ORIGINAL ARTICLE

INJECTION BOTULINUM IN PARALYTIC STRABISMUS
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ABSTRACT: AIM: To assess the effectiveness of botulinum toxin injection to the antagonist muscle in paralytic strabismus. OBJECTIVE: To study the effect of botulinum toxin a injection into the antagonist muscle in cases of paralytic strabismus to alleviate diplopia. MATERIAL AND METHODS: This was a tertiary eye care hospital based prospective interventional study in the department of Orthoptycs over a period from October 2011 to October 2013. 36 patients with paralytic strabismus of recent onset within 3 months, with chief complaint of double vision were included. RESULTS: The study data analysis of 36 patients of paralytic strabismus of recent onset (within 3 months) with chief complaints of double vision showed age wise distribution as 3(8.33%) in 0-20 years, 16(44.44%) in 21-40 years, 16(44.44%) in 41-60 years, 1(2.78%) > 60 years. gender wise 26(72.22%) males, 10 (27.28%) females, aetiology wise 15(41.67%) were diabetic, 4(11.11%) were traumatic, 11(30.56%) were Idiopathic, 2(5.56%) were due to CSOM and 4(11.11%) due to Diabetes and Hypertension. All patients were treated with botulinum toxin injection to the antagonist nonoparotic muscle and were followed at an interval of 1 week, 1 month and 3 months. Thorough clinical examination and Diplopia charting were done before and after treatment. CONCLUSION: Injection botulinum into the antagonist muscle during the first three months after the onset allows the patients to enjoy and appreciate fusion in primary gaze without necessity for head turn, Prevents contracture of antagonist muscle. Thus botulinum toxin is useful in the treatment of acute paretic loss of ocular muscle function when surgical treatment of the ocular muscles is not yet possible but the patient is obviously disturbed by diplopia or forced head posture. The procedure is simple, safe and effective method. KEYWORDS: Botulinum, Double Vision Paralytic Strabismus.

INTRODUCTION: Strabismus is the condition where the visual axes of two eyes do not meet at the point of object of regard. Strabismus may occur in one of two major forms: either comitant or incomitant. In comitant strabismus, the deviation for a given fixation distance, is same in all directions of gaze. In Incomitant strabismus, one or more extra ocular muscles show signs of under action or paralysis. The deviation therefore varies in different direction of gaze and is larger when the eyes are turned in the direction of action of under acting or paralytic muscle.¹

Binocular patients who develop strabismus before the age of 7-9 years usually develop the sensory adaptions of suppression and anomalous retinal correspondence to obviate diplopia and visual confusion. Older patients who develop strabismus for the first time suffer from diplopia and visual confusion as long as vision remains in both eyes, until the eyes are aligned. To achieve binocular single vision to avoid diplopia and confusion they adopt anomalous head posture such head turn, head tilt, and chin elevation or depression. Surgery is indicated only when spontaneous resolution does not takes place after 6 months of follow up.

During this period injection of botulinum toxin into the overacting unopposed antagonist of a paralysed muscle causes temporary paralysis, preventing its contracture and allowing the paralysed muscle to take up the slack and reduce or correct the ocular misalignment and provides the patient
with a useful zone of single binocular vision and avoid a compensatory and uncomfortable head postures until such time that the function of the paralysed muscle returns.\textsuperscript{2}

In the early 1970 Alan B. scott of san Francisco first established that injection with botulinum toxin type A (Botox allergen) is the most effective method to paralyse a muscle temporarily\textsuperscript{3,4}

By this study an effort has been made by us to highlight the effects of botulinum injection in the treatment of paralytic strabismus.

**MATERIALS AND METHODS:** This is a prospective interventional study done at a tertiary eye care government medical college hospital from October 2011 to October 2013. The study included 36 patients who attended strabismus O.P.D with paralytic strabismus of recent onset within 3 months with chief complaint of double vision.

**Inclusion Criteria:** All cases of paralytic strabismus of recent onset within 3 months with chief complaint of double vision attending strabismus O.P.D.

**Exclusion Criteria:**
1. All cases of paralytic strabismus of more than 3 months of duration of onset.
2. Paralytic strabismus without diplopia in primary gaze.
3. 6th nerve palsy with papilledema on fundus examination.
4. Complete 3rd nerve palsy.

