# Efficacy of Botulinum toxin type A in the treatment of benign essential blepharospasm and hemifacial spasm

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## Abstract

**Purpose:** To study the efficacy of botulinam toxin type A injection in benign essential blepharospsm and hemifacial spasm.
**Methods:** This quasi interventional study was done in a tertiary eye care centre in Dhaka, Bangladesh from January 2013 to April 2016. We included all patients of benign essential blepharospsm and hemifacial spasm those who had consented for the study.
**Results:** 60 patients was benign essential blepharospasm and 60 patients was hemi facial spasm. Female was 61.3% and male was 38.7%.The mean age of BEB was 57.38 years and the mean age of HFS was 44.72 years. The mean baseline score of eyelid spasm was 3.60 in BEB and 3.40 in HFS. The mean score of eyelid spasm was 3.31±1.54 in benign essential blepharospasm and 2.67±1.39 in hemifacial spasm after 24 weeks of treatment.
**Conclusion:** Outcome of botulinam toxin type A injection was more effective in hemifacial spasm than benign essential blepharospasm.

## Introduction

Benign essential blepharospasm (BEB) is a progressive disease characterized by spontaneous, spasmodic, bilateral, intermittent or persistent involuntary contractions of orbicularis oculi muscles often involving procures and corrugator's muscles. The onset of blepharospasm is heralded by various episodes of increased blinking lasting from seconds as long as to 20 minutes. The spasmodic and repetitive eye contractions can lead to functional blindness in up to15% of patients. Benign idiopathic blepharospasm affects usually above 50 years of age. It accounts approximately300 of every 1 million people.[1-3] Hemi facial spasm (HFS) is a rare neuromuscular disease characterized by irregular, involuntary muscle contractions (spasms) on one side (hemi) of the face (facial). HFS is typical and atypical.

The most common is typical form that accounts about 97-98%.In typical form, the twitching usually starts in the orbicularis oculi muscle of the lower eye lid and gradually spreads to the whole lid, then to the orbicularis oris muscle around the lips, and buccinators muscle in the cheek. Middle aged women are preponderance for HFS. It may be caused by facial nerve injury or tumor compressing facial nerve. It is diagnosed by magnetic resonance imaging or electromyography or angiography.[4-6] Botulinum toxin is a potent neurotoxin derived from Clostridium botulinum. Botulinum toxin type A alters receptor proteins in the presynaptic neuron, inhibiting the release of acetylcholine.

Injection of this agent at the therapeutic doses results in chemical denervation and localized muscle paralysis. Average onset of action is 2 to 3 days and average peak effect occurs at about 7 to 10 days following injection. The duration of effect is different but is typically 3 to 6 months. The treatment of benign essential blepharospasm and hemifacial spasm with Botulinum toxin A injections seems to safe, simple and easily repeatable and symptomatically helpful.[7-8] We attempt to assess the outcome of botulinam toxin type A injection in the patients those who were suffering from benign essential blepharospasm and hemifacial spasm.

## Patients and Methods

This quasi interventional study was done in the orbit and ophthalmic plastic services of Bangladesh eye hospital, Dhaka, Bangladesh from January" 2013 to April" 2016 (40 months). We included all patients of benign essential blepharospasm and hemi facial spasm those who had consented for the study. We excluded patients from this study those who were suffering from acute and chronic systemic illness, neoplastic diseases, and facial nerve compression due to any cause, pregnant and lactating mother, inflammatory and infectious ocular diseases. All patients were examined clinically in details. Variables like as mean age, gender, result of schemer test I, scoring of eyelid spasm, onset of action, spasm free period, and occupation were evaluated in this study.

### Baseline preinjection and postinjection evaluation of the score of eyelid spasm in blepharospasm

The following scoring system was used according to Scott *et al* to evaluate eyelid spasm.[9-10]

| Event | Score | | | | |
|---|---|---|---|---|---|
| Eyelid Spasm | 0 | 1 | 2 | 3 | 4 |

Interpretation of eyelid spasm scoring:
0=none, 1=increased blinking caused by stimuli, 2=mild noticeable fluttering no incapacitating, 3=moderateto very noticeable spasm mildly incapacitating, 4=severely incapacitating i.e. unable to read, drive, write etc.

