

Clinical Outcome of Botulinum Toxin Injection in Benign Essential Blepharospasm and Hemifacial Spasm

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Abstract

Purpose: To Assess the results of botulinum toxin injection on benign essential blepharospasm and hemifacial spasm.

Methods: Prospective follow up study in the department of oculoplasty, National Institute of Ophthalmology & Hospital, Dhaka. From 1st November 2014 to 31st March 2016. Assess all the patients with essential blepharospasm and hemifacial spasm attending in the department of oculoplasty.

Results: 2 groups of patients of which 30 is essential blepharospasm and 30 is hemifacial spasm assessed. Evaluation of spasm done before and after Botulinum toxin injection for both groups. Before injection spasm score usually 3-4 in both groups. After injection 2 weeks, 1 month, 2 months evaluation found that spasm down to 0-1, but they reappear after 3 months and need re-injections. Onset of effect starts 2-15 days. Complications are also very less, such as ptosis, pain in rare cases. For all parameters botulinum toxin is better in hemifacial spasm than essential blepharospasm.

Conclusion: Botulinum toxin is more effective in hemifacial spasm than benign essential blepharospasm.

Introduction

Benign essential blepharospasm is a bilateral focal dystonia characterized by increased blinking and spontaneous, spasmodic, intermittent or persistent involuntary contractions of orbicularis oculi, procerus and corrugator muscles. The mean age of onset is 56 years and affects nearly 300 of every 1 million people. The onset of blepharospasm starts as increased blinking lasting from seconds to as long as 20 minutes. Blinking gradually intensified insidiously becoming a spasm of eyelid that is not under voluntary control. The spasm generally starts as mild twitches and progresses over time to forceful contracture. Initially it may start unilaterally but

eventually become bilateral and limits the patient's ability to drive, perform activity daily living. As the episodes progress eye closure become so frequent and prolonged that patients become functionally blind. The cause is unknown, but is probably central in origin, in the basal ganglia of brain. Spasm may be precipitated by air pollution, wind, noise, eye movement, head movement, watching television, reading, driving, stress or bright light and alleviated by talking, walking and relaxation. Essential blepharospasm is a diagnosis of exclusion based on clinical findings.

Essential blepharospasm is difficult to treat. Pharmacological drugs provide only partial relief but their efficacy is limited and temporary in most

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cases. Lists includes anticholinergic, antihistamine, benzodiazepine, antispasticity agents, neuroleptics or antipsychotics. Most patients respond incompletely or not at all to pharmacotherapy.

The success rate in surgical treatment is 50-70%. But surgery is complicated to perform. In spite of beneficial results spasm returns in many patients after a while.

Doxorubicin chemotherapy is a permanent or long term therapy but associated with higher incidence of complications including skin ulcerations, cicatricial ectropion or entropion.

The introduction of botulinum neurotoxin in the 1980s was a milestone for patients suffering from focal dystonias including blepharospasm. It is a potent neurotoxin derived from *Clostridium botulinum*. Botulinum toxin type A alters receptor proteins in presynaptic neuron, inhibiting the release of acetylcholine. Injection of these agents at the therapeutic doses results in chemical denervation and localized muscles paralysis. Average onset action is 2 to 3 days and average peak effect occurs at about 7 to 9 days following injection. Duration of effect varies but is typically 3 to 4 months. At which points recurrence of spasm anticipated. Botulinum toxin A injections is safe, simple and easily repeatable and relief symptoms for a different duration of time in different patients. Transient ptosis and diplopia are commonest side effect.

So botulinum neurotoxin injection is now considered the treatment of choice for benign essential blepharospasm.

Hemifacial spasm is a rare neuromuscular disease characterized by irregular involuntary muscle contractions on one side of face. The facial muscles are controlled by facial nerve originates at brainstem and exits below ear where it separates into five main branches. This disease takes two forms : typical and atypical. In typical form ,the twitching usually starts in lower eye lid in orbicularis oculi muscle. As time progresses ,it spreads to the whole lid, then to the orbicularis oris muscle around the lips and buccinator muscle in

the cheekbone area. The reverse process occurs in atypical hemifacial spasm. The most common is typical form and atypical form only seen in 2-3% of patients .The incidence is approximately 0.8 per 100, 000 persons.

This disorder occurs in both men and women and affects middle aged or elderly. Hemifacial spasm is more common in Asian populations. It may be caused by a facial nerve injury or tumor or no apparent cause. Spasm on both sides of face is very rare .