All cases were examined under similar conditions. A detailed history is taken with reference to following points:
1. Subjective symptoms such as double vision-Mode of onset, constant or intermittent, distance at which diplopia is noticed, field where greatest separation of images occurs, any change since onset, does diplopia disappear when eye is occluded.
2. Any attributed cause.
3. Any previous ocular problem and treatment taken or any squint surgery done in the past.
4. General health.
5. Family history of squint.

A thorough examination of the anterior segment was done under slit lamp. Best corrected visual acuity was recorded. A detailed orthoptic examination was done for all cases which includes:
- Facial symmetry and compensatory head posture.
- Hirschberg corneal reflex test.
- Cover test and uncover test.
- Alternate cover test to establish whether the squint is unilateral or alternate and also to differentiate comitant from paralytic squint (Where secondary deviation is greater than primary deviation)
- Prism bar cover test- done for near and distance with appropriate refractive error correction appropriate prisms (Base- in/Base- out) The deviation was measured in all the directions of gaze.
- Ocular motility was tested in all cases.
• Diplopia charting- The patient is asked to wear red green goggles; red glass being in front of right eye and green in front of left eye. The patient is made to sit with his/her head straight in a semi dark room and is shown a fine linear light from a distance of gaze. For each direction, the patient is asked to comment on the position, brightness and separation between the red and green images.

• FDT- Forced Duction test for diagnosing the presence of mechanical restriction of ocular motility. After anesthetizing the conjunctiva with 4% xylocaine eye is moved with two toothed forceps applied to the conjunctiva near the limbus in the direction opposite to that in which mechanical restriction is suspected. For instance to distinguish between lateral rectus paralysis and mechanical restriction involving the medical aspect of the globe, we apply the forceps at the 6 and 12.00 0 clock positions and move the eye passively into abduction. If no resistance is encountered the motility defect is clearly caused by paralysis of the lateral rectus muscle.

All patients were given a single injection of 0.1 ml Botox containing 2.5 units of botulinum toxin A into the antagonist muscle by a single surgeon under sterile conditions. In patients with esotropia due to 6th nerve palsy, injection was given to the medical rectus muscle and in patients with exotropia due to partial 3rd nerve palsy without ptosis; injection was given to the lateral rectus muscle.

Procedure for the Administration of Botulinum Toxin: Topical local anesthetic agent (Ex proparacine eye drops) was administered in the affected eye after cleaning and draping the eye in the operation theatre.

An eye speculum is used to keep the lids apart.

Patient is asked to look in the direction of paralyzed muscle and 0.1 ml of Botox containing 2.5 units is injected into the overacting antagonist muscle by grasping the muscle tendon with fixation forceps. For example 5.5mm from the limbus to grasp Medial rectus, 7mm from the limbus to grasp Lateral rectus muscle. Applied Anatomy of the extra ocular muscles were followed.5,6,7,8,9

After injecting the eye is closed with a sterile pad and taped. Patient is asked to remove the pad after 2hrs and to start topical antibiotic drops (flouroquinolones) every 8th hourly for 1 week.

All patients who were treated with botulinum toxin injection to the antagonist muscle were followed at regular intervals of 1 week, 1 month and 3 months. Through clinical examination including orthoptic measurements and diplopia charting were done.

![Procedure for the administration of botulinum toxin](image-url)
RESULTS: Our study included 36 patients of paralytic strabismus of recent onset within 3 months presenting with chief complaint of double images.

The effects of the botulinum toxin treatment were measured as the change in the strabismus angle in relation to the pre-injection value, presence of diplopia in primary gaze, relation between duration of presentation and the reduction in deviation, relation between aetiology of paralytic strabismus and reduction in deviation, the extent of recovery of movement and the results were statistically analyzed.

The data after statistical evaluation were presented as mean±SD.

Among 36 patients with neurogenic palsy, 32 patients were with esotropia due to 6th nerve palsy and 4 patients were exotropia due to partial 3rd palsy. All cases had chief complaint of double vision. All cases of 6th nerve palsy had restriction of abduction movement due to lateral rectus palsy and all cases of 3rd nerve palsy had restriction of adduction movement due to medial rectus palsy.