### Doses

After baseline evaluation of the patient a standard dose of 25 unit of botulinum toxin type A injection was injected in each patient.

### Preparation of injection

At first ice pack massage was done on the injection area to every patient for 5 minutes. Peri-ocular skin was washed with 5% povidone iodine, 25 unit of Botulinum Toxin Type A injection was injected in each patient. It was supplied in a frozen, sterile, lyophilized form in a vial of 100 units. This type-A toxin was reconstituted with 4 ml of sterile 0.9% saline prior to injection, so each ml of solution contain 25 units of Botulinum toxin type A. The reconstituted solution was drawn into a 1 ml tuberculin syringe and injection was pushed with 30 G needle within 4 hours. The fragile toxin molecules are susceptible to damage by mechanical stress, hence rapid injection and frothing during reconstitution were avoided. The solution was injected subcutaneously over the orbicularis oculi and intramuscularly over the thicker corrugator and procures muscles at 13 points around both eyes in case of benign essential blepharospasm and 11 points in case of Hemi facial spasm. We followed all patients after two weeks, six weeks, twelve weeks, eighteen weeks, and twenty four weeks of treatment. Data were collected in a pre-designed data collection sheet and appropriate statistical analysis was done. Paired "t" test was done.

### Results

We evaluated one hundred twenty cases involving sixty cases of benign essential blepharospasm (BEB) and sixty cases of hemifacial spasm (HFS). Male patients were forty six (38.3%) and female was seventy four (61.7%). Female was preponderance in this study. We categorized the age of the study subjects into five groups. In BEB, most of the patients (58.3%) were in the group of 56-70 years of age and 75% of the patient was above the 50 years of age. In HFS, 51.7% of the patient was in the 41-55 years of age group and more than 75% of the patient was 26 to 55 years. The mean age of the patients suffering from BEB was 57.38 years and the mean age of HFS cases was 44.72 years. Dry eye was associated with 20% of BEB and 10% in cases of HFS. Apraxia of eyelid opening was associated in 15% cases of BEB and 5% was meige syndrome among the cases of BEB. Botulinum toxin type-A was poorly response in the cases of apraxia of lid opening with BEB and meige syndrome. The mean baseline eyelid spasm score was 3.60 in BEB and 3.40 in HFS according to Scott *et al.* The mean eyelid spasm score was 0.41, and 3.31 after two weeks, and twenty four weeks of botulinum toxin type A injections in the cases of BEB.

| Parameters | BEB | HFS |
|---|---|---|
| Mean age ± SD | 57.38±8.64 | 44.72±5.43 |
| Gender: Male: Female | 1.9:1 | 1.4:1 |
| Eyelid spasm: | | |
| (Mean score± SD) | -------- | ----- |
| Baseline | 3.60±0.56 | 3.40±0.50 |
| 2 wks after inj | 0.41±0.63 | 0.39±1.19 |
| 4 wks after inj | 0.63±0.48 | 0.60±0.81 |
| 8 wks after inj | 0.83±1.37 | 0.79±1.37 |
| 12 wks after inj | 1.63±1.29 | 1.26±1.03 |
| 18 wks after inj | 2.27±0.87 | 1.73±0.96 |
| 24 wks after inj | 3.31±1.54 | 2.67±1.39 |
| Onset of action of inj (days) | 3.54±3.41 | 4.08±3.79 |
| Dry eye | 20% | 10% |
| Apaxia of lid opening | 15% | 0% |
| Meige syndrome | 05% | 0% |

The mean eyelid spasm score was 0.39, and 2.67 after two weeks, and twenty four weeks of botulinam toxin type-A injections in the cases of HFS. The mean onset of action of botulinam toxin type A was 3.54 days in BEB and 4.08 days in HFS. The right side was involved in 44% cases and left side was involved in 56% cases in HFS. The common aggravating factor was bright light (66.6%) and the common relieving factor was rest (83.3%) in the study subjects of BEB. The common occupation of the study subjects was house hold worker (65%). The mean onset of effect started after botulin-am toxin injections type a injection was 3.54 days in BEB. The mean onset of effect after injection was 4.08 days in HFS. Mild ptosis was found in two cases after giving botulin-am toxin injections in BEB cases. Epiphora was evaluated in HFS cases after injections in two cases. The outcome of botulin-am toxin type A injections was statistically significant difference between BEB & HFS after 24 weeks of treatment.

**Scoring of the eyelid spasm at baseline and follow-up periods of treatment in BEB**

| Mean score of baseline period ± SD | Mean score after injection ± SD | | t value (two-tailed) | P value |
|---|---|---|---|---|
| 3.60±0.56 | After 2 weeks | 0.41±0.6 | 19.73 | <0.0001 |
| | After 8 weeks | 0.83±1.3 | 24.31 | |
| | After 12 weeks | 1.63±1.2 | 18.57 | |
| | After 24 weeks | 3.31±1.5 | 23.57 | |

**Scoring of the eyelid spasm at baseline and follow-up periods of treatment in HFS**

| **Mean score of baseline period±SD** | **Mean score after injection ± SD** | | **t value (two-tailed)** | **P-value** |
|---|---|---|---|---|
| 3.40±0.50 | After 2 weeks | 0.39±1.19 | 18.06 | <0.0001 |
| | After 8 weeks | 0.79±1.37 | 13.86 | |
| | After 12 weeks | 1.26±1.03 | 05.00 | |
| | After 24 weeks | 2.67±1.29 | 04.08 | |

**Compare of outcome of BEB & HFS after 24 weeks of botulin am toxin injection**

| **Parameter** | **BEB** | **HFS** | **t test value** | **p value** |
|---|---|---|---|---|
| Mean | 3.31 | 2.67 | | 0.0150 <0.05* |
| SD | 1.54 | 1.29 | 2.4677 | |
| N | 60 | 60 | | |

The difference of the result of botulinum toxin type A injection in BEB and HFS after 24 weeks is considered to be statistically significant.

## Discussion

Benign Essential Blepharospasm and Hemi facial Spasm both are devastating condition. Patients become functionally blind and unable to perform their daily work and gradually they become handicapped.[11] It is challenging to treat the patients those are suffering from two diseases. Neurologist, Ophthalmologist and psychiatrist of the world are trying to treat the diseases. Botulinum toxin type A injections have become widely popular for combating the functional recovery of benign essential blepharospasm and hemi facial spasm.[5,6,12] Most of the patients are treated with partially effective or ineffective remedies like anxiolytic or sedative agents by general ophthalmologist and general practitional.[2] Recent trend is referring the patient to oculoplastic specialist and neurologist for better management of the diseases.

Injection of this botulinum toxin type A at therapeutic doses results in chemical denervation and localized muscle paralysis. We injected 25 units of botulimatoxin type A (Botox) in both benign essential blepharospasm and hemifacial spasm. The mean injection dose of BEB and HFS per visit injected during the last year compared with the first year was 26.8±10.3 and 22.5±7.5 units (p=0.003), respectively in a study.[13]

In our study, benign essential blepharospasm affected the middle age to elderly commonly and hemifacial spasm commonly involved the young adult to middle age patients. We categorized the age of the patients in to five groups. In 26-40 years, BEB was six (10%) and HFS (25%) was fifteen. In 41-55 years, BEB was fourteen (23.3%) and HFS was 31 (51.7%). In 56-70 years, BEB was thirty five (58.3%) and HFS was twelve (20%). And seventy years above, BEB was five (8.3%) and HFS was two (3.3%). Benign essential blepharospasm was found about 75% above fifty years of age and hemifacial spasm was most frequently affected in the age of twenty six to fifty years. The mean age was 57.38 years in the cases of BEB and 44.72 years in HFS cases. Grandas et al. did a review of 264 patients of BEB and they found mean age ± SD 55.8±12.76 years. BEB usually occurs over forty years of age.[8]

Female was most frequently affected in both benign essential blepharospasm (73%) and hemifacial spasma (60%).Female was 39% and male was 61%in benign essential blepharospasm and hemifacial spasm subgroups.[13]Female: male was 3:1.[11]There are some aggravating and relieving factors in benign essential blepharospasm. Bright light (66.6%) is the most common aggravating factor, followed by walking (46.6%), watching television (43.3%), talking (30%), and stress 26.6%. Rest is the most common relieving factor (83.3%) followed by touching the face, at morning, walking, reading religious book.

