Original Article

EFFICACY OF A SINGLE SUBCONJUNCTIVAL INJECTION WITH DISPORT FOR LID RETRACTION TREATMENT

Khataminia Gh R[1], Moosavian J[2]

ABSTRACT

Objective: To evaluate the safety and efficacy of dysport injection via a subconjunctival approach in the management of upper lid retraction at 3 months follow up.

Methodology: It is a prospective, non comparative, interventional case series study. It enrolled 22 patients (34 lids) with upper scleral exposure mainly associated with thyroid eye disease who were referred to the ophthalmic department of Ahwaz Imam Khomeini Hospital. A single injection of botulinum toxin A (dysport) was injected into the subconjunctival space at the superior margin of the tarsal plate by conjunctival approach. Main outcome measurements included upper lid position in relation to the upper limbus, patient satisfaction and any complication in the period of the study.

Results: All patients experienced some improvement in the amount of lid retraction after injection. The amount of lowering varied between patients and lasted at least 3 months. A lid repositioning acceptable to the patient was obtained in 19 patients (26 lids) one patient had ptosis lasting 3 weeks and one patient had transient diplopia lasting 4 weeks.

Conclusion: Subconjuntval injection of dysport provides a safe and effective treatment for upper eyelid retraction associated with thyroid eye disease. It is easy to adminster and is well tolerated by patient with few minor and transient side effects, such as diplopia and ptosis.

KEY WORDS: Lid retraction, Dysport, Sub conjunctival injection.

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INTRODUCTION

The characteristic features of thyroid eye disease include upper lid retraction and proptosis resulting in upper scleral exposure. Other causes of lid retraction can be due to psychotropic drugs, recession of vertical rectus muscle, aggressive skin excision in blepharoplasty, brain tumor, congenital abnormality.[1,2] This may results in corneal and conjunctival exposure problems such as ocular irritation and discomfort, exposure keratitis and corneal ulcer as well as being cosmetically unacceptable for the patients.[1,3]

Conventional treatment of thyroid eye disease consist of conservative or surgical interventions. Surgical procedures include lowering the upper lid by recessing the levator muscle, excision of muller's muscle, introducing a spacer, or myotomies.[1-4] These options involve relatively complex procedures and have significant risks as well as an unpredictable course and outcome in some cases.[2,4]

For patients who do not wish to undergo a surgical procedure, there are no generally accepted alternatives, although non surgical approach such as topical guanethidine have been tried to control upper lid position but results are generally considered disappointing.[5]

Botulinum toxin type A is a very potent neurotoxin that acts at the motor- end plate (neuromuscular junction)[6] and blocks the release

1. Khataminia Gh.R
2. Moosavian J
1-2: Ophthalmology Department, Imam Khomeini Hospital, Jondi-Shapour University of Medical Sciences, Ahwaz, Iran.

Correspondence

Khataminia Gh. R
E-Mail: khataminia@hotmail.com

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of acetyl- cholin. It has many ophthalmic uses including management of blepharospasm,[6-8] strabismus,[8] sixth nerve palsy,[9] nystagmus[10] and entropion.[11]

A temporary ptosis is a well-recognized complication of strabismus and blepharospasm treated with botulinum toxin type A injection, possibly by diffusion of the toxin to the levator muscle.[12,13]

A few clinical trials were conducted that considered botulinum toxin type A injection into the upper lid via a percutaneous approach to lower the upper lid, creating a protective ptosis in the treatment of corneal disease.[12-17]

All cases had dysthyroid upper lid retractions that were treated with percutaneous botulinum toxin type A injection. Injections were given into the area of the levator complex, via the skin, aiming at the levator aponeurosis and muller's muscle, without myographic control.[12-17] Present report is the results of the use of botulinum toxin type A injection in the upper lid through subconjunctival approach in patients with cosmetically unacceptable upper scleral exposure.

PATIENTS AND METHODS

Twenty two patients (15 male and 7 female) aged between 17 and 66 years with upper scleral exposure were enrolled into the study from 2004 to 2005. The retraction was bilateral in 12 patients and unilateral in 10 patients. The upper eyelid position ranged between 1 and 5 millimeters above the superior limbus. (Table-I)

Twenty patients had thyroid eye disease and two patients (patients 8 and 11) had no history of thyroid or other diseases. All 20 patients with thyroid eye disease were euthyroid at the time of botulinum toxin type A treatment, but only 7 patients had thyroid eye disease documented to be stable for at least 6 months. Duration of systemic thyroid disease was from 5 months to 10 years. (Table-I)

Patients underwent full ocular examination and management options were discussed. Informed consent was obtained with knowledge of possible side effects. The upper lid position above (positive value) and below (negative value) the superior limbus was measured in millimeter. Patients were reviewed at 3 and 10

Table-I: Characteristics of patients referred to Imam Khomeini Hospital from 2003-2004

Patient No	*Age (years)*	*sex*	*Lid involved*	*Duration of thyroid disease months*	*Upper lid retraction (pre treatment)*	*porptosis*
1	37	M	L	20	+4	+
2	64	M	Bi	84	+3,+2	+
3	14	F	R	8	+3	-
4	37	M	Bi	36	+3,+2	-
5	66	M	Bi	60	+4,+4	+
6	17	F	R	5	+2	+
7	27	M	R	30	+2	-
8	34	M	R	-	+3	-
9	26	F	R	36	+2	+
10	45	F	L	24	+3	-
11	64	M	Bi	-	+4,+4	-
12	29	F	Bi	24	+2,+1	-
13	50	F	R	24	+2	-
14	52	M	Bi	120	+2,+3	+
15	25	M	Bi	32	+2,+1	-
16	27	M	Bi	12	+5,+2.5	-
17	35	M	Bi	8	+4,+5	+
18	33	F	R	48	+3	-
19	28	M	R	12	+2	-
20	50	M	Bi	24	+3,+1	-
21	48	M	Bi	24	+2,+1	-
22	24	M	Bi	12	+3,+4	-

M= male F= female L=left R=right Bi=bilateral

days after treatment and then after one, two and three months. Side effects including pain, lid ecchymosis, visually impairing ptosis and diplopia were noted.

Dysport (Botulinum toxin type A) was administered by anesthetizing the conjunctiva with topical anesthetic (tetracain 0.5%) and then everting the upper eyelid, with the patient looking down (Fig-1), three injections were applied, one –third of the dose (10 units) was administered at each site (medial, central, and lateral). Dysport was injected transconjunctivally using a 1-ml insulin syringe into the subconjunctival space at the superior margin of the tarsal plate. (Figure-1)

RESULTS

All patients experienced some improvement in the amount of lid retraction after injection. The amount of lid lowering varied in patients. Of 34 lids treated (22 patients), 26 lids achieved lid position to the level of the limbus or below that persisted at least 3 months after receiving a single dose treatment. Another 8 lids achieved incomplete but significant reduction of lid retraction (Table-II).

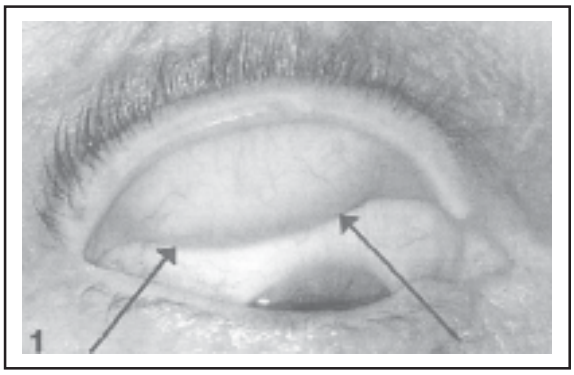

Fig-1: Approach to subconjunctival space.

All patients were dissatisfied with their pretreatment upper lid position and scleral exposure. Treatment achieved a satisfactory lid position in 19 patients (Fig 2&3) and the others requested further treatment for more improvement in lid retraction. The results can be classified in two categories:

1. Achievement of lid position below or at the limbus (26 lids in 19 patients) (Fig-4).
2. Improvement in lid position but inability to maintain lid position at or below limbus (8 lids in 5 patients) (Fig-4).

One patient had ptosis lasting 3 weeks and one patient had transient diplopia lasting 4

Table-II: Results showing upper lid position at follow – up period, and dose of botulinum toxin and complication

Patient. No	*Side*	*Upper lid retraction(mm)After injection*			*Total dose of injection (unit)*	*Complication*
		1 week	*1 month*	*3 months*		
1	L	-2	-1	-1	30	NO
2	Bi	+1,-1	+1,-1	+2,0	30	NO
3	R	-1	-1	0	30	NO
4	Bi	-2,-2	-1,0	0	30	NO
5	Bi	+2,+1	+2,+2	+2,+3	30	NO
6	R	-1	-1	0	30	NO
7	R	-0.5	-1	-1	30	NO
8	R	-1	-1	0	30	NO
9	R	-2	-1	0	30	NO
10	L	-2	-1	-.05	30	diplopia
11	Bi	-0.5,+1	0,+1	0,+1	30	NO
12	Bi	-1,-1	0,-0.5	0	30	NO
13	R	-1	-1	-0.5	30	NO
14	Bi	+1,+2	+1,+1	+1,+1	30	NO
15	Bi	-1.5,-2	-1,-1	0	30	NO
16	Bi	+0.5 ,-1	0,0	0	30	NO
17	Bi	+2,+2	+1,+2	+1,+2	30	NO
18	R	-1.5	-0.5	0	30	NO
19	R	-2	-1	0	30	NO
20	Bi	-5,-4.50	-2,-1	0	30	ptosis
21	Bi	-1,-1	-1,-1	-1,0	30	NO
22	Bi	-2,-1	-1,-1	0	30	NO

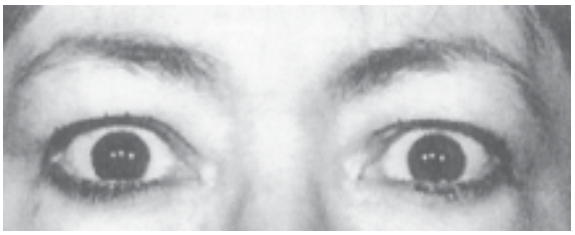

Fig-2: Patient with eyelid retraction before injection.

weeks (Table-II). The procedure was well tolerated. No patient developed new persistent motility problem, in particular hypotropia or superior rectus underaction.

DISCUSSION

The results of this study indicated that injection dysport (botulinum toxin type A) into subconjunctival space at the superior margin of the tarsal plate through conjunctival approach is temporarily effective and safe treatment for upper lid retraction.

There appears to be an inverse corrolation with the age and satisfactory outcome, in that young patients appearing to respond better to treatment (6 lids of 8 lids in group 2 were in patients older than 50 years). It further appears to be an inverse correlation between the amount of upper lid retraction and satisfactory results, with initial upper lid retraction between +1 and +2 millimeters appearing to respond well to treatment. Lid retraction of +3 to +5 millimeters has poorer outcomes. No significant relationship between duration of the thyroid eye disease with response to treatment was observed in this study.

Our results show that dysport injection using a subconjunctival approach is more effective than previous percutaneous studies, which may be the result of the more accurate and reproducible placement of the botulinum toxin type A into the levator and muller's muscle rather than of the relatively blind placement percutaneously into the levator region.[16-22]

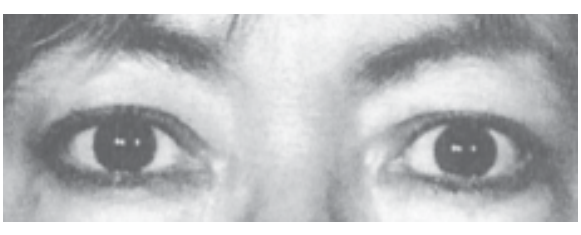

Fig-3: Same patient in (Fig-2), 3 months after injection.

Persistent hypotropia when using the percutaneous approach for induction of protective ptosis is an expectant complication.[21] This complication was not seen in our study. Most of our patients had no motility problems before treatment. In one patient who had vertical diplopia and hypotropia before treatment (patient number 20) no worsening of his motility problem occurred after treatment. An explanation for the lack of superior rectus involvement may be the subconjunctival injection in the region of the aponeurosis as it inserts onto the tarsal plate of the upper lid, which is anatomically distinct from superior rectus whereas when the percutaneous approach is used, the dysport is placed further back in the orbit where the levator muscle and superior rectus share a common sheath.[20,21]

In conclusion, the subconjunctival method of dysport (botulinum toxin type A) injection provides an effective treatment for majority of patient with eyelid retraction which is easy to administer and well tolerated by patients with few temporary side effects. However, more studies are required to determine whether permanent contracture of muller's muscle can be avoided with botulinum toxin injections. As botulinum toxins type A works to relax both

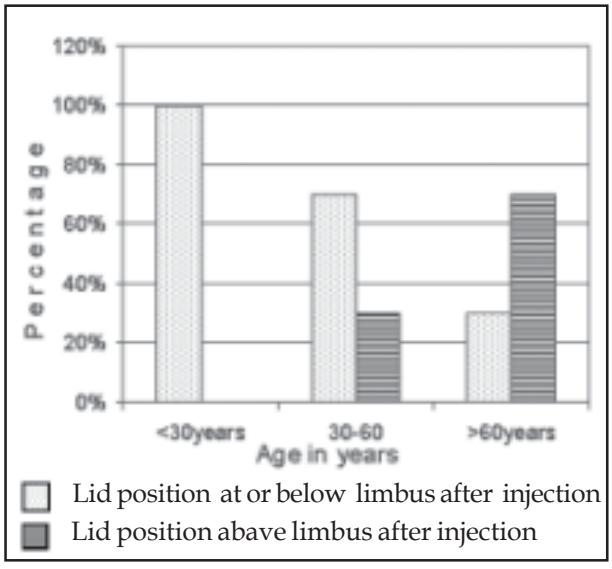

Fig-4: Achievement of lid position

skeletal and smooth muscle, it holds promise in helping patients with active lid retraction.

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REFERENCES

1. American Academy of ophthalmology. Eyelid malpositions and involutional changes. In: Basic and clinical science course: Orbit, eyelid and lacrimal system. San Francisco: The Academy 2002-2003;204-6.
2. Ophthalmic plastic and reconstructive surgery. Eyelid surgery for Thyroid ophthalmopathy. ST. Louis. Washington DC. Toronto: The CV. Mosby Company 1987;1401-14.
3. Grove AJ. Upper eyelid retraction and grave's disease. Ophthalmology 1981;88:499-506.
4. Hedin A. Eyelid surgery in dysthyroid ophthalmopathy. Eye 1988;2:201-6.
5. Melling J, Hambleton P, Shone CC. Clostridium botulinum toxins: nature and preparation for clinical use. Eye 1988;2:16-23.
6. Elston JS. The management of blepharospasm and hemifacial spasm. J Neurol 1992;239:5-8.
7. Riordan–Eva P, Lee JP. Management of VIth nerve palsy avoiding unnecessary surgery. Eye 1992;6:386-90.
8. Repka MX, Savino PJ, Reinecke RD. Treatment of acquired nystagmus with botulinum neurotoxin A. Arch ophthalmol 1994;112:1320-4.
9. Steel DH, Hoh HB, Harrad RA, Collins CR. Botulinum toxin for the temporary treatment of involutional lower lid entropion: A clinical and morphological study. Eye 1997;11:472-5.
10. Burns CL, Gammon JA, Gemmill MC. Ptosis associated with botulinum toxin treatment of strabismus and blepharospasm. Ophthalmology 1986;93:1621-7.
11. Kirkness CM, Adams GG, Dilly PN, Lee JP. Botulinum toxin A- induced protective ptosis in corneal disease. Ophthalmology 1988;95:473-80.
12. Scott AB, Rosenbaum A, Collins CC. Pharmacologic weakening of extraocular muscles. Invest ophthalmol 1973;12:224-7.
13. Scott AB. Injection treatment of endocrine orbital myopathy. Doc Ophthalmol 1984;58:141-5.
14. Ebner R. Botulinum toxin type A in upper lid retraction of grave's ophthalmopathy. J Clin Neuro Ophthamol 1993;13:258-61.
15. Biglan AW. Control of eyelid retraction associated with gvave's disease with botulinum A toxin. Ophthalmic Surgery 1994;25:186-8.
16. Ozkan SB, Can D, Soylev MF. Chemodenervation in treatment of upper eyelid retraction. Ophthalmologica 1997;211:387-90.
17. Holds JB, Alderson K, Fogg SG, Anderson RL. Motor nerve sprouting in human orbicularis muscle after botulinum A injection. Invest Ophthalmol Vis Sci 1990;31:964-7.
18. Heyworth PL, Lee JP. Persisting hypotropias following protective ptosis induced by botulinum neurotoxin. Eye 1994;8:511-5.
19. Shih MJ, Liao SL, Lu My. A single transcutaneous injection with Botox for dysthyroid lid retraction. Eye 2004;18(5):466-9.
20. Cheryl Guttman. Subconjunctival botulinum toxin help treat eyelid retraction. Ophthalmology 2003;111:82-9.
21. Jimmy M, Uddin MA, Peter D. Treatment of upper eyelid retraction associated with thyroid eye disease with subconjunctival Botulinum toxin injection. Ophthalmology 2002;11:83-5.
22. Gay AJ, Wolkstein MA. Topical guanethidine therapy for endocrine lid retraction. Arch ophthalmol 1966;76:364-7.