SEX DISTRIBUTION: Our study had 26 males (72.22%) and females (27.78%)

| Sex   | No. of Patients | Percentage |
|-------|-----------------|------------|
| Male  | 26              | 72.22%     |
| Females | 10              | 27.78%     |

Table 1: Sex Distribution

AGE DISTRIBUTION:

The age of the patients in the study ranged from 8-65 years.

The mean age was 39.63±13.41 years.

| Age | No. of Patients | Percentage |
|-----|-----------------|------------|
| 0-20| 3               | 8.33%      |
| 21-40| 16              | 44.44%     |
| 41-60| 16              | 44.44%     |
| >60 | 1               | 2.78%      |

Table 2: Age Distribution

DURATION OF PRESENTATION:

The mean duration of presentation was 42.83±29.18 days

Minimum duration of presentation was 5 days and maximum was 3 months.

| Duration in days | No. of Patients | Percentage |
|------------------|-----------------|------------|
| 1-30             | 21              | 58.33%     |
| 31-60            | 8               | 22.22%     |
| 61-90            | 7               | 19.44%     |

Table 3: Duration of Presentation
Aetiology of Paralytic Strabismus: The causes of paralytic strabismus were vascular in 19 patients, idiopathic in 11 patients, traumatic in 4 patients, chronic suppurative otitis media in 2 patients.

| Aetiology     | No. of Patients | Percentage |
|---------------|-----------------|------------|
| DM            | 15              | 41.67%     |
| Trauma        | 04              | 11.11%     |
| Udiopathic    | 11              | 30.56%     |
| CSOM          | 02              | 5.56%      |
| DM&HTN        | 04              | 11.11%     |

Table 4: Aetiology of Paralytic Strabismus

Amount of deviation before and after injection- effect of the botulinum toxin treatment.

| Visit      | Deviation in Prism Diopters mean +/- SD |
|------------|----------------------------------------|
| Pre treatment | 33.83 +/-12.29                         |
| 1 week      | 7.48 +/-15.33                           |
| 1 month     | 6.58 +/-15.50                           |
| 3 months    | 5.59 +/-15.66                           |

Table 5: Mean deviation in prism diopters before and after injection
The pre injection deviations ranged from 18 to 60 prism Diopters. At 1 week post injection the full effect had developed in most of the cases the mean maximal effect was reduction of strabismus from 33.83 prism diopters to 7.48 prism diopters i.e. 26.35 reduction at 1 week after injection when the difference was statistically analyzed the p value was found to be < 0.0001.

As p-value is <0.0001 the reduction in the degree of deviation at 1 week after treatment with botulinum toxin is considered extremely significant.

At 1 month the mean deviation was 6.58 prism Diopters and 3 months the mean deviation was 5.59 prism Diopters. The reduction in the deviation after treatment was maintained at subsequent follow up.

Of the 36 Patients having received Injections, at 1 week after Injection;

- 31(86.12%) patient had no deviation on Hirschberg corneal reflex test i.e. restored orthotropia and binocular single vision in primary gaze position i.e., there was no diplopia in primary gaze.
- 5 (13.89%) patients did not achieve binocular single vision as there was no significant reduction in the deviation before and after treatment. Among these 5 patients 2 cases were diabetic, one case was both diabetic and hypertensive, and 2 were due to unknown aetiology. When these 5 cases were subsequently followed up at 1 month and 3 months, there was no change in the degree of deviation and there was no improvement.

| Deviation on HCRT        | No. of Patients | Percentage |
|--------------------------|-----------------|------------|
| No. Deviation            | 31              | 86.12%     |
| Persistent Deviation     | 05              | 13.89%     |

Table 6: Deviation on HCRT at 1 week after injection

Of 31 Patients who had no Deviation on HCRT:

- 22 (61.12%) patients had no deviation on prism bar cover test.
- 9 (25%) patients had deviation within 10 prism dioptres on prism bar cover test. However when these patients were subsequently followed at 1 month and 3 months there was no deviation on prism bar cover test.
Relation between Duration of Presentation and Effect of Botulinum Toxin: Of 21 patients presenting within 1 month of duration, mean deviation before treatment was 30.10 prism dioptres. After treatment at 1 week, mean deviation was 2.58 prism Diopters i.e., 27.52 prism diopters reduction was observed at 1 week after injection.

