Coll. Antropol. **33** (2009) 4: 1155–1161
Original scientific paper

Effect of Botulinum Toxin-A Injection on Intraocular Pressure and Proptosis in Thyroid Associated Orbitopathy

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A B S T R A C T

The aim of this study was to evaluate the effects of extraocular muscle injection of botulinum toxin-A (BTX-A) on intraocular pressure (IOP) and proptosis in patients with ocular motility disturbances in thyroid associated orbitopathy (TAO). In 17 patients (20 eyes) with restrictive strabismus and diplopia, BTX -A injections were applied. Intraocular pressure was measured with a Goldmann applanation tonometer in primary gaze position before and 2–4 weeks after BTX-A injection. Extraorbital prominention of the eyeball was measured before and after BTX -A injection using a Hertel instrument. Before the injection, the mean IOP in primary position of gaze was 18.6± 2.8 mmHg and 2–4 weeks after BTX-A injection was 16.9±3.3 mmH; (p=0.001). There was no statistically significant difference in Hertel egzophthalmometer readings before and after BTX-A injection, 21.5±2.7 mm vs 22.0± 2.6 mm; (p=0.678). In conclusion, BTX-A injection has a secondary lowering effect on IOP in TAO due to relaxation of extraocular muscles, but with no influence on proptosis.

Key words: *thyroid related orbitopathy, botulinum toxin-A, intraocular pressure, proptosis*

Introduction

The thyroid associated orbitopathy (TAO) is characterized by proptosis and extraocular muscle involvement which can cause restrictive strabismus and increased intraocular pressure (IOP)[1].Causes of elevated IOP in patients with TAO have been reported to be associated with the mechanical effect of extraocular thickening, elevated episcleral venus pressure, pressure of swollen orbital tissues, accumulation of mucopolysaccharide in the trabecular meshwork and finally coexistent open angle glaucoma[2–7].

Elevated IOP in up gaze is a common finding and is explained by a tight inferior rectus muscle that blocks the episcleral equeous outflow and orbital congestion[2,8]. It was found that in the Graves disease of recent unset, the raised muscle tension and reduced elasticity of the affected muscles, and hence strabismus, were caused primarily by active muscle contraction, not by fibrosis[9]. Treatment with botulinum toxin-A (BTX) in TAO has been shown previously[10–13]. In a small retrospective series of cases BTX-A caused decreased IOP on restrictive strabismus associated with thyroid-related orbitopathy[7].

The aim of this study was to assess the effects of BTX-A on IOP and proptosis in patients with TAO and related restrictive strabismus in observational case-study.

Material and Methods

We retrospectively studied the records of 17 patients (20 eyes, 14 female aged 49.9, range, 40–61 years and 3 male aged 50.4, range, 50–57 years, with TAO and related restrictive strabismus or diplopia treated at the Department of Ophthalmology University Hospital Split during the period from January 2004 to December 2006. Patient data are shown in Table 1.

Received for publication June 20, 2007

TABLE 1
PATIENTS CHARACTERISTICS

	Characteristics	Number	Age
Patients	Male	3	50.4 (3.7)
	Female	14	49.9 (6.9)
Thyroid status	Euthyroid	2	
	Hyperthyroid	15	
Smokers		12	
Duration of Disease		9–15	

Before the therapy two patients were euthyroid and the others were hyperthyroid. In the time of therapy they were either euthyroid or with a stable hormonal status of the thyroid gland under medication for at least two months.

Considering the time of initial complaints and the unset of the thyroid gland disease, 5 patients simultaneously developed symptoms of the thyroid and eye disease. Twelve patients developed eye symptoms after the unset of the thyroid gland disease.

There were twelve active smokers. The median time of duration of the eye signs of TAO was 11 months, ranged 9–15 months.

All patients had a history of TAO based on the presence of typical clinical ophthalmic findings (eyelid retraction, limitation of ocular motility, strabismus, proptosis and computed tomography (CT) that revealed evidence of extraocular muscle enlargement). All the patients were with active TAO and according to CAS score were with CAS 4 and more. Seven eyes were with CAS 4 and 5 and 13 eyes with CAS 6 and 7.