The causes areas follows. Three theories exists to explain the facial nerve dysfunction. The first proposed theory is ephaptic transmission which is electrical activity crossing from one demyelinated neuron to another resulting in a false synapse. The second theory involves abnormal activity of axons at facial nerve root end zone secondary to compressive damage/ demyelination. The third theory or kindling theory involves increased excitability of facial nerve nucleus due to feedback from a damaged facial nerve.

There are several tests to diagnose hemifacial spasm including complete neurological exam, electromyography, magnetic resonance imaging, computed tomography and angiography.

Mild cases may be managed with sedation or carbamazepine. Microsurgical decompression and botulinum toxin injection are the current main treatments used for hemifacial spasm.

There is no known way to prevent hemifacial spasm.

Methodology

This prospective study was conducted in department of Oculoplasty, National Institute of Ophthalmology, Dhaka from November 2014 to March 2016 on 60 patients of which 30 with essential blepharospasm and 30 with hemifacial spasm. They were selected by consecutive sampling technique and inclusion criteria including aged 40-70 years, both sexes, all occupation and excluding secondary causes such as tumors, aneurysm, allergic reaction to botulinum toxin, area of infection or inflammation,

Myasthenia gravis, pregnancy or lactation and muscular spasm not consistent with essential blepharospasm or hemifacial spasm.

All patients were examined clinically before applying injection Botulinum toxin and recorded in 2 proforma 1 for essential blepharospasm and 1 for hemifacial spasm. They containing name, age, sex, occupation, address, chief complain, aggravating and relieving factors, family history, treatment history, DM, HTN, general and systemic examination. Ocular examination includes visual acuity, peri-ocular skin and spasm score 0-4 (Jancovic rating scale: Jancovic and Orman 1987).

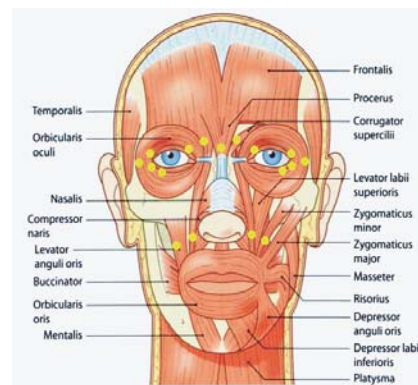


Photograph 1: Botox (Allergan Inc, Irvine, USA) commercially available Botulinum toxin type A

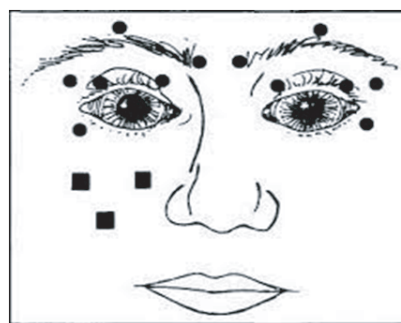
After baseline evaluation a standard dose of 25 units (1 ml) of Botulinum injection (Botox, Allergan Inc, USA) was injected to each patients. Follow up was done after 2 weeks, then monthly for 3 months and assessed visual acuity, peri-ocular skin, blepharospasm score, onset and duration of treatment effect and complications. After collecting data statistical analysis was done using computer based software SPSS program.



Photograph 2: showing technique of Botulinum toxin type-A injection



Photograph 3: Sites (round yellow mark) of Botulinum toxin type-A Injection in Benign Essential Blepharospasm



Photograph 4: Sites of Botulinum toxin injection in Hemifacial spasm.

Observation and Results

Table-1 : Aggravating factors for Benign Essential Blepharospasm (n=30)

Factors	No of cases	Percentage
Bright light	20	66.6
Walking	14	46.6
Hot	5	16.6
Watching television	13	43.3
Fatigue	4	13.3
Eating	3	10.0
Talking	9	30.0
Stress	8	26.6
Whole day	4	13.3
Wind	1	3.0
Morning	1	3.0
Evening	1	3.0
Antipsychotic drug	1	3.0
Sweating	1	3.0
Sunlight	1	3.0
Reading	1	3.0

Table-1 shows symptoms majority patients aggravate during bright light, walking, watching television, talking, and stress and eating.

Table-2 : Relieving factors for Benign Essential Blepharospasm (n=30)

Factors	No of cases	Percentage
Rest	25	83.3
Touching the face	7	23.3
Morning	5	16.7
Sleeping	4	13.3
Walking	3	10.0
Night	1	3.0
Reading Al-Quran	2	6.0
No	2	6.0
Evening	1	3.0
Talking	1	3.0
Cold	1	3.0
Awakening	1	3.0
Concentration on a task	1	3.0

Table-2 shows symptoms of majority patients relieve during rest. Other factors are touching the face, at morning, sleeping, walking, reading holy Quran and at night. 2 patients have found no relieving factor.

Table- 3 : Distribution of onset of treatment effect by group (n=30)

Onset of effect (Post Inj. day)	Benign essential blepharospasm	Hemifacial spasm	p value*
2	5 (16.7)	4 (13.3)	
3	8 (26.7)	10 (33.3)	
4	4 (13.3)	7 (23.3)	
5	4 (13.3)	2 (6.7)	
6	2 (6.7)	1 (3.3)	
7	3 (10.0)	4 (13.3)	
8	1 (3.3)	0 (.0)	
9	1 (3.3)	0 (.0)	
10	1 (3.3)	1 (3.3)	
15	1 (3.3)	0 (.0)	
16	0 (.0)	1 (3.3)	
Total	30 (100.0)	30 (100.0)	
Mean ± SD	4.83 ± 2.90	4.53 ± 2.87	
(Median)	(4)	(4)	
Mean Rank	31.45	29.55	0.667

*Mann-Whitney U test was done to measure the level of significant

Table-3 shows onset of treatment effect in essential blepharospasm in most patients have 2-15 days; majority are within 3 days(26%). In case of hemifacial spasm have 2-16 days; majority are within 3 days (33%).

Table-4 : Distribution of eyelid spasm score in both group (n=60)

Follow up	Benign essential blepharospasm	Hemifacial spasm	p value*
Baseline	3.47± 0.51 (3.0) (4.0)	3.63 ± 0.56	
Mean Rank	27.77	33.23	0.160
1 st follow up	0.37 ± 1.39 (.0) (.0)	0.37 ± 0.72	
Mean Rank	31.98	29.02	0.415
2 nd follow up	0.47 ± 0.73 (0) (.0)	0.40 ± 0.56	
Mean Rank	30.57	30.43	0.972
3 rd follow up	1.03 ± 1.33 (0.5) (.0)	0.60 ± 0.81	
Mean Rank	32.53	28.47	0.322
4 th follow	1.23 ± 1.28 (1.0) (1.0)	1.23 ± 1.07	
Mean Rank	30.02	30.98	0.823

Table-4 shows comparison between two groups. Baseline eyelid spasm score were 3.47 and 3.63. After Botox injection on 1st and 2nd follow up symptoms improved and on 3rd and 4th follow up spasm begins to reappear and more improved in HFS than BEB.

* Mann-Whitney U test was done to measure the level of significant

Figure within bracket indicates in percentage.

Table-5 : Duration of treatment effect (spasm free period)

Spasm free period	Benign essential blepharospasm	Hemifacial spasm	p value*
2 Months	8 (26.7)	0 (.0)	
3 Months	15 (50.0)	20 (66.7)	
4 Months	4 (13.3)	4 (13.3)	
6 Months	2 (6.7)	3 (10.0)	
8 Months	1 (3.3)	2 (6.7)	
12 Months	0 (.0)	1 (3.3)	
Total	30 (100.0)	30 (100.0)	
Mean \pm SD	3.23 \pm 1.36	4.06 \pm 2.10	
(Median)	(3)	(3)	
Mean Rank	26.07	34.93	0.028

*Mann-Whitney U test was done to measure the level of significant

Figure within parenthesis indicates in percentage.

Table -5 shows majority patients (53%) have 3 months spasm free period. Some have 2month (26%), 4months (10%), 6 months (6%) and 8 (3%) months spasm free period.

Discussion

This prospective follow up study was designed to assess the role of Botulinum toxin injection on the rate of eyelid spasm in essential blepharospasm and hemifacial spasm patients attending at National Institute of Ophthalmology and Hospital, Dhaka from November 2014 to March 2016.

In both essential blepharospasm and hemifacial spasm 11 patients(36%)(majority) were within the age group 41-50 years, followed by 51-60 years. Mean age was 51.73 years (SD \pm 9.06) in essential blepharospasm and 49.40 years (SD \pm 2.43) in hemifacial spasm.

Considering sex females are more commonly affected in both benign essential blepharospasm (73%) and hemifacial spasm (60%). Clinical and experimental Ophthalmology showed no significant gender difference.

Most females were engaged with housewives. Others were teachers, office workers, farmers, businessman, engineers, students.

To evaluate the role of Botulinum toxin injection baseline eyelid spasm was recorded, following a scoring system as follows: Eyelid spasm scoring:

0 =none, 1 =increased blinking caused by stimuli, 2 =mild noticeable fluttering no incapacitating, 3= moderate very noticeable spasm mildly incapacitating, 4=severally incapacitating i.e. unable to read, drive, write etc.

There are some aggravating and relieving factors in benign essential blepharospasm. Bright light(66%) is the most common aggravating factor, followed by walking, watching television, talking, stress, hot, fatigue and eating.

Rest is the most common relieving factor(83%) followed by touching the face, at morning, walking, reading holy Quran at night.

Table-1 shows symptoms majority patients aggravate during bright light, walking, watching television, talking, and stress and eating.

Table-2 shows symptoms of majority patients relieve during rest. Other factors are touching the face, at morning, sleeping, walking, reading holy Quran and at night. 2 patients have found no relieving factor.

In case of hemifacial spasm, left side(56%) is commonly affected followed right side(43%).

In this study mean baseline eyelid spasm score was found 3.40 \pm 0.50 (SD) and 3.60 \pm 0.56 between essential blepharospasm and hemifacial spasm respectively. Then 50 unit of Botulinum toxin type- A injection(Botox, Allergan Inc, Irvine, CA, USA) was injected in each patients under all aseptic precaution. Eyelid spasm was again evaluated after 2 weeks; 1 month, 2 months and 3 months using same scoring system.

All patients experienced some relieve of symptoms. Time of onset of effect(the period from the injection until the patient experienced some relief from their symptoms) was estimated by the patients at 1st follow up visit. Mean time of onset of treatment effect amounted to 4.83 \pm 2.90 and 4.53 \pm 2.87 days in essential blepharospasm and hemifacial spasm respectively.

Table- 3: shows onset of treatment effect in essential blepharospasm in most patients have 2-15 days; majority are within 3 days(26%). In case of hemifacial spasm have 2-16 days; majority are within 3 days (33%).

After 2 weeks of Botulinum toxin injection mean score of eyelid spasm become 0.37 \pm 1.39 and 0.37 \pm 0.75 between essential blepharospasm and

hemifacial spasm respectively which is highly significant, p value <0.0001 (p value reached from paired 't' test; d.f=58). About 80% patients show very good response (score level 0-1), 17% show moderate improvement (score-2), 3% shows less improvement (score level-3).

Effect was maintained at 2nd (1st month) & 3rd (2nd month) follow up with mild variation. After 1 month, mean score of eyelid spasm was 0.83±1.37 and 0.33±0.48 respectively. After 2 months 2/3rd of patients remains happy (spasm score 0-2), mean score was 0.83±1.37 and 0.60±0.81 respectively.

Table-4 shows comparison between two groups. Baseline eyelid spasm score were 3.47 and 3.63. After Botox injection on 1st and 2nd follow up symptoms improved and on 3rd and 4th follow up spasm begins to reappear and more improved in HFS than BEB.

* Mann-Whitney U test was done to measure the level of significant

Figure within bracket indicates in percentage.

At 4th follow up visit (after 3 months)- mean eyelid spasm score become 1.63±1.38 and 1.23±1.07 which is significantly lower (p value <0.0001) than baseline eyelid spasm score. 20% and 13% patients of essential blepharospasm and hemifacial spasm respectively had spasm score 3-4. They require re-injection.

p value indicates changes of mean eyelid spasm before and after injection. Both benign essential blepharospasm and hemifacial spasm shows p value is <0.0001 which is extremely significant. Here, p value reached from paired t test.

Comparison between two groups: baseline eyelid spasm score were 3.47 and 3.63 respectively before injection. After injection on 1st and 2nd follow up symptoms improved and on 3rd and 4th follow up spasm begins to reappear and more improved in HFS than BEB.

Duration of effect (period from injection until decline of effect) was assessed by patients and mean duration of treatment was found 3 months 50% and 66% respectively.

Table -5 shows majority patients (53%) have 3 months spasm free period. Some have 2 month (26%), 4 months (10%), 6 months (6%) and 8 (3%) months spasm free period.

No systemic complications were observed. Some patients developed haematoma, ptosis, pain and lagophthalmos temporarily.

Conclusion

Based on the present follow up study and with previous case reports, case series and controlled studies, one may conclude that botulinum toxin injection is very good option for relieving spasm in benign essential Blepharospasm and Hemifacial spasm. It has no systemic complications and patients are highly satisfied. But outcome remains temporary for three months and repetitive injections are necessary. Duration of action of botulinum toxin is more in hemifacial spasm than essential blepharospasm. It acts quickly in hemifacial spasm. Complications are also less in hemifacial spasm than essential blepharospasm. So Botulinum toxin injection is more effective in Hemifacial spasm than Benign essential blepharospasm.

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