other drugs for at least 2 weeks before the study.

The severity of spasm was graded clinically from grade 0 to grade 4 according to Jankovic disability rating scale: 0-normal, 1-slight disability, no functional impairment, 2-moderate disability, no functional impairment, 3-moderate disability, functional impairment and 4-incapacited.

Botox, Allergan was used for treatment in all cases due to easy availability in the market. The manufacturer's instructions were carefully followed. The toxin was used within 1 hour of its reconstitution. A vial of 50 units freeze dried BTX was reconstituted with 2 ml of preservative free 0.9% saline solution to yield toxin in a concentration of 2.5 ml per 0.1 ml. The toxin was injected subcutaneously into selected sited using 1 ml tuberculin syringe with a gauge of 27-29 needles.

The dose was calculated on the basis of severity and location of patient's spasm. In Blepharospasm, four to five periocular injections at the medial and lateral aspects of upper and lower eyelids near orbital rim were injected with due technical considerations. Both pretarsal and preseptal injections were administered accordingly. In Hemifacial spasm, four to five periocular sites as above were selected. The cheek was injected in cases having a severe degree of retraction of angle of mouth. The dose of BTX A was calculated according to the prevalent reports in literature and modified according to the severity of clinical status. The dystonia was reassessed before each injection. Patients were evaluated at two weeks, four weeks and 6 months after treatment with BTX A. Diary was provided to record the onset of clinical response, peak effect, duration of clinical improvement and complications on follow-up assessment. Telephone contact with the patients was encouraged for follow up assessment.

Magnitude of subjective responsive considering functional improvement (0to 4) was conducted by the following grading system in all cases on follow-up: 0-no effect, 1-mild effect but no functional improvement, 2-moderate change in both severity and function, 4-marked improvement in severity and function. Results were expressed as mean ± SD.

Complications were looked for and noted if any blepharoptosis, deviation of angle of mouth, bruises and ecchymosis. Patients were told to note the date and follow up immediately as soon as significant spasm occurred. A proforma was maintained to record all the particulars regarding patient, treatment and follow-up visits and significant events. Useful data was recorded in the database for statistical analysis.

Results

A total of 35 patients were studied, 29 cases were HFS, five cases were of BS and one case of MS. Out of 35 (thirty-five) patients, 29(85.7%) were females and 5(14.2%) were males. The mean age of females and males were 47.72 and 49.24 years with standard deviation being 9.92 and 10.48 respectively, in HFS and BS when botulinum toxin treatment was started. More than 90% of the patients were from north-eastern region. More than 50% were professional and rests were house wives. Various exacerbating factors for both movement disorders were described by the patients stress was the commonest exacerbating factors for spasm(77.5%), similarly, sunlight(70%), talking (48.84%), lack of sleep(25%), watching TV(30%), reading (13.6%), eating (7.3%) were other important exacerbating factors for the spasm. By Jankovic disability rating, 29 cases with HFS were functionally disabled or incapacitated 2.86 ± 0.54SD (range 2 to 4) and 5 cases with BS had mean disability score of 2.51 ± 0.58 SD (range 2 to 4). Mean Jankovic disability grading was more in case of MS followed by HFS and BS.The mean duration of spasm before botulinum toxin treatment was 5.47 ± 3.68 SD years (range 7months to 15 years) in HFS and 3.67 ± 3.68 years (range 3 months to 16 years) in BS.HFS and MS required a higher doses of botulinum toxin injections when compared with BS [Table 1]. 55 units were used in single patient of MS.

Table 1: Shows dose of injection botulinum toxin A in BFS, HFS & MS.

Botulinum toxin A in units	Blepharo-spasm	Hemifacial spasm	Meige's syndrome	Total
20	1	1	-	2
23	-	2	-	2
25	1	2	-	3
28	-	4	-	4
30	2	2	-	4
38	-	13	-	13
40	-	2	-	2
45	1	1	-	2
50	-	2	1	3
Total	**5**	**29**	**1**	**35(100%)**

(p<0.001)

After two weeks, mean follow-up improvement in functional impairment rating in study subgroups was excellent in all patients. Similar results were noted in four weeks and six months follow up periods. The effect of BTX A in treating these cases were remarkable and lasted long enough it was slightly more in BS and was of shorter duration in MS. Blepharoptosis was the commonest complications in both BS and HFS groups accounting for 55.7%, which, however, cleared after a few days, followed by deviation of angle of mouth, bruises and ecchymosis. However, no systemic complications were recorded in any case included in present study.

Mean improvement in functional scale score was 3.4 ± 0.7SD in HFS and 3.9 ± 0.3 in BS. The onset of beneficial effect after botulinum toxin ranged from 3 to two weeks (mean 3.29 ± 1.07 SD) in BS and 2 to 9 days (mean 3.31 ± 3.5 SD) in HFS. The effect peaked at 8 ± 1.66SD (range 3-16) days in BS and 10.6 ± 5.24) (range 4-21) days in HFS. Benefit from each session lasted in HFS and BS, respectively lasted a mean of 4.5 ± 2.8

SD (range 2.5 to 6.5) months and 4.3 ± 1.6 (range3.0 to 7.5) months [Table 2]. Age, sex, age of onset of dystonia, duration of symptoms before injections did not influence relief response.

Table 2: Showing the duration of effect lasted the longest in HFS comparison to BS and Meige's syndrome.

Diagnosis	Number with spasm reappearance	Duration in months			
		Min	Max	Mean	Standard deviation
Hemifacial Spasm	29	2.5	6.5	4.5	2.8
Blepharospasm	5	3.0	7.5	4.3	1.6
Meige's syndrome	1	-	-	-	-
Total	**35**	**2.5**	**7.5**	**4.4**	**1.9**

Discussion

BTX exerts its effects by preventing the release of acetylcholine from presynaptic vesicles. The active form of toxin produces denervation through a three step process: 1) toxin binding to nerves, 2) internalization and 3)inhibition of neurotransmitter release. [4] In our study, both preseptal as well as pre tarsal injections of BTX A was given, and the outcome was better in cases where pretarsal injections of BTX A was given, which again correlated with the study done where the results of injecting BTX A in pretarsal portion of orbicularis oculi muscle was more effective. [9,12] To the best of our knowledge this study is one of the rare studies from Northeastern India.

Among 35 cases that were enrolled in the study, 29(82.85%) cases were of HFS (26 females and 3 males), 5(14.2%) of BS (3 females and 2 males) and 1 female (2.85%) of MS. In present study, the cases of HFS outnumbered the cases of BS while only one was MS. Reported prevalence of HFS in general population is higher than BS and MS. The mean age in years of the female patients was 53.00(± 9.29 SD) with the age range from 21 to 63 years, while the mean age of the male patients was 51.72(± 10.62 SD) range from 33 to 67 years. It was found that there was a female predominance in these kinds of movement disorders in our study, which correlated with other published studies. [1-4]

The present results confirm that patients with HFS, BS and MS can benefit from local injections of botulinum toxin. As in previous studies, almost all of the cases with BS, HFS and MS reported subjective improvement with botulinum toxin injections in the present study as well. [6,7] The onset of beneficial effect, peak effect and duration of clinical benefits in response BTX A are comparable with those observed, by various investigations who used botulinum toxin to treat focal dystonias, muscle cramps, spasticity and rigidity. [7,9,11,17-20]

The mean value for reappearance of significant spasms (in months) in present series was 4.4(± 1.9 Std deviation, range 2.5 to 7.5).In study subgroups, the range of value for reappearance of significant spasms (in months) was 4.5(± 2.8 Std deviation, range 2.5 to 6.5), 4.3(± 1.6SD, range 3 to 7.5) respectively in cases of HFS and BS and in MS lasted for 3 months. The study of Jankovic et al, revealed that patients with HFS had longer lasting improvement than those with other focal dystonias as our present study also confirms same. [9] Subclinical denervation in patients with HFS was hypothesized for longer duration of improvement. [6] These findings are similar studies done in past. [17]

A large number of exacerbating factors like stress, sunlight, talking, watching TV, etc were observed by the patients in present study. Similar situational exacerbating factors have been reported in literature. [6] Despite the considerable variations in dose, in previous publications, the total complications accounted for 12.3 %(range 0-52.3%). [17] In present series, ptosis was noticed in 55.7% of all treatment sessions. This blepharoptosis may be due to toxin diffusion into muscular portion of the levator palpebrae superioris muscle causing chemodeneravation which disappeared in few days. Deviation of angle of mouth was noticed in 2 cases of HFS, bruises were present in 2 cases one each of BS and HFS.Ecchymosis was present in 1 case of HFS. No systemic complications were noted during the study. The complications noted in present study were comparable noted in other studies. [6,10,16,18]

Age, sex, age of onset of dystonia, duration of symptoms before injections did not influence relief response. In comparison to the use of BTX A for major dystonias i.e, cranio cervical and spasticity management as is frequently used in western world, its use would be more appropriate in our setup considering that a much smaller dose of BTX A is required hence, affordable to our economically constrained northeastern population for management of these movement disorders. We strongly recommend its use as a first line management drug for HFS, BS and MS which responds poorly to oral medications. Its use by neurologist trained in movement disorders management cannot be overemphasized considering the toxicity of BTX A.

Conclusion

Our present study strengths the fact that local botulinum toxin treatment provides safe, effective and long lasting relief of spasms and botulinum toxin treatment holds promise for hemifacial spasm, blepharospasm and meige's syndrome. Hence, an acceptable and effective treatment modality has been long felt needed in these neurological disorders. Our study has established that BTX A has been an effective and safe method of treating these movement disorders in Northeast Indian population. Our results are promising and show a possibility for wider use of this treatment modality in our economically constrained developing country.

Conflict of Interest

All authors disclose that there was no conflict of interest.

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