Botulinum toxin-A (Botox-Allergan) is a vial of 100 units of the medication in the form of crystal powder which is dissolved with 1.0 ml 0.9% solution of natrium chloride so that 0.1 ml of the solution consists 10 IU of Botulinum toxin A. 0.2 ml (20 IU) were applied with an insulin syringe under topical anesthesia in the site of the inferior rectus muscle of the affected side.

None of the patients was taking antiglaucoma medications, glucocorticoids or was treated with orbital radiotherapy; only local supportive lubricants were used. Examination of all patients included in the study was performed before and 2–4 weeks after the treatment (visual acuity, inspection of the eyelids and cornea, ocular motility measurement, Hess-Lancaster test, ophthalmoscopy). Preinjection and postinjection IOP was measured by an unmasked physican using a Goldmann aplanation tonometer in the primary position. Extraorbital prominention of the eyeball was measured using a Hertel instrument.

Statistical analysis was performed using t-test, χ^2-test, Mann-Whitney U-test, Wilcoxon test, Mc Nemar test and descriptive statistics.

Results

IOP and proptosis measured by Hertel egzophthalmometry taken before and after the injection of BTX-A are shown in Table 2.

Before the injection, the mean IOP was 18.6±2.8 mm Hg (range, 12–22 mmHg). After 2–4 weeks following BTX-A injection, the mean IOP was significantly decreased (16.9±3.3 mmHg, range 13–22 mmHg, p=0.001).The decrease in IOP was maintained in seventeen eyes for four weeks of the observed period of time. In three eyes the slight increase of IOP (1–3 mm Hg) was noticed two weeks following BTX-A injection and maintained in the observed period of four weeks. After BTX-A injection 8 of the eyes with CAS 6 and 7 reduced CAS score to 4 and 5 (61.5 %) (Mc Nemar test: p=0.008).

Using Wilcoxon test we did not find a statistically significant difference in proptosis before and after treatment with BTX-A; 21.5±2.7 mm vs 22.0±2.6 mm; (p=0.678).

Discussion

In Graves' disease increased IOP and proptosis are the results of orbital tissue infiltration and active extraocular muscle contraction[13–14].

Increased IOP in TAO has been attributed to increased episcleral venous pressure resulting from orbital congestion and venous outflow obstruction, increased resistance of trabecular outflow, restriction and compression of the globe by fibrotic and enlarged rectus muscles, a genetically linked predisposition to glaucoma, or increased mucopolysaccharide deposition in the trabecular meshwork[16]. In courses of Graves' ophthalmopathy of recent unset, raised muscle tension and reduced elasticity of the affected muscles were caused primarily by active muscle contraction, not by fibrosis[13].

Kikkawa and associates reported a significant decrease in IOP following BTX injections[7]. The limitation of their study was a small number of patients. In that study only 5 patients were without treatment at the time of BTX injection. The IOP measurements performed in our study were taken in primary gaze position. We didn't perform IOP measurements in up gaze position neither in down gaze position because the aim of

TABLE 2
INTRAOCULAR PRESSURE AND HERTEL EGZOPHTHALMOMETRY BEFORE AND AFTER BOTULINUM TOXIN-A (BTX-A) INJECTION

	Before BTX-A injection	After BTX-A injection	p-value*
IOT (mmHg)	18.6±2.8 (12–22)	16.9±3.3 (13–22)	0.001
Hertel egzophthalmometry (mm)	21.5±2.7 (16–24)	22.0±2.6 (16–25)	0.678

* Wilcoxon test

the study was to define changes in IOP following BTX-A injections, but not to determine ocular hypertension. Ocular hypertension is defined only if IOP is increased in all positions of gaze. We considered that IOP measured in primary position was sufficient to assess the effect of BTX-A injection on IOP. We speculate that the effect of BTX-A injection into the inferior rectus muscle relieves the muscle contraction and in turn has a lowering effect on IOP.

To the best of our knowledge this is the first study on the effect of applied BTX-a injection on proptosis in restrictive myopathy related to TAO.

We didn't find a significant difference in proptosis measured by Hertel egzophthalmometry. This could be explained solely by the effect of BTX-A on extraocular muscle contraction but not on muscle augmentation.

In conclusion, this study clearly demonstrates that BTX-A injections applied in patients with restrictive myopathy related to TAO have a lowering effect on IOP but without influence on proptosis.

The limitation of our study was a relatively small number of patients and IOP measurements were not performed in up gaze position which is probably more sensitive.

REFERENCES

1. SUTULA FC, Orbital decompression surgery. In: ALBERT DM (Eds) Ophthalmic surgery: Principles and techniques (Malden MA, Blackwell Science, 1999) — 2. OHTSUKA K, NAKAMURA Y, Am J Ophthalmol, 129 (2000) 613. — 3. COCKERHAM KP, PAL C, JANI B, WOLTER A, KENNERDELL JS, Ophthalmology, 104 (1997) 914. — 4. OHTSUKA K, Am J Ophthalmol, 124 (1997) 570. — 5. ALLEN C, STETZ D, ROMAN SH, PODOS S, SOM P, DAVIES TF, J Clin Endicrinol Metab, 61 (1985) 183. — 6. NORDI M, BARTOLOMEI MP, ROMANI A, BARCA L, Graefes Arch Ophthalmol, 226 (1988) 8. — 7. KIKKAWA DO,CRUZ RC, CHRISTIAN WK, RIKKERS S, WEINREB RN, LEVI L, GRANET DB, Am J Ophthalmol, 135 (2003) 427. — 8. FISHMAN DR, BENES SC, J Clin Neuro-ophthalmol, 11 (1991) 162. — 9. SIMONSZ HJ, VINGERLING JR, Orbit, 17 (1998) 173. — 10. SCOTT AB, Ophthalmology, 87 (1980) 1044. — 11. DUNN WJ, ARNOLD AC, O'CONNOR PS, Ophthalmology, 93 (1986) 470. — 12. LYONS CJ, VICKERS SF, LEE JP, Eye, 4 (1990) 538. — 13. STIGLMAYER N, LEŠIN M, JURI J, IVANIŠEVIĆ M, BOIĆ L, ROGOŠIĆ V, Coll Antropol, 29 (2005) 41. — 14. KALMANN R, MOURITS MP, Br J Ophthalmol, 82 (1998) 754. — 15. KAZIM M, KENNERDELL JS, Orbit, 10 (1991) 211. — 16. DANESH-MAYER HV, SAVINO PJ, DERAMO V, SERGOTT RC, SMITH AF, Ophthalmology, 108 (2001) 145.

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UTJECAJ LOKALNE PRIMJENE BOTULINUM TOKSINA-A NA INTRAOKULARNI TLAK I PROPTOZU KOD TIROIDNE ORBITOPATIJE

SAŽETAK

Cilj istraživanja je bio ispitati utjecaj injekcije Botulinum toksina-A (BTX-A) u područje ekstraokularnih mišića na intraokularni tlak (IOP) i proptozu u pacijenata sa poremećajima bulbomotorike u tiroidnoj orbitopatiji (TO). Injekcije BTX-A primjenjene su u 17 pacijenata (20 očiju) sa restriktivnim strabizmom i dvoslikama. Mjerenje IOT-a aplanacionom tonometrijom po Goldmannu načinjeno je u primarnom položaju oka prije i 2–4 tjedna nakon injekcije BTX-A. Ekstraorbitalna prominencija očne jabučice mjerena je egzoftalmometrom po Hertelu prije i 2–4 tjedna poslije BTX-A injekcije. Srednja vrijednost IOT-a prije injekcije u primarnom položaju oka bila je 18,6±2,8 mm Hg, a 2–4 tjedna poslije BTX-A injekcije iznosila je 16,9±3,3 mm Hg; (p=0,001). Nije bilo statistički značajne razlike u vrijednosti egzoftalmometrije prije i nakon injekcije BTX-A, 21,5±2,7 mm prema 22,0±2,6 mm; (p=0,678). Zaključno, injekcija BTX-A ima sekundarno djelovanje na sniženje IOT-a u pacijenata sa TO zbog relaksacije ekstraokularnih mišića, ali bez utjecaja na proptozu.