

The use of botulinum toxin in acquired nystagmus: literature review and case presentation

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Abstract

Aim: To review the literature on the use of botulinum toxin (BT) in the treatment of symptoms associated with acquired nystagmus and to present a case report of a patient who experienced relief of symptoms with an injection of only one horizontal rectus muscle.

Method: A literature-based review on the use of BT in acquired nystagmus. A case is presented of a 40-year-old woman with multiple sclerosis who had BT injection to relieve symptoms of reduced vision and oscillopsia due to horizontal nystagmus. Orthoptic findings before and after the injection are documented and the management of the case described.

Results: It has been reported that BT can be injected into both the horizontal recti of one eye, or the retrobulbar space of one eye, to alleviate the symptoms of oscillopsia associated with acquired nystagmus. Numerous detrimental side-effects associated with the injections have been reported. In the case presented the patient reported an improvement in vision and oscillopsia following a BT injection into the left lateral rectus muscle. This was substantiated by an objective improvement in the visual acuity, with few side-effects.

Conclusion: BT injections into selected extra-ocular muscles can temporarily reduce the amplitude of nystagmus and relieve the symptom of oscillopsia. The case presented shows that a subjective improvement in symptoms can be achieved by a BT injection in only one horizontal rectus muscle

Key words: Acquired nystagmus, Botulinum toxin (BT), Oscillopsia, Visual acuity (VA)

Introduction

Acquired nystagmus is a debilitating disorder. Ruben *et al.* stated that vision is impaired in acquired nystagmus because of a defect in fixation and suppression of vision during eye movements.¹ The eye movements themselves do not require treatment, but if they result in visual symptoms then treatment is advocated.² The main incapacitating symptom of acquired nystagmus is oscillopsia, which is the illusory motion of the environ-

ment, and the associated reduction in visual acuity (VA).³ The treatment of acquired nystagmus should ideally be aimed at the pathophysiological mechanism causing the nystagmus.⁴ When the main cause cannot be treated, treatment is aimed at reducing the symptom of oscillopsia and improving VA by reducing the amplitude and frequency of the nystagmus.⁵

Treatment options for acquired nystagmus include pharmacological agents, optical and surgical procedures. These treatment options have all been reported in the literature with varied, but mainly limited success; a good summary is provided by Ruben *et al.*¹

Botulinum toxin for acquired nystagmus

Botulinum toxin (BT) has been reported to be of therapeutic value in the treatment of neurological and ophthalmological diseases^{6–8} and has been described as an alternative treatment option for acquired nystagmus.^{1,5,9,10–12} The use of BT in nystagmus has been advocated in two ways: either injection into the horizontal recti of one eye^{1,9,10,11} or injection into the retrobulbar space of one eye.^{1,5,11,12}

BT injection into the horizontal recti of one eye

Leigh *et al.* reported on the use of BT injection into the horizontal recti of one eye in 2 patients with acquired pendular nystagmus associated with multiple sclerosis (MS).⁹ Both patients reported a subjective improvement in their horizontal oscillopsia following the injections, and eye movement recordings after the injection revealed the horizontal component of the nystagmus had been essentially abolished. However, both patients reported previously unnoticed vertical or torsional components to their oscillopsia. Both patients declined further injection.

Ruben *et al.* reported that uniocular BT injection of both horizontal recti is only beneficial when the nystagmus is purely horizontal.¹ They reported on 3 patients with purely horizontal nystagmus who had this BT procedure, and despite all 3 having an objective improvement in VA, only 1 reported a subjective improvement in oscillopsia and vision.¹

BT injection into the retrobulbar space of one eye

Helveston and Pogrebniak were the first to report on the injection of BT into the retrobulbar space to improve the symptom of oscillopsia by reducing the amplitude of vertical, horizontal and rotary components to pendular

acquired nystagmus following a brainstem stroke.¹¹ It is proposed that the retrobulbar injection of BT causes a paralysis of all the extra-ocular muscles, resulting in reduced ocular movement and the subjective improvement in oscillopsia and VA.¹¹ Helveston and Pogrebniak reported on 2 patients who had an objective improvement in VA and a subjective improvement in oscillopsia and vision following retrobulbar injection. Only 1 of the patients had repeated injections; the other did not feel the improvement in vision warranted repeat injection.¹¹

Repka *et al.* reported on 6 patients who underwent one or more BT injections into the retrobulbar space. The subjects reported a subjective improvement in the vision of the injected eye. Eye movement recordings objectively confirmed a significant decrease in the oscillations of the nystagmus and reduced saccadic oscillations.⁵

Ruben *et al.* reported on 9 patients who underwent one or more BT injections into the retrobulbar space.¹ Four had an objective improvement in VA and 2 reported a subjective reduction in visual symptoms. For 1 patient this was relief of hallucinations, which moved in synchrony with the nystagmus despite a level of vision that was no light perception, and for the other patient this was a reduction in oscillopsia. These authors advocated the use of uniocular retrobulbar space BT injection for oscillopsia in cases that are not responsive to more conventional treatment options.¹ Patients should be prepared to view monocularly following retrobulbar injection in order to gain benefit from the treatment.^{1,12}

Side-effects of BT injection

As with BT injections for other conditions, side-effects can occur following injection of the horizontal recti of one eye and retrobulbar space injections.^{1,5,9,10-12} These include unmasking secondary components of the nystagmus in the recti muscle injections, diplopia, reduced ocular motility of the injected eye, increased amplitude of nystagmus in the non-injected eye, ptosis and the need for repeat injections.

An increase in the amplitude of the nystagmus in the non-injected eye following injection into the horizontal recti of the fellow eye has been reported.⁹ Leigh *et al.* noted that the saccadic, smooth pursuit and vestibular movements of the non-injected eye all increased and these gain changes were all restricted to the horizontal plane. They concluded that adaptive changes of these eye movements had occurred in response to the paresis caused by the toxin. As the horizontal component of the nystagmus in the injected eye returned, the vestibular movements of the non-injected eye declined.⁹

Not all authors have noted this trend. Tomsak *et al.* reported on 3 patients who had retrobulbar BT injection in whom eye movement recording showed there was no increase in the nystagmus of the non-injected eye after the injection.¹² In fact 1 patient had a reduction in the nystagmoid movements of their non-injected eye, which the authors could not explain. It has been proposed that an increase in the eye movements of the non-injected eye is not a problem provided the eye with the better VA is treated.⁵

Leigh *et al.* reported that the saccadic eye movements of the injected eye following BT injection into the

horizontal recti became hypometric with reduced velocity and dynamic overshoots. The corresponding saccades of the non-injected eye were reported to be hypermetric.⁹ Similarly it is reported that the horizontal and vertical saccades were moderately decreased in the injected eye following retrobulbar space injection.⁵

Limitations of ductions following BT injections into the retrobulbar space and horizontal recti have been reported to vary from slight^{5,9,11,12} to total ophthalmoplegia.^{5,12} Disorders of ocular movement are reportedly maximal 1 month following retrobulbar injection, but resolve within 2 months of the injection.⁵ However, the duration of the subjective improvement in symptoms is reported to last from 3 to 12 months following a single uniocular retrobulbar injection.⁵

Diplopia may occur as the result of inducing a manifest deviation by BT injection into the horizontal recti^{1,9} or retrobulbar space.^{5,12} The reported incidence varies but appears to be greater following retrobulbar injections and has been reported to be intolerable in some cases.¹²

Ptosis usually occurs following retrobulbar BT injections but may also occur following BT injections into individual horizontal rectus muscles. The incidence of ptosis following retrobulbar BT injection varies from 11.76%⁵ to 100%¹² compared with 0¹¹ to 50%⁹ following injection into the horizontal recti.

Case report

A 40-year-old woman with MS was referred to the neuro-ophthalmology service at the Birmingham and Midland Eye Centre. Orthoptic and ophthalmic examination revealed bilateral internuclear ophthalmoplegia with purely horizontal pendular nystagmus and no manifest deviation in the primary position. VA was right eye 1.300 (6/120), left eye 1.120 (6/75). At the time of referral the patient was taking 500 mg of gabapentin with the aim of reducing her main symptom of oscillopsia. Although the patient reported that the gabapentin did reduce her oscillopsia, she still complained of reduced vision, oscillopsia and dizziness.

The patient underwent an injection of BT into the left lateral rectus muscle. Three weeks after the injection the VA was unchanged for the right eye at 1.300 (6/120), but had improved for the left eye to 0.940 (6/48-2). On cover test the patient had a constant right esotropia with diplopia. In addition to the previously diagnosed bilateral internuclear ophthalmoplegia, left eye abduction was limited following the BT injection. The patient reported an improvement in her vision and oscillopsia, and although she complained of diplopia, she utilised an abnormal head posture of face turn to the left to alleviate this.

Three months after the injection the patient reported a reduction in VA to the pre-injection levels. On examination VA had reduced in the left eye to 1.00 (6/60) but had improved in the right eye to 1.12 (6/75). The limitation of abduction of her left eye was noted to have resolved. At the patient's request she underwent a second injection of BT into the left lateral rectus muscle. One month later the patient reported no improvement in her vision following the second BT injection. As a

consequence the patient had a third injection of BT into the left lateral rectus muscle. After the injection she reported an improvement in her oscillopsia and vision although there was no change on VA testing.

The patient remained under review for 4 years during which she received a further 11 BT injections into her left lateral rectus muscle. The patient reported a subjective improvement in her oscillopsia and vision following each repeat injection. The limitation of the left eye abduction was noted to improve between injections but returned following each injection without diplopia.

Discussion

This patient was initially treated with gabapentin with the aim of reducing her visual complaints. Gabapentin is often the drug of choice for the treatment of acquired pendular nystagmus resulting from MS.^{2,3,4,13} Following an injection of BT into the left lateral rectus muscle this patient's VA improved and she reported an improvement in her symptoms of reduced vision, oscillopsia, dizziness and instability.

Due to the detrimental effect of MS on this patient's health, which resulted in her being wheelchair-bound, management of her oscillopsia was aimed at improving her quality of life. To keep the treatment and therefore patient distress to a minimum, it was decided to undertake a BT injection into just one horizontal rectus muscle to ascertain whether a beneficial outcome could be obtained. This patient reported a subjective improvement in her oscillopsia and vision following the BT injection. Although these BT injections induced a strabismus, the patient only reported diplopia following the first injection. Furthermore the improvement in her oscillopsia and vision resulted in her being able to undertake activities that the oscillopsia had prevented her from doing. Therefore she continued to receive repeat BT injections into her left lateral rectus muscle to reduce her symptom of oscillopsia.

In contrast Leigh *et al.* reported little change in the eye movement recordings after BT injection into one horizontal rectus muscle. The authors did not state whether there was any subjective improvement in symptoms, but it could be assumed that as the other horizontal rectus muscle of the same eye was injected 2 weeks later, there was no subjective improvement in symptoms following the first injection. They reported a reduction in the eye movement recordings following the second BT injection and as a consequence advocated injection into both horizontal rectus muscles.⁹

It is likely that this patient's improvement in VA was due to the reduction in nystagmus of that eye. However, it should be noted that any reduction in the nystagmus is assumed, as no pre- or post-injection eye movement recordings were made for this patient due to her failing health. It is possible that this variation in VA may be due to variation between tests or the fact that MS patients can be suggestible.

The actual improvement in this patient's VA is not as substantial as that reported by other authors who injected

BT into either both horizontal recti of one eye or the retrobulbar space.^{1, 5,9-12} It is possible that there would have been a greater improvement in this patient's acuity if both horizontal recti of the left eye had been injected.

In accordance with previous reports on the side-effects of BT, the initial injection of the left lateral rectus resulted in a slight limitation of abduction of the injected eye and an esotropia with diplopia. However, this did not trouble the patient, who adopted a head posture to alleviate the diplopia.

This patient had repeat toxin injections at 3 monthly intervals when she felt that the improvement in her acuity and oscillopsia had diminished. This duration of effect of the injections is similar to that reported in the literature of 6-8 weeks after horizontal recti injections⁹ and retrobulbar injection.¹¹ Three months after the injection, acuity and visual function will reportedly have returned to the pre-injection levels.^{9,11}

Conclusion

BT injections into selected extra-ocular muscles can temporarily reduce the amplitude of nystagmus and relieve the symptom of oscillopsia. Previous reports have advