Botulinum Toxin A in Surgically Overcorrected and Undercorrected Strabismus

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Objective: *To evaluate the effectiveness and safety of botulinum toxin A injection in treating overcorrected and undercorrected strabismus after unsatisfactory postoperative alignment.*

Material and Method: *The authors reviewed the outcomes of 20 patients aged 5 to 56 years (mean 29.1 years) who had botulinum toxin A injection following their unsatisfactory operation. The motor outcomes (percentage of successful motor outcome and percentage change in deviation) were recorded at 1 month, 3 months, 6 months, 1 year, 2 years, 3 years, and 4 years after botulinum toxin injection.*

Results: *The mean pre-botulinum toxin injection angle of deviation was 20.6 prism dioptors (PD). Six of 20 (30%) patients maintained the successful position for the average of 2.66 years (range 1-4 years) with single injection. The mean percentage change of the deviation was 87.50%, 87.93 %, 73.05 % at 1, 2, and 3-year visit respectively. In 3 of 5 (60%) patients of consecutive esotropia, 4 of 8 (50%) residual esotropia, 1 of 4 (25%) of consecutive exotropia and 1 of 3 (33.33%) of residual exotropia had successful motor alignment at 6 month visit. There was no scleral perforation, visual loss, or retrobulbar hemorrhage from the injection treatment in the present study.*

Conclusion: *Botulinum toxin A injection appears to be a safe and effective treatment for overcorrected and undercorrected strabismus after unsatisfactory surgery. It is very effective in rapid elimination postoperative diplopia. When the result is not adequate or the effect does not last long, repeat the injection or reoperation can be chose to perform later.*

Keywords: *Botulinum toxin, Consecutive esotropia, Residual esotropia, Consecutive exotropia, Residual exotropia*

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The most common complication of surgery for strabismus is unsatisfactory alignment[1]. Reoperation is frequently required to correct the misalignment or diplopia. Botulinum toxin injection has been reported to be effective in treating children who had previous operation[2,3]. The present study showed the effectiveness and safety of botulinum toxin injection in surgically overcorrected and undercorrected strabismus in adult and children.

Material and Method

The patients who had unsatisfactory surgical alignment and did not want reoperation were included in the present study. The patients were divided into 4 groups: consecutive esotropia, residual esotropia, consecutive exotropia, and residual exotropia. The angles of deviation were measured by alternate prism cover test at 6 and 0.33 meters or with the Krimsky method when the cover tests were not possible. The Worth 4 dot and synoptophore were used to assess the sensory status before and after the botulinum toxin injection. In all adults, botulinum toxin type A (Botox) was administered under topical anesthesia alone (0.5% tetracaine hydrochloride) with electromyographic control. Only two children had botulinum toxin injection under general anesthesia. The concentration of botulinum toxin 2.5 U in 0.1 ml per muscle was used in all cases. In consecutive esotropia and residual esotropia, the medial rectus muscle was injected. In consecutive exotropia and residual exotropia, the lateral

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rectus muscle was injected. The information recorded included the following: age at presentation, refraction, best corrected visual acuity, diagnosis, sensory status, types and numbers of operations performed, angle of deviation before botulinum toxin injection, the duration between the last operation and the time of injection, dose of botulinum toxin, numbers of injections, angles of deviation within 1 month after the injection, at 6 months, 1 year, 2 years, 3 years, and 4 years post injection. The follow up ranges from 3 months to 4 years. At any time post injection, if the patient is not satisfied with the deviation of the eye or the diplopia recurs, the patient can choose to have reoperation or repeated botulinum toxin injection in the same dose. In the patient who chooses repeated injection, the follow up protocol will be the same as the first injection. Successful motor alignment was defined as a distance deviation of within 10 PD of orthophoria by the alternate prism cover test.

Results

There were 20 patients in the present study. The mean age was 29.1 years (range 5-56 years). In 10 of 20 patients, the visual acuity in one eye was equal or worse than 20/70, the other 10 patients had best corrected visual acuity 20/20 in both eyes. For the causes of strabismus, 13 in 20 patients were infantile strabismus; the other seven patients had strabismus acquired by trauma. In 19 of 20 patients, there was no fusion potential before and after injection. Of the 19 patients without fusion potential, nine patients (47.36%) achieved and maintained good ocular alignment and resolution of their diplopia more than 6 months. In the only one patient with fusion potential, she achieved and maintained successful alignment for 3 years after a single botulinum injection.

Before toxin treatment, an average of 1.2 operations (range 1-3 times) had been performed per patient. The mean pre-botulinum toxin injection angle of deviation was 20.6 PD (SD 7.32). The average angle of deviation was 12.8 PD in consecutive esotropia, 22.12 PD in residual esotropia, 22.75 PD in consecutive exotropia and 26.6 PD in residual exotropia. The time elapsed between the last surgery and botulinum toxin injection ranges from 1 to 260 weeks (median = 4 weeks). In 18 of 20 patients, the interval between the last surgery and botulinum toxin injection was within 12 weeks, only two patients had long interval (208 and 260 weeks). The average number of injections was 1.95 (range 1 to 10) per patient. In the patient having 10 injections, the angle of deviation frequently decreased following each injection but the effect lasted only for 3 months. This patient prefers repeated injection to reoperation. In 4 of 20 patients suffered from diplopia following the last surgery, the diplopia was eliminated in all four cases after botulinum toxin injection.

Nine patients were overcorrected strabismus (five consecutive esotropia and four consecutive exotropia) and nine patients were undercorrected strabismus (8 residual esotropia and 3 residual exotropia).

In table 1, the results of the first injection were showed in mean percentage change in the deviation (preoperative deviation postoperative deviation/ preoperative deviation 100%) at 1, 3, 6 months, 1, 2, 3, and 4 years after the injection of the four groups.

Successful motor alignment was defined as a distance deviation of within 10 PD of orthophoria by the alternate prism cover test. Of 20 patients, 12 had only one injection and eight had multiple injections. In 12 patients with single injection, successful alignment was achieved in seven patients (58.33%) at 3-month follow-up. Six of seven patients maintained the successful position for the average of 2.66 years (range 1-4 years) without any further management. Of 8 patients with multiple injections, seven got the successful motor alignment for less than 6 months each times, only one patient maintained good alignment for 4 years after two injections. In two patients who had injection 208 and 260 weeks after the last surgery, did not have successful motor alignment at 3-month visit.

Long-term successful motor alignment was defined as maintain a distance deviation of within 10 PD of orthophoria for 6 months. According to the present findings, nine in 20 patients (45%) had longterm successful motor alignment. All the nine patients had injection within 12 weeks. In three of five (60%) patients of consecutive esotropia, four of eight (50%) residual esotropia, one of four (25%) of consecutive exotropia and one of three (33.33%) of residual exotropia had a long-term successful motor alignment.

In two children who had single injection, one patient in the residual esotropia group maintain a distance deviation of within 10 PD of orthophoria for 1 year while the other child in consecutive exotropia group was in the motor successful alignment for 3 years after injection then the angle start to gradually increase.

Of 39 injections of botulinum toxin, transient ptosis occurred in four of the 39 (10.25%) and secondary vertical deviation was momentary in only one of them (2.56%). In the present study, there was no globe perforation, visual loss, papillary dilatation, persistent

Table 1. Mean percentage change in the deviation (pre-operative deviation - post-operative deviation/preoperative deviation ◊ 100%)

Group	1 Month		3 Months		6 Months		1 Year		2 Years		3 Years		4 Years	
	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD
Consecutive esotropia	145.00	62.25	91.00	35.78	100.00	0.00	100.00	0.00	100.00	0.00	100.00	0.00	-	-
Residual esotropia	109.75	66.10	64.75	37.17	74.67	30.35	81.33	16.65	85.71	0.00	72.62	79.13	-	-
Consecutive exotropia	105.63	53.48	55.75	38.11	69.00	55.15	78.00	53.74	83.00	46.67	60.00	56.57	116.00	0.00
Residual exotropia	72.89	24.60	32.00	30.20	-	-	-	-	-	-	-	-	-	-
	112.21	58.99	64.60	38.36	81.13	30.36	87.50	24.51	87.93	28.15	73.05	51.30	116.00	0.00

diplopia, or retrobulbar hemorrhage from the botulinum toxin injection.

At final follow-up, 12 patients were still having small and stable deviation, two patients went on to the strabismus surgery and six patients failed to follow up.

Discussion

Overcorrection and undercorrection of the alignment are the most common complication following strabismic surgery. With new alignment, the image may be moved out of the suppression scotoma of the deviated eye, the diplopia can develop. Therefore, the overcorrection and undercorrection are not only cause misalignment, but also disturbing diplopia. The majority of patients do not want another surgery and occasionally the angle of deviation is too small to do reoperation. The postoperative inflammation of the eye prevents the reoperation to be appropriate in the early postoperative days. Most surgeons will wait for 6 weeks before doing another surgery[4]. In a patient who has postoperative diplopia will be troubled during 6 weeks. Half of the patients in the present study had poor vision in one eye; therefore, the operations were already done in that eye. When overcorrection or undercorrection occurred, they did not want the good eye to be operated. Hence, the author was interested in other management that is safe, more rapid and less invasive, such as botulinum toxin injection.

Botulinum toxin injection has been report to be effective in treating previously operated strabismic children[2,3]. Tejedor et al[5] compared botulinum toxin injection with reoperation in the management of previously operated acquired esotropic children and suggested that botulinum toxin injection may be as effective as reoperation, particularly in early failures. For previously operated infantile esotropia, Tejedor et al[6] found that botulinum toxin injection and reoperation are equally effective after 3 years of follow up.

Botulinum toxin causes paralysis of injected extraocular muscle within 2-4 days after injection and lasts clinically for at least 5-8 weeks[7]. In the present study, the percentage change in the deviation from first injection is highest (112.21%) within 1 month after injection then declined at 3 months. After 6 months, the percentage change is quite stable. Even it is high again at 4-year visit, there was not statistic significant because there was only one patient who is still successful and come to follow up. For previously operated infantile esotropia, the successful alignment rates obtained with both botulinum injection and reoperation decline only slightly with time[6].

Following botulinum injection, that extraocular muscle is paralyzed and lengthen while its antagonist contracts. The long-term successful alignment of the eyes may be explained by the contraction of the antagonist of the injected extraocular muscle. Repeated injection of botulinum toxin is necessary in some cases to maintain the satisfactory alignment.

In the present study, the successful motor alignment (60% of consecutive esotropia and 50% of residual esotropia) in the esotropia group seems to be better than the exotropia group (25% of consecutive exotropia and 33.33% of residual exotropia). It is interesting to note that the greater concentration of singly innervated fibers in the medial rectus muscle[8] makes it easier to paralyze than the lateral rectus. In the present study, the percentage of long-term success in motor outcome was highest in the consecutive esotropia group. The medial rectus is shorten and reattached to the previous insertion in consecutive esotropia, therefore it can be relaxed from botulinum injection. Whereas in residual esotropia, the medial rectus is already recessed and has less potential to be more weaken. In consecutive exotropia, the lateral rectus is injected but the previous recessed medial rectus has less potential to strengthen or shorten in response to the paralysis of the lateral rectus. In residual esotropia and residual exotropia, the technique seem to be difficult because the needle has to be penetrated deeper and through scar tissue to inject the recessed medial rectus and lateral rectus, respectively. A previous investigation[2] considered that botulinum injection is more effective in small deviations (10-20 PD) than larger deviations (20-110 PD). In the present study, the highest long term success in the consecutive esotropia group might be related to the smallest mean pre-injection deviation in this group. However, the sample sizes in the present study may be considered a design limitation to compare among four groups statistically.

The previous study[5] showed that botulinum injection was probably more effective when performed within 3 months following initial surgery. It is most likely that the lower efficacy following injection in the late state is due to the restriction of scar tissue and adhesions. In the present study, 90 % of the patients had injection within 3 months and the long-term success rate was 50%. While the other 10% who had late injection, had angle decreased following injection but only for 3 months. The influence of postoperative delay after initial surgery on the efficacy of botulinum injection cannot be accurately compared from the present data because of the different numbers of members in each group. However, it seems reasonable to treat unsatisfactory cases with botulinum toxin injection earlier because it is less invasive and more effective in early state.

Scott et al[2] considered that previously operated adult was not so effectively treated by botulinum toxin injection, whereas there was only a small difference in the success rates between previously operated and non-operated children. This is attributed to the retained elasticity of the extraocular muscles in children. In the present study, there were only two children. Long-term successful motor alignment with single injection was achieved in all children.

Almost none of the patients in the present study had fusion potential therefore, it is difficult to compare the effect of injection between the group with and without fusion potential. Though botulinum toxin injection has been reported to be more effective in those with fusion potential[2,3,9], the present study has 47.36% satisfactory alignment at 6 months in patients without fusion potential. The author agrees that fusion potential contributes to long-term success with botulinum toxin treatment as it does with surgery, but it may not compulsory for successful alignment improvement from botulinum toxin.

The author expects that the incidence of side effects following botulinum toxin injection should be higher in previous operated patients. This might be related to the difficulty of penetration of needle through the scar tissues and the anatomical change of extraocular muscle in patients who have undergone prior surgery. Comparing to the study[10] done by the same surgeon in the comitant strabismus without previous operation, the occurrence of diplopia in the present study is 1.45% higher while the occurrence of secondary deviation is 1.84% lower. A previous investigation also showed that the frequency of ptosis following botulinum toxin injection was higher in previous operated patients[11].

Botulinum toxin treatment can avoid the creation of more scar tissue from repeated surgery and, if unsuccessful, another surgery can be performed. At final follow-up of the present study, 12 patients had satisfactory alignment and two patients who failed from injection, had successful alignment from reoperation. The injection could affect the result of the surgery. The toxin-induced paralytic deviation may last for more than 6 months[6], the surgery should be delayed until the effect of the toxin subsided.

Conclusion

The present study suggests that the use of botulinum toxin A is effective and safe in treating overcorrected and undercorrected strabismus after unsatisfactory surgery. With this procedure, many patients may avoid reoperation and eliminate diplopia with a rapid and less invasive technique. Another advantage is an opportunity to repeat the injection or to perform another surgery if the result is inadequate or the effectiveness does not last long.

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การใช้โบทูลินุมทอกซินเอ ในผู้ป่วยตาเขหลังผ่าตัดกล้ามเนื้อตา

โสพส วุฒิพันธุ์

วัตถุประสงค์: *เพื่อศึกษาผลและความปลอดภัยของการฉีดยา botulinum toxin A ในผู้ป่วยที่ยังเป็นตาเขหลังจากการผ่าตัดกล้ามเนื้อตา*

วัสดุและวิธีการ: *ได้ทำการฉีด botulinum toxin A ในผู้ป่วย 20 คนอายุ 5-56 ปี (อายุเฉลี่ย 29.1 ปี) ที่เป็นตาเขหลังจากการผ่าตัดกล้ามเนื้อตา ได้วัดขนาดของมุมเขที่ 1 เดือน, 3 เดือน, 6 เดือน, 1 ปี, 2 ปี, 3 ปีและ 4 ปีหลังการฉีด*

ผลการศึกษา: *ค่าเฉลี่ยของมุมเขก่อนฉีดยาคือ 20.6 ปริซึม ในผู้ป่วย 20 คนมี 6 คน (30%) ที่ดำรงความตาตรงได้นานเฉลี่ย 2.66 ปี (1-4 years) ด้วยการฉีดเพียงครั้งเดียว ค่าเฉลี่ยของการเปลี่ยนแปลงของมุมเขเป็น 87.50%, 87.93 %, 73.05 % ที่ 1 ปี, 2 ปี, 3 ปีหลังการฉีดตามลำดับ เมื่อ 6 เดือนพบว่า 3 ใน 6 คน (60%) ของกลุ่ม consecutive esotropia, 4 ใน 8 คน (50%) ของกลุ่ม residual esotropia, 1 ใน 4 คน (25%) ของกลุ่ม consecutive exotropia และ 1 ใน 3 คน (33.33%) ของกลุ่ม residual exotropia สามารถดำรงความตรงของตาได้ ไม่พบภาวะแทรกซ้อนที่อันตรายจากการฉีดเช่น การฉีดทะลุตา การสูญเสียสายตาหรือการมีเลือดออกหลังตา*

สรุป: *การใช้ botulinum toxin A มีประสิทธิภาพและมีความปลอดภัยในการรักษาตาเขหลังจากการผ่าตัดกล้ามเนื้อตาแล้วไม่ได้ผล มีประโยชน์ในการกำจัดการเห็นภาพซ้อนหลังผ่าตัด ข้อได้เปรียบอีกประการหนึ่งคือสามารถฉีดซ้ำได้หรือเปลี่ยนเป็นการผ่าตัดได้ถ้าการฉีดไม่ได้ผล หรือได้ผลแค่ในช่วงระยะเวลาสั้น*