Jundishapur Journal of Natural Pharmaceutical Products 2009; 4(1): 41-46

Jundishapur Journal of Natural Pharmaceutical Products

EVALUATION OF THE DISPORT INJECTION FOR TREATMENT LID RETRACTION IN THYROID OPHTHALMOPATHY VIA SUB-CONJUNCTIVAL APPROACH

Khataminia GR[1]*, Feghhi M, Sadegian MR, Latify M, Moosavian J

[1]Department of Ophthalmology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Received:*14 December 2009* ***Accepted:*** *19 April 2010*

Abstract

lid retraction is the most common presenting sign of thyroid Ophthalmology, which can cause several ophthalmologic problems such as dry eye, redness, lacrimation, exposure keratitis, and corneal ulcer or blindness. In this study, we evaluated disport injection via sub-conjunctival for management of lid retraction. This study is a prospective, non comparative, interventional case series. The study enrolled 25 patients (38 lids) with lid retraction secondary to thyroid Ophthalmopathy. The disport was injected in sub-conjunctival space at the superior margin of the tarsal plate. One –third of the total dose (10 unite) was administrated in three points of the lid and if eyelid retraction recurs another dose of disport was injected. Patient followed up for 12 months. In this study 8 patients (10 lids) showed improvement with single injection for 12 months or more. Other cases need more than one injection. There was negative correlation between age and satisfactory outcome. So that young patients had the best response, but with increasing age, especially above 50 years, amount and duration of response have decreased. Furthermore, other factors such as sex, duration of the systemic thyroid disease and proptosis lid have no influences on drug effectiveness. Our study shows sub-conjunctival injection of disport provides an effective and safe treatment for eyelid retraction due to thyroid Ophthalmopathy.

Keywords: Lid retraction, disport, sub-conjunctival injection

Introduction

The characteristic features of thyroid ophthalmopathy include lid retraction and proptosis resulting in upper sclera exposure, which may results in conjunctival exposure problems. Furthermore, this may result in many problems for patients both cosmetically and functionally, such as dry eye, redness, lacrimation, exposure keratitis and cornea ulcer or blindness (1, 2,3).

The cause of lid retraction in thyroid ophthalmopathy has long been disputed, while sympathicotonia has often been advanced as the causes. The lid retraction is present in patients who are euthyroid as well as are hyperthyroid. Thus, the level of thyroxin in the blood appears not to be responsible for this phenomenon (4).

Conventional treatment of lid retraction due to thyroid ophthalmopathy consists of conservation or surgical intervention.

Surgical procedures include lowering upper lid by recessing the levator muscle, excision of Muller's muscle introducing a spacer or myotomy (1-4). The primary goals of surgery for patients are to maintain the normal position lids and protected cornea against exposure and the secondary is cosmoses.

Email: Khataminia @ Hotmail.com

These options involve relatively complex procedures and have significant risks as well as an unpredictable course and outcome in some cases(2,5). For patients who do not wish to undergo a surgical procedure generally there are no accepted alternatives , although non surgical approach such as topical guanethidine have been tried to control upper lid position ,results are generally considered disappointing (6).

Botulinum toxin type-A is a very potent neurotoxin that acts at the motor – end plate and blocks the release of acetylcholine (6). It has many ophthalmic uses including management of blepharospasm (7) strabismus (7,8) sixth nerve palsy (8) nystagmus (9) and spasmatic entropion (10) 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 (11, 12). Nowadays, there are two productions of botulinum toxin- A include Botox and disport with different potential and side effect), although Botox is 3-5 time more potent than disport (13). A few clinical trials were conducted test considered Botox injection into the upper lid via a percutaneous approach to lower the upper lid, creating a protective ptosis in the treatment of corneal disease and lid retraction in thyroid ophthalmopathy (12-18). There are three clinical trials that considered Botox injection via sub conjunctival l for treatment of lid retraction (19, 20).

On the basis of our knowledge, there was no lecture or clinical trial which used disport injection into upper eyelid through sub-conjunctival approach in patients with unacceptable upper sclera exposure, cosmetically or functionally with long follow-up. So, this study aimed to evaluate disport injection via sub-conjunctival for management of lid retraction.

Materials and Methods

This study is a prospective, non comparative, interventional, cases series. Twenty five patients (14 male-11 female) between 14 and 66 year-old with upper sclera exposure were enrolled into the study from 2004-2006. The lid retraction was bilateral in 15 and unilateral in 12 patients. All patients with thyroid of ophthalmopathy were euthyroid at systemic of disport injection duration of systemic thyroid disease was from 5 to 120 months. The patients underwent full ocular examination and management options were discussed with them. The study was approved by the University Hospital and Ahvaz Jundishapur University of Medical Sciences Ethics Committees, and all subjects granted informed consent to participate.