Of 8 patients presenting within 1-2 month of duration, mean deviation before treatment was 35.13 prism diopters. After treatment at 1 week, mean deviation was 14.63 prism diopters i.e., 20.50 prism diopters reduction was observed at 1 week after injection.

Of 7 patients presenting within 2-3 months of duration, mean deviation before treatment was 43.58 prism diopters. After treatment at 1 week, mean deviation was 12.58 prism diopters i.e., 31 prism diopters reduction was observed at 1 week after injection.

When the difference between pre injection and post injection deviation was compared in cases presenting with in <1 month of duration, 1-2 months of duration and 2-3 months of duration, it was observed that there was no difference in between the patients with different onset of duration. All patients had significant reduction in the deviation.
However the reduction in the mean deviation after injection was more in cases presenting within 2-3 months of onset of duration when compared to other two groups, this could probably because of an element of spontaneous recovery of nerve function in these cases.

**RELATION BETEEN AETIOLOGY AND EFFECT OF BOTULINUM TOXIN:**

| Aetiology | Pre-Treatment Deviation in Prism Diopters | Post-Treatment Deviation (1week) in Prism Diopters |
|-----------|------------------------------------------|--------------------------------------------------|
| DM        | 34.86±11.70                              | 5.47±12.78                                      |
| Trauma    | 41.25±13.15                              | 13.50±24.41                                     |
| Idiopathic| 31.45±12.31                              | 6.73±15.37                                      |
| CSOM      | 31.50±19.09                              | 3±4.24                                          |
| DM&HTN    | 30.25±14.29                              | 13.25±21.50                                     |

Table 9: Comparison of effect of Botulinum toxin in patents with different Aetiology

Out of 36 Cases:
- Diabetic cases were 15. In them mean deviation before treatment was 34.86 prism diopters. At 1 week after treatment, mean deviation was 5.47 prism diopters i.e., 29.39 prism dioptres reduction was observed at 1 week after injection.
- Idopathic cases were 11, in them mean deviation before treatment was 31.43 prism dioptres. At 1 week after treatment, mean deviation was 6.73 prism diopters i.e., 24.72 pirsmdioptres reduction was observed at 1 week after injection.
- Traumatic cases were 4. In them mean deviation before treatment was 41.25 prism dioptres. At 1 week after treatment, mean deviation was 13.45 pirsmdioptres i.e., 27.80 prism dioptres reduction was observed at 1 week after injection.
- Four cases had diabetes and hypertension. In them mean deviation before treatment was 30.25 prism diopters. At 1 week after treatment, mean deviation was 13.25 prism diopters i.e .17 prism diopters reduction was observed at 1 week after injection.
Two cases had chronic suppurative otitis media. In them mean deviation before treatment was 31.50 prism dioptres. At 1 week after treatment, mean deviation was 3 prism dioptres i.e., 28.50 prism dioptres reduction was observed at 1 week after injection.

There was no correlation between the effect of botulinum toxin injection and the etiology of paralytic strabismus.

**Relation between Recovery of Restricted Movement and Effect of Botulinum Toxin:** The abduction movement in 6th nerve palsy and the adduction movement in 3rd nerve palsy were measured before and after treatment and the results were analyzed.

The mean movement in mm before injection was 3.67, at 1 week after injection the mean movement was 4.75 at 1 month the mean movement was 7.48 at 3 months the mean movement was 8.47. There was no significant improvement in movement at 1 week after injection. Botulinum toxin injection does not effect the recovery of the movement.

| Visit     | Restricted Movement in mm mean +/– SD |
|-----------|--------------------------------------|
| Pre treatment | 3.67±2.0                           |
| 1 week       | 4.75±2.05                           |
| 1 month       | 7.48±2.85                           |
| 3 months      | 8.47±2.94                           |

**Table 10: Restricted movement in mm before and after injection**

Of the 36 patients in our study, 21 (58.33%) patients had full recovery of movement at 1 month.

Of the remaining 15 patients, 10 (27.78%) patients had full recovery and 5 (13.89%) patients had no recovery of movement at 3 months.

| Visit     | No. of patients with full recovery of movement | Percentage |
|-----------|-----------------------------------------------|------------|
| At 1 month| 21                                            | 58.33%     |
| At 3 months| 10                                           | 27.78%     |

**Table 11: No. of patients with full recovery of movement**
Thus at 3 months, of 36 patients 31 patients (86.12%) patients recovered adequately while 5 (13.89%) patients did not recover.

| Visit          | No. of patients | Percentage |
|----------------|-----------------|------------|
| Complete recovery | 31              | 86.12%     |
| No recovery     | 05              | 13.89%     |

Table 12: No. of patients with complete recovery at 3 months

**COMPLICATIONS:** Out of 36 patients having injection, 4(11.12%) patients had subconjunctival haemorrhage which resolved in 2-3 weeks.
DISCUSSION: Paralytic strabismus presents with chief complains of diplopia and confusion due to motor imbalance arising from paralysis of extraocular muscles. To achieve binocular single vision to avoid diplopia and confusion they adopt anomalous head postures such as head turn, head tilt, and chin elevation or depression. Surgery is indicated only when spontaneous resolution does not take place after 6 months of follow up.

Conservative measures to avoid diplopia and confusion include occlusion therapy and use of Fresnel prisms. Occlusion of only the involved eye predisposes to contracture of the antagonist muscle, while occlusion of only the uninvolved eye results in past pointing and disturbed mobility. Fresnel prism blurs vision slightly and patients with this form of early treatment find some difficult to tolerate.

Patients with acute onset nerve palsies can be considered excellent candidates for botulinum therapy. Botulinum is thought to be useful because it eliminates diplopia in primary gaze by causing a temporary paralysis of the antagonist muscle. Thus fusion may be obtained within a few days without a marked head turn. In addition the induced paralysis prevents contracture of the antagonist muscle (which can result in a residual deviation due to mechanical factors, even if there has been recovery from the nerve palsy).10,11

Our study included 36 patients with paralytic strabismus of recent onset (within 3 months). Among 36 patients with neurogenic palsy, 32 patients were with esotropia due to 6th nerve palsy and 4 patients were with exotropia due to partial 3rd nerve palsy. All cases had chief complaint of horizontal diplopia. All cases of 6th nerve palsy had restriction of abduction movement due to lateral rectus palsy and all cases of 3rd nerve had restriction of adduction movement due to medial rectus palsy. All patients were treated with 2.5 units of botulinum toxin a injection to the antagonist nonparetic muscle only one time and were followed at regular intervals of 1 week, 1 month and 3 months.

The study had 26 males and 10 females. The age of the patients in the study ranged from 8-65 years. The mean age was 39.63±13.41 years. The mean duration of presentation was 42.83±29.18 days. Minimum duration of presentation was 5 days and maximum was 3 months. The causes of paralytic strabismus were vascular in 19 patients idiopathic in 11 patients traumatic in 4 patients, chronic suppurative otitis media in 2 patients.

The preinjection deviations ranged from 18 to 60 prism dioptres. At 1 week post injection the full effect had developed in most of the cases. The mean maximal effect was a reduction of strabismus from 33.83 prism diopters to 7.48 prism Diopters i.e., 26.35 prism diopters reduction at 1 week after injection. The results of our study were comparable with the values mentioned in the literature.

In a study by Gunnar lennerstand, odd AsmundNorbo, SunaTian, which was on evaluation of effects and complications of botulinum toxin in strabismus12, the mean maximal effect was a reduction of strabismus of 24.2 prism diopters at 1 week after injection into the antagonist muscle in paralytic strabismus.

Of the 36 patients having received injections, at 1 week after injection 31(86.12%) patients had no deviation on Hirschberg corneal reflex test i.e., restored orthotropia and binocular single vision in primary gaze position i.e., there was no diplopia in primary gaze. Of these 31 patients, in 22(61.12%) patients there was no residual deviation on prism bar cover test. 9(25%) patients has deviation within 10 prism dioptres on prism bar cover test. 9(25%) patients had deviation within 10 prism dioptres on prism bar cover test. However when these patients were subsequently followed at
1 month and 3 months there was no deviation on prism bar cover test. 5(13.89%) patients did not achieve binocular single vision as there was no significant reduction in the deviation before and after treatment.

Thus our study suggests that early botulinum toxin injection of patients with recent onset (Acute) nerve palsy appears to be beneficial allowing the patient to enjoy and appreciate fusion without the necessity of a marked head turn. Thus botulinum toxin is useful in the treatment of acute paretic loss of ocular muscle function when surgical treatment\textsuperscript{13} of the ocular muscles is not yet possible but the patient is obviously disturbed by diplopia or a forced head posture.

In a study by Quah BL, Ling YL, Cheong PY, Balakrishnan V2, A total of 25 injections were given to 19 patients. Seven patients (36.8%) had final ocular alignment within 10 prism dioptries of orthotropia of which six achieved fusion at primary gaze position.

Scott and Kraft,\textsuperscript{14} injected three patients within eight weeks of the onset of the palsy and all three patients recovered fully with orthophoria in the primary position.

In a study by A.D.N Murray,\textsuperscript{5} University of Cape Town, South Africa, Six patients were treated within eight weeks of the onset of the palsy. Within a few days five of the six gained fusion, without the necessity of a marked head turn and none complained of diplopia. The same five recovered full function.

Metz and Mazow,\textsuperscript{15} injected 34 patients with sixth nerve palsy, within 12 weeks of onset of the palsy. 16 Of the 31 patients that could be followed, 22(71%) recovered adequately without surgery, while 9(29%) developed chronic paralysis requiring strabismus surgery.

Of the 36 patients in our study 21(58.33%) patients had full recovery of movement at 1 month. Of the remaining 15 patients, 10(27.78%) patients had full recovery 5(13.89%) patients had no recovery movement at 3 months. At 3 months of 36 patients 31(86.12%) patients recovered adequately, while 5(13.89%) patients did not recover. In our study the sample size is less and does not have controls and since some patients may recover spontaneously a randomized double-blind study is necessary to more precisely determine the effectiveness of this form of therapy.

In our study when the difference between preinjection and postinjection deviation was compared in case presenting with in <1 month of duration, 1-2 months of duration and 2-3 months of duration, it was observed that there was no difference in between the patients with different onset of duration. All patients had significant reduction in the deviation. Thus our study suggests that there is no correlation between the effect of botulinum toxin injection and the duration of presentation in patients presenting within 3 months.

When the difference between preinjection and postinjection deviation was compared in cases with different aetiologies, it was observed that there is no correlation between the effect of botulinum toxin injection and the etiology of paralytic strabismus.

In our study the mean of the restricted movement in mm before injection was 3.67, at 1 week after injection the mean movement was 4.75, at 1 month the mean movement was 7.48, at 3 months the mean movement was 8.47. There was no significant improvement in movement at 1 week after injection. This implies that botulinum toxin injection doesn’t appear to be effective in facilitating recovery of the paralysed muscle function.

The most of the previous studies,\textsuperscript{16,17,18,19} have proven the safety and effectiveness of botulinum injection in paralytic strabismus.

The side effects of the botulinum toxin treatment are mainly due to spread of toxin to non-injected muscles, particularly to the levator muscle, causing ptosis and to the inferior rectus muscle.
causing vertical diplopia. In literature it was observed that side effects were generally more frequent with the higher doses. In our study we used a standard low dose of 2.5 units thus we did not have any complications except for subconjunctival haemorrhage. Of 36 patients in our study only 4(11.12%) patients had subconjunctival haemorrhage which resolved in 2-3 weeks.

CONCLUSION: Botulinum toxin injection into the antagonist extra-ocular muscles in an ideal and safe therapy for the treatment of paralytic strabismus of recent onset.

Injection of botulinum into the antagonist muscle during the first 3 months after the onset allows the patient to enjoy and appreciate fusion in the primary gaze without the necessity of a marked head turn till surgery is done and prevents contracture of antagonist muscle.

In our study the sample size is less and does not have controls and since some patients may recover spontaneously a randomized double blind study is necessary to more precisely determine the effectiveness of this form of therapy.

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