Paralytic strabismus: the role of botulinum toxin

J S ELSTON AND J P LEE

From the Institute of Ophthalmology and Moorfields Eye Hospital, London

SUMMARY Five adults with acute extraocular muscle palsies followed by limited recovery of muscle function were treated with injections of botulinum toxin A to the ipsilateral antagonist of the affected muscle. Three were cases of unilateral sixth nerve palsy, one of bilateral sixth nerve palsy, and one of third nerve palsy. After a period of paralysis, during which the strabismus was overcorrected, the injected muscle recovered and binocular sensory and motor functions were restored and have been maintained for periods of up to 21 months. The treatment is a safe and effective alternative to surgery, particularly in cases in which a general anaesthetic is not advisable.

Adult neurogenic ocular palsies present problems of both diagnosis and management. Despite full neurological investigation the underlying cause may not be established,^{1,2} and, even if specific treatment can be instituted, recovery of function may not be complete. Binocularity may not be restored even with a compensatory head posture, or prisms, and despite alternate patching suppression frequently develops. The timing of surgical treatment and the choice of procedure in the individual case are difficult decisions,³ and the functional result of surgery is unpredictable, particularly after head injury or neurosurgical procedures, when fusional mechanisms may have been disrupted.⁴

In sixth nerve palsy the choice of operation depends on the extent of recovery. If the eye cannot be abducted beyond the midline, a vertical rectus muscle transposition procedure with medial rectus recession will be required.^{3,5} Surgery may have to be in two stages, since the anterior ciliary arteries associated with three ipsilateral rectus muscles cannot be simultaneously operated upon in a patient over the age of 20 without risking anterior segment ischaemia.³ When the affected eye can abduct at least 10° beyond the midline, and saccadic velocity for this is normal, a medial rectus recession and lateral rectus resection should suffice.^{3,6} In either case the contralateral medial rectus may have to be recessed and adjustable or posterior fixation sutures used.⁷ Surgery in third nerve palsy is less satisfactory.⁸ The combination of the size of the exodeviation, the presence of a vertical deviation, and, frequently, acquired oculomotor synkinesis means that normal

binocular control cannot be achieved. A satisfactory appearance in the primary position with a small field of binocular single vision will usually require operations on both eyes.^{3,8}

Botulinum toxin A (BTXA) causes a flaccid paralysis of skeletal muscle by preventing the release of acetylcholine at the neuromuscular junction.⁹ New junctions are formed over six to eight weeks, and the muscle gradually recovers normal activity.¹⁰ In appropriate dosage individual extraocular muscles can be paralysed by direct injection of BTXA under local anaesthetic and the position of the eye within the orbit altered.^{11,12} If binocular functions are re-established when the eyes are realigned, as the treated muscle recovers function the inconstant strabismus may not recur.¹² Five adults who would otherwise have been treated surgically for partly recovered neurogenic ocular palsies have therefore had injections of BTXA into the ipsilateral antagonist of the palsied muscle.

Patients, materials, and methods

There were three cases of unilateral sixth nerve palsy, one of bilateral sixth nerve palsy, and one of third nerve palsy (Table 1). The aetiology had been established in all cases and appropriate treatment carried out where indicated. At least six months had been allowed for spontaneous recovery to occur. The patients' general health had been assessed, particularly their suitability for general anaesthetic (Table 1). The visual acuity and visual fields were normal in all cases.

Orthoptic assessment included measurement of the angle of strabismus at near and distance fixation, and the extent of the extraocular movements (Table

Correspondence to Mr J S Elston, FRCS, Moorfields Eye Hospital, City Road, London EC1V 2PD.

Table 1 *Description and aetiology of paralytic strabismus: five cases*

Patient	Sex	Age	Nerve	Aetiology	General health	Fit for general anaesthetic	Interval from palsy to treatment
1	F	19	Right VI	Infectious polyneuritis	Normal	Yes	6 Months
2	F	37	Left III	Trauma	Normal	Yes	5 Years
3	M	45	Bilateral VI	Trauma	Left hemiparesis, bulbar palsy	Yes	9 Months
4	F	73	Right VI	Hypertension	Bronchiectasis, depression	No	3 Years
5	F	18	Right VI	Pontine arteriovenous malformation	Right V and VII nerve palsies, left hemiparesis	No	8 Months

Table 2 *Pretreatment orthoptic assessment*

Patient	Deviation prism dioptres at 6 m	Ocular movements	Saccadic velocity	Suppression	Binocular function	
					Fusion	Stereopsis
1	55	Reduced right abduction	Normal	Intermittent	Yes	Gross
2	65	Limited adduction, vertical: acquired oculomotor synkinesis	Slow adduction	Left	Yes	Nil
3	50	Reduced abduction bilateral	Slow abduction	Intermittent	Yes	Gross
4	30	Reduced abduction	Normal	Intermittent	Yes	Gross
5	45	Reduced right abduction	Slow abduction	Intermittent	Yes	Gross

Table 3 *Treatment schedules*

Patient	Muscle treated	Subsequent treatment	Period of overcorrection	Period to stable result
1	Right medial rectus	Nil	5 Weeks	8 Weeks
2	Left lateral rectus	Left lateral rectus at 4 weeks	3 Weeks	16 Weeks
3	Left medial rectus	Left medial rectus at 4 weeks	3 Weeks	14 Weeks
4	Right medial rectus	Right medial rectus at 10 weeks	4 Weeks	6 Weeks
5	Right medial rectus	Nil	3 Weeks	8 Weeks

Table 4 *Results of treatment*

Patient	Cover test	Binocular function			Period of follow-up after stable result achieved	
		Stereopsis in seconds of arc (Titmus stereotest)	Fusion range (degrees)			Area of binocular single vision
			Abduction	Adduction		
1	Esophoria	40 Seconds	4	10	Normal	21 Months
2	Exophoria	40 Seconds	4	6	30° From fixation	10 Months
3	Esophoria	40 Seconds	4	8	Normal vertical, 30° horizontal	4 Months
4	Esophoria	40 Seconds	4	10	Normal vertical, 30° horizontal	4 Months
5	Esophoria, distance esotropia Controlled by AHP	40 Seconds	2	4	Full in L gaze, 10° R gaze	4 Months

2). The saccadic velocity in the direction of the palsied muscle was judged clinically to be either normal or slow. Fusion and stereopsis were investigated on the synoptophore.

BTXA, 3.12×10^{-4} μ g, was injected under electro-

myographic control as previously described¹² into the muscle indicated in Table 3. Clinical assessment and orthoptic measurements were repeated at one, two, and four weeks after treatment, and the injections repeated at the same dosage if necessary to produce

Fig. 1A

Fig. 1B

Fig. 1 Hess charts showing the effect of botulinum toxin treatment of the lateral rectus in partly recovered IIIrd nerve palsy.

an overcorrection of the original strabismus (Table IV). In case 2 pilocarpine drops 0.1% were applied twice a day to the left eye to mediate accommodation in an attempt to re-establish fusion.⁸ Follow-up thereafter has been from 4 to 21 months.

Results

There were no local or systemic side effects of the treatment.

The ocular deviation was overcorrected in all cases for a period of between three and five weeks (Table 3), when single vision could be obtained in only one position of gaze. As the treated muscle recovered function, however, the area of binocular single vision (BSV) gradually enlarged. Fig. 1A shows the Hess chart in case 2 before treatment. After the left lateral rectus had been treated, the horizontal muscles on the right eye overacted in both adduction and abduction, but there was a small central area of single

Fig. 1C

Fig. 2A

vision (Fig. 1B). The area enlarged as the lateral rectus recovered function (Fig. 1C).

Fig. 2A shows the Hess chart in case 3 before treatment. In Fig. 2B, after the left medial rectus had been treated, single vision could be obtained in left gaze, but the patient showed an increasing exotropia as he moved into right gaze. In Fig. 2C the final stable result is shown with minimal bilateral lateral rectus weakness.

Normal stereopsis and fusion were achieved in all

patients after between six and 16 weeks; the field of binocular single vision was then normal in cases 1 and 4 but remained limited in cases 2, 3, and 5 because of permanent nuclear or supranuclear abnormalities of eye movement. The functional results have been maintained for periods up to 21 months (Table 4).

Discussion

Conventional treatment of these patients would

Fig. 2B

Fig. 2C

Fig. 2 Hess charts showing the effect of botulinum toxin treatment of the left medial rectus in bilateral VIth nerve palsy.

require surgery on both eyes for the third and bilateral sixth nerve palsies and, in two of the three cases of unilateral abduction deficit, operation under local anaesthesia. While the benefit of surgery, provided the suppression of the deviating eye was overcome, would be immediate, the potential area of binocular single vision, already limited in cases 2, 3, and 5, would be further compromised by operative reduction of ocular rotations in cases 2 and 3. The patients would be in hospital for three days and need

to have local anti-inflammatory treatment for one to two weeks.

In contrast, BTXA treatment of strabismus is an outpatient procedure under local anaesthetic, and, if the muscle to be injected has not been previously operated on, the treatment is easy and painless. There are no systemic side effects,^{11 12} and, while there is a theoretical danger of ocular perforation, this has not occurred in over 400 injections by the authors. The eye is padded for two hours,

and thereafter no local treatment is needed.

The period of reversal of the diplopia and horizontal incomitance associated with the newly paralysed muscle was disturbing for all the patients treated. Although there was one position of gaze in which single vision could be obtained, overaction of the contralateral synergist of the injected muscle made this difficult to maintain, and the two images slipped past one another. As the paralysis recovered, the area of binocular single vision gradually increased. In case 2, after five years with suppression of the deviating image and no stereopsis demonstrable, stereo acuity of 40 seconds of arc and a near normal fusion range were achieved, and in general the quality of stereopsis and fusion regained was better than had been expected before treatment. The period of overcorrection when the deviating image is moved well away from the suppression scotoma may explain this finding.

Experience with BTXA treatment of strabismus in patients without binocular functions¹² suggests that the eye tends to drift back to the original position as the paralytic effect of the injection declines. If stereopsis and fusion had not been re-established in these cases therefore, the pretreatment status would have been restored, whereas surgery may have led to intractable diplopia.

BTXA has also been advocated in the management of acute microvascular lateral rectus palsy, when injection of the ipsilateral medial rectus, by allowing the eye to abduct passively, enables a small central area of binocular co-operation to be achieved. It is expected that the two paralysed horizontal muscles would regain function at the same rate, gradually enlarging the area of the binocular single vision. We consider that these benefits to a group of patients with a good prognosis for recovering lateral rectus function are outweighed by disadvantages. A change in neurological signs may be obscured, and the reversal of diplopia on either side of the central binocular area is likely to be very uncomfortable. We are, however, extending the use of BTXA to the treatment of the medial rectus prior

to surgery in cases of persistent abduction weakness requiring vertical muscle transposition, with encouraging results.

Conclusion

BTXA treatment of partly recovered adult paralytic strabismus is a simple, safe, cheap, and effective method which avoids the risks of a general anaesthetic. A larger area of binocular single vision may be achieved than by conventional surgery.

We thank Miss C Smyth for secretarial assistance.

References

- 1 Rush JA, Younge BR. Paralysis of cranial nerves III, IV and VI: cause and prognosis in 1000 cases. *Arch Ophthalmol* 1981; **99**: 76-9.
- 2 Jampolsky A. Management of acquired (adult) muscle palsies. In: *Transactions of the New Orleans Academy of Ophthalmology, Symposium on Neuro-ophthalmology*. St Louis: Mosby, 1976: 148-66.
- 3 Fells P. The treatment of non-comitant strabismus. In: Van Balen AT, Houtman WA, eds. *Doc Ophthalmol Proc Ser* 1982; **32**: 197-201.
- 4 Stanworth A. Defects of ocular movement and fusion after head injury. *Br J Ophthalmol* 1974; **58**: 266-71.
- 5 Carlson MR, Jampolsky A. An adjustable transposition procedure for abduction deficiencies. *Am J Ophthalmol* 1979; **87**: 382-87.
- 6 Fells P. Vertical rectus muscle transplantation to restore abduction. In: Mein J, Bierlaagh JJM, Brummel Kamp-Davis TEA, eds. *Orthoptics, Proceedings of Second International Orthoptic Congress, 1972*. Amsterdam: Excerpta Medica, 1973: 229-37.
- 7 Scott AB. The Faden operation: mechanical effects. *Am Orthopt J* 1977; **27**: 44-7.
- 8 Elston JS. Traumatic third nerve palsy. *Br J Ophthalmol* 1984; **68**: 538-43.
- 9 Dolly JO, Black J, Williams RS, Melling J. Acceptors for botulinum neurotoxin reside on motor nerve terminals and mediate its internalization. *Nature* 1984; **307**: 457-60.
- 10 Duchon LW. An electron microscopic study of the changes induced by botulinum toxin in the motor end plates of slow and fast muscle fibres of the mouse. *J Neurol Sci* 1979; **14**: 47-60.
- 11 Scott AB. Botulinum toxin injection into extra-ocular muscles as an alternative to strabismus surgery. *Ophthalmology (Rochester)* 1980; **87**: 1044-7.
- 12 Elston JS, Lee JP, Powell CM, Hogg C, Clark P. Treatment of strabismus in adults with botulinum toxin A. *Br J Ophthalmol* 1985; **69**: 718-24.