In case of hemi facial spasm, left side (56%) was commoner than right side (43%).The mean time of onset of effect amounted to3.54days in benign essential blepharospasm. Most patients had onset of treatment effect from two to seven days and only few patients had onset of effect was eight to twelve days in BEB cases. The mean onset of action was 4.08±3.79 days in hemifacial spasm but very few patients were started delayed onset effect that was eleven to fifteen days in HFS. 08% patients of hemifacial spasm showed rapid onset of action that was one to two days. The time to onset of treatment effect was estimated by the patient at 1st follow up visit in all study patients. Average onset of action following botulinam toxin type A is two to three days and average peak action occurs up to seven to ten days.[12,14] Roggen K.P *et al*. reported mean onset of action was 4 days.[15] The response of the effect was 3.18 days after the first injection session.[16]

The effect of botulinum toxin injection after two weeks in both diseases showed significant relief of symptoms. The mean score of eyelid spasm in both BEB and HFS were 0.37±0.73 and 0.39±1.19 (mean±SD) respectively. The mean score (mean±SD) following injection was 0.63±0.48, 0.83±1.37,1.63±1.29, 2.27±0.87, 3.31±1.54, after4 weeks,8weeks,12 weeks, 18 weeks and 24 weeks respectively in BEB. The mean score of eyelid spasm±SD was 0.60±0.8, 0.79±1.37, 1.26±1.03, 1.73±0.96, 2.67±1.29 after 4 weeks, 8 weeks, 12 weeks, 18 weeks and 24 weeks of botulinum toxin type A injections in HFS. The difference of the outcome is statically significant in benign essential blepharospasm and hemicial spasm after 24 weeks of botulinum toxin type A injection. The most of the patients need injections after 3 to 4 months of the first treatement.[11,12,14] The mean durations of action during the first and last years in both Benign essential blepharospasm and hemifacial spasm were 12.4±7.1 and 14.6±7.0 weeks, respectively and *P* value was 0.076.[13] Czyz CN et al. reported that mean duration of treatment efficacy was 18 weeks.[6] The duration of response free time after the initial injection was 16.33 weeks.[16] In our study some patients showed spasm free period from 6 months to 9 months in Hemifacial spasm. The changes of mean eyelid spasm score before and after injection in both benign essential blepharospasm and hemifacial spasm shows *p* value was <0.0001which is extremely significant. Here, t value reached from unpaired t test.

Botulin am toxin was less effective in other associated condition like as dry eye, apraxia of lid opening and meige syndrome. Periocular hematoma (10%) reported in both diseases which was temporary. Other minor temporary complications were ptosis, pain and lagophthalmos. Two patients had developed mild ptosis and epiphora respectively, which subsided over four weeks. Ababneh OH et al mentioned that most common adverse effects were ptosis, lagophthalmos and dry eye.[13] Another study done by Roggen KP et al. showed that ptosis, diplopia, ecchymosis and localized bruising like adverse effects was occurred after botulinum injections in BEB.[15] Botulinum toxin type A is the treatment of choice as the first line therapy for BEB and HFS. The only drawback is that the effect was temporary and the injections are to be repeated every three to six months. Patients' motivation and affordability is essential to manage the disorder.

## Conclusion

Botulinum toxin type A is an effective, safe, long-term treatment for patients to relieve benign essential blepharospasm and hemifacial spasm. Botulinum toxin is effective in long term for hemifacial spasm than benign Essential Blepharospasm.

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