

Fixed Dose Botulinum toxin therapy for Blepharospasm

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Purpose: To find the efficacy of a fixed dose of Botulinum toxin A for the treatment of Blepharospasm.

Study Design: Quasi experimental study.

Place and Duration of study: Yaqin Vision Clinic, Lahore from (August 2010 – August 2015).

Material and Methods: All patients of Blepharospasm treated with botulinum toxin included in the study were assessed on first visit for the presence of blepharospasm and graded into 4 patterns from mild to severe. Ocular examination was done to rule out any cause of secondary blepharospasm due to trichiasis or entropion. CT or MRI scan was performed to rule out any neurological cause of the disease. Injections were given at 7 periorcular sites in a fixed dose. Follow up was done at 2 weeks, 6 weeks and 3 months.

Results: There were 53 cases of blepharospasm, 27 males and 26 females, which were treated with botulinum toxin. Average age of the patients was 55.3 +/- 8.4. Out of these only 34 patients (64%) had regular injections while 19 patients (36%) had only one injection and did not turn up for further treatment. Average number of injections given to each patient was 5.5 +/- 4.7. The average duration of relief of symptoms was 3.1 +/- 1 month with 25 units of Botulinum toxin at 7 periorcular sites on each side. Relief of symptoms started after 3.6 +/- 1.8 days in most of the patients. Pre-op 23 patients had moderate and 11 had severe spasms. Average spasms at 1 month post injection were slight to mild with better response in patient with moderate pre-op spasms. One patient each had post injection headache and drooping of lid after injection.

Conclusion: Fixed dose therapy gives satisfactory results in patients with moderate blepharospasm.

Key words: To Severe Botolinum Toxin, Blepharospasm, Injections.

Blepharospasm is characterized by abnormal, involuntary over contraction of orbicular muscle and occasionally underlying aetiology is basal ganglia disease¹. Blepharospasm affects women more commonly than men by a 3:1 ratio and has an onset in the sixth decade². Increased frequency of blinking, eyelid spasm, mid facial or lower facial spasm, eyelid tics and involuntary chronic contractions affecting both eyes are the main symptoms of blepharospasm. In cases with

blepharospasm, reading, writing and driving becomes difficult for the patient because of spasms of the orbicular muscle causing closure of both eyelids³ leading to a disaster effect on the quality of life⁴.

Botulinum toxin A (Botox A, Allergan) prevents acetylcholine secretion from pre synaptic vesicles thus causing neuromuscular blockade. Due to its efficacy and safety, Botulinum toxin A is the only best therapy for Blepharospasm now-a-days⁵.

Botulinum toxin is an expensive drug therapy for patients with blepharospasm in our country. Therefore the rationale of our study was to assess the results of fixed dose (50 units for both sides) therapy with Botulinum toxin in all patients presenting with Blepharospasm. This treatment regimen is the most economical as the injection cost can be shared between two patients.

MATERIALS AND METHODS

The study was prospective case series conducted in the last 5 years (August 2010-August 2015) at Yaqin Vision clinic, Lahore. Patients of all ages with essential blepharospasm) were included in the study Patients who were non-willing, had neurologic or psychiatric disease, and had history of eyelid surgery on initial presentation were excluded from the study. Pre-injection CT/MRI was done in all patients to rule out any neurological cause of the disease. Informed consent was taken from all the patients and they were explained about the procedure and the study. Standard precautions of injecting Botox injection were taken and 7 periocular sites were selected e.g. nasally and temporally in upper brow, upper lid (Pre-tarsal area), lower lid (pre-tarsal area) and one below lateral canthus on the orbital rim. These patients were seen on follow up after one week, 6 weeks and at 3 months.

RESULTS

There were 53 cases of blepharospasm, 27 males and 26 females, which were treated with botulinum toxin. Average age of the patients was 55.3 +/- 8.4. Severity of blepharospasm at initial visit and average 4 years response at 1 month is given in table 1 and grade of orbicularis tone is given in table 2. Twenty five units of botulinum toxin were distributed over 7 periocular sites in fixed doses (Fig. 1). Out of these only 34 patients (64%) had regular injections while 19 patients (36%) had only one injection and did not turn up for further treatment. Average number of injections given to each patient was 5.5 +/- 4.7 (Fig. 2). The average duration of relief of symptoms was 3.1 +/- 1 month with 25 units of Botulinum toxin at 7 periocular sites on each side. Relief of symptoms started after 3.6 +/- 1.8 days in most of the patients. Average spasms at 1 month post injection were slight to mild with better response in patient with moderate pre-op spasms. One patient had post injection headache. One patient had drooping of lid after injection.

Table 1: Severity of Blepharospasm pre op and post injection after 1 month.

| Grade | Clinical Features | Pre-op n (%) | Average Post-op 1 Month (n%) |
|-------|--|--------------|------------------------------|
| 0 | None | 0 | 21 (61) |
| 1 | Slight. Increase blinking in response to external stimulus | 0 | 10 (30) |
| 2 | Mild, spontaneous lid flutter | 0 | 3 (9) |
| 3 | Moderate, very noticeable spasm of eyelids only | 23 (67) | |
| 4 | Severe, incapacitating eyelids and facial muscles spasm. | 11 (32) | |

Table 2: Grades of Orbicularis tone at initial Presentation.

| Grade | Clinical Features | No. of Patients n (%) |
|-------|--|-----------------------|
| 0 | Incomplete closure of eyelids | 0 |
| 1 | Eyelids just closing with minimal resistance | 0 |
| 2 | Good eyelids closure with some resistance | 0 |
| 3 | Strong eyelids closure but can be overcome with difficulty | 0 |
| 4 | Very strong closure of eyelids that cannot be overcome | 18 (100) |

DISCUSSION

Benign essential blepharospasm (BEB) is 2 - 3 times more common in women than men and more so in people over the age of 50 years⁶. But in our study we found males were affected slightly more probably due to easy access of males to medical examination. Post-menopausal women using phenothiazine's and with thyroid dysfunction are more prone to develop BEB⁷. Incidence of blepharospasm in USA is 2000 cases annually while prevalence is 1.6-30/100,000⁸.

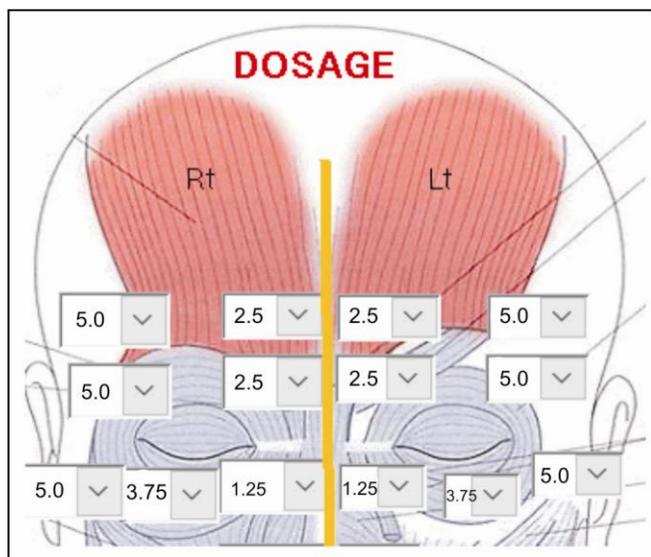


Fig 1: Periocular sites for botulinum toxin injection.

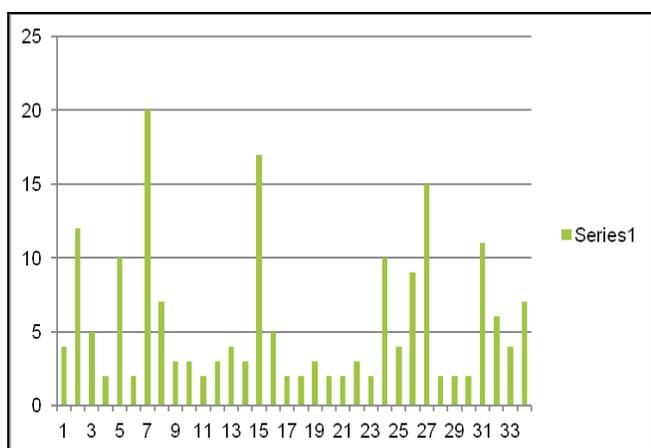


Fig. 2: Number of injections in each patient (n = 34).

Clostridium botulinum is the bacterium which produces Botulinum toxin. The FDA approved its usage in the late 1980s when they discovered that Botulinum toxin could help in diseases like blepharospasm (uncontrolled blinking) and strabismus (lazy eye)⁹. In April 2002, FDA approved it for the treatment of glabellar lines as well¹⁰. But it can be used for other areas of the face as well. Blepharospasm and dystonia of muscles of the face and neck are not only the source of physical discomfort but also result in significant social blemishers. Best available treatment is botulinum toxin injection into the muscles¹¹. Response is best in pure essential blepharospasm. Duration of action is

variable ranging from 6 weeks to 6 months. Because of financial constraints, many patients cannot afford to have repeated injections. Oral medication including tri-cyclic anti-depressants and anti-cholinergic have been tried but the results are not very encouraging¹². In our study some of the patients had tried these medications with poor results.

Botulinum toxin is available in Pakistan¹³. One vial contains 100 units for one patient and is quite expensive. We shared one vial between 2 patients by using a fixed dose treatment of 50 units which was more economical for the patient. Other studies have reported this as well¹³. It is injected in pretarsal and preseptal regions of the eyelids for the treatment of blepharospasm. One of its complication is that when we inject it in the upper lid, it can migrate to the orbit and can lead to temporary ptosis. It is highly recommended that the toxin dose should not exceed 200 IU in a 1 month period and the injection should not be repeated before 90 days. We preferred the pretarsal injection as in other studies because with site of injection there are few complications due to less diffusion into the levator muscle¹⁴. It has been stated in different studies that the initial dose of Botulinum toxin is between 1.25 – 5 units for the treatment of blepharospasm at each site¹⁵. In our patients, the dose that was enough for all patients was 2.5 to 5 units at each site.

In our study, although the treatment needed to be repeated after every 90 days but we found Botulinum very effective in the control of blepharospasm. The sign and symptom free duration with every injection remained same over the long term treatment. Almost same results are found in studies carried out by Ainsworth, Burns and Czyz¹⁶. Our patients were satisfied because of better quality of life, both socially and physically due to its long symptom free periods. Our experience was similar from studies carried out at other centers where Blepharospasm Disability Index (BSDI) scoring was done¹⁷. A national study having 4 patients of blepharospasm found botulinum toxin effective in its treatment.¹³ Same results were also shown by Iwashige¹⁸, Parsuad R¹⁹ and Park YC²⁰.

Our study has some limitations like low patient compliance, due to infrequent referrals from other centres of the country.

CONCLUSION

The therapeutic use of botulinum toxin for the diseases of the face and periocular region is safe,

repeatable and temporarily effective. Patients should be selected carefully and before injection potential complications should be discussed with the patient thoroughly. Botulinum toxin type A is the standard treatment of choice as the first line therapy for essential blepharospasm. The only drawback is that the effect wears off in about 3 months and the injections need to be repeated every 12 weeks. This demands good counselling by the doctor and patients' motivation and affordability.

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