Before injection upper eyelid position above the superior limbus, upper lid marginal –reflex distance, lower lid marginal –reflex distance, upper lid crease, levator muscle function and proptosis were measured. Patients were examined at 3 and 14 days after treatment and then monthly until one year. Side effects including, pain, lid ecchymosis, visually impairing, ptosis, dryness, lacrimation and diplopia were recorded. Disport was administrated by anesthetizing the eye with topical anesthetic (tetracaine 0.5%) and then everting the upper eyelid, with the patients looking down, three injections were applied, on-thired of the total dose (10 unite) was administered at each point of lid (medial, central and lateral); disport was injected using a insulin syringe into the sub-conjunctival apace at the superior margin of the tarsal plate .Through a conjunctival approach (Figure 1). The patients were followed-up 12 months and disport was injected again if eyelid retraction and sclera show recurs. Two patients were excluded due to refusal follow-up. Successful treatment is lowering upper lid to normal position.

Figure 1: Method of injection

Results

Although, the amount of lid lowering varied between patients, all of them experienced some improvement in the mount of lid retraction after injection. The 34 lids treated, 27 lids achieved to the level of the limbus or below that persisted at least 3 months after receiving treatment. The other 7 lids underwent incomplete but significant reduction of lid retraction. Among total 25, in 8 patients (10 lids) the upper lid retraction resolved within one year or more with only single injection (table1),10 patients (15 lids) needed two injections in follow-up period (table2), and the rest 5 patients (9 lids) received three or more injection in one year (table3). Two patients had blepharoptosis lasting 2-3 weeks and one patient had transient vertical diplopia lasting 2 weeks. The procedure was well tolerated. No patient developed new persistent motility problem in particular hypotropia or superior rectus underaction.

Table 1. Characteristic Group 1(resolved within one year or more only single injection)

Proptosis	Amount of lid retraction (mm)	Duration thyroid disease	Sex	Age	Patient
+	4	20	M	37	1
-	3	8	F	14	2
+	2	5	F	17	3
+	2	36	F	26	4
-	2, 3	?	M	32	5
-	2	18	F	20	6
+	5, 2.5	12	F	27	7
-	2	12	M	28	8

M = Male
F= Female

Table 2. Characteristic Group 2(needed two injections)

Proptosis	Amount of lid retraction (mm)	Duration thyroid disease	Sex	Age	Patient
-	2	84	M	64	1
-	2	30	M	26	2
-	2, 3	36	M	37	3
-	3	?	M	34	4
-	1, 2	24	F	29	5
-	2	24	F	36	6
-	3, 3	60	F	41	7
-	2	36	F	41	8
-	1, 3	24	M	50	9
-	1, 2	24	M	25	10

M = Male
F= Female

Table 3: Characteristic Group 3(needed three or more injections)

Proptosis	Amount of lid retraction	Duration thyroid disease	Sex	Age	Patient
+	4, 6	60	F	66	1
-	5, 4	?	F	64	2
-	3, 5	12	F	66	3
+	3	84	F	64	4
-	1, 2	24	F	50	5

M = Male
F= Female

Discussion

The results of our study shows that injection of Disport into sub-conjunctival space at the superior margin of the tarsal plate through conjunctival l approach is a effective and safe treatment for upper lid retraction. There was negative correlation with the age and satisfactory outcome, that means young patients respond better to treatment ($P<0.05$). In patients under 30 years old, the duration of single injection was 10 months but in patients with 30-50 years old was seven months and over 50 years old was 2-5 months respectively.So it can be concluded that with increasing age especially above 50 years, amount and duration of response decreased. In our study, no significant relationship was founded between the amount of eyelid retraction and duration of the thyroid disease. Other factor such as sex and proptosis had no influences on drug effectiveness. Our results show that disport injection using a sub-conjunctival approach is more effective and safer than previous percutaneous studies , which may be due to the more accurate and reproducible placement of the Botox into the levator and muller's muscle rather than of the relatively blind placement percutaneously into the levator region (12,14,15,16).

This study revealed that effect disport injection via subconjunctival l approach is similar Botox injection vi subconjunctival

l approach (19,20). Persistent hypotropia when using the percutaneous approach an expectant complication. This complication has not seen in our study. An explanation for the lack of superior rectus involvement may be due to sub-conjunctival injection is 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 disport is placed further back in the orbit where the levator muscle and superior rectus share a common sheath (22, 23).

Conclusion

The sub-conjunctival method of disport injection provide an effective treatment for patient with eyelid retraction which easy to administer and well tolerated by patient with few temporary side effects. More studies will be require to determine whether permanent contracture of muller's muscle can be avoided with disport botulinum toxin type A works to relax both skeletal and smooth muscle , it hold promise in helping patients with active lid retraction .

References

1. Eyelid malpositions and involutional changes. In: Basic and clinical science course: orbit, eyelid and lacrimal system. San Francisco: The Academy; 2002- 2003: 204-206.
2. Wsley RF, Jackson CG. Facial palsy. In: Hornblass A. (ed) Oculoplastic, Orbital and Reconstructive Surgery, Vol 1. Baltimore, Willams and Wilkins, 1988, pp 325-340.
3. Grove A. Upper eyelid retraction and grave's disease. Ophthalmol. 1981; 88: 499-506.
4. Frederick A. Orbital inflammation In: Duan's Clinical Ophthalmology 2nd ed, J.B Lippincott Co. London, 1990.
5. Hedin A. Eyelid surgery in dysthyroid Ophthalmopathy. Eye 1988; 2: 201-6.
6. Melling J, Hambleton P, Shone CC. Clostridium botulinum toxins: nature and preparation for clinical use. Eye 1988; 2:16-23.
7. Elston JS. The management of blepharospasm and hemifacial spasm. J Neurol. 1992; 239:5-8.
8. Riordan-Eva P, Lee JP. Management of VIth nerve palsy avoiding unnecessary surgery. Eye 1992; 6: 386-90.
9. Repka MX, Savino PJ, Reinecke RD. Treatment of acquired nystagmus with botulinum neurotoxin A. Arch. Ophthalmol. 1994; 112: 1320-4.
10. Kataminia GR. Feghhi M. Miralaie Z. Botulinum-A toxin in the treatment of Spastic Entrapion. Bina 2003; 7(3): 20-33 .
11. Burns CL, Gammon JA, Gemmill MC. Ptosis associated with botulinum toxin treatment of strabismus and blepharospasm. Ophthalmology 1986; 93: 1621-7.
12. Kirkness CM, Adams GG, Dilly PN, Lee JP. Botulinum toxin A- induced protective ptosis in corneal disease. Ophthalmology 1988; 95: 473-80.
13. Scott AB, Rosenbaum A, Collins CC. Pharmacologic weakening of extraocular muscles. Invest. Ophthalmol. 1973; 12: 224-7
14. Traisk F, Tallstedt L. Thyroid associated ophthalmopathy: botulinum toxin A in the treatment of upper lid retraction. Acta Ophthalmol. 2001 ; 79: 585 – 8.
15. Ebner R. Botulinum toxin type A in upper lid retraction of Graves ophthalmopathy. J. Clin. Neuroophthalmol. 1993 ; 13: 258-61
16. Ozkan SB, Can D, Soyler MF, et al. Chemodenervation in treatment of

upper eyelid retraction. Ophthalmologica. 1997; 211: 387-90 .
17. Fagien S. Temporary management of upper lid ptosis, lid malposition, and eyelid fissure asymmetry with Botulinum toxin type A. Plastic Reconstrictive Surg . 2004; 114: 1892 –1902
18. Shih MJ, Liao SL, Lu H. A single transcutaneous injection with Botox for dysthyroid lid retraction. Eye. 2004; 18: 46-69.
19. Uddin JM, Davies PD. Treatment of upper lid retraction associated with thyroid eye disease with subconjunctival l Botulinum toxin Injection. Am. Acad. Ophthalmol. 2002; 85: 1183-87.
20. Morgenstern KE, Evanchan J. Botulinum toxin type A for dysthyroid upper eyelid retraction. Ophthalmic plastic Reconstrictive Surg. 2004; 20: 181 –5
21. Khataminia GR ,Moosavian J. Efficacy of a single subconjunctival 1 injection with disport for lid retraction treatment. Pakistan J. Med. Sci. 2007; 23: 609-624.
22. Lewallen WM. Lid retraction syndrome. Am. J. Ophthalmol. 1975, 45: 562-567.
23. Schechter RJ. Ptosis with contralateral lidretraction due to excessive innervations of the LPS. Am. J. Ophthalmol. 1978; 10: 1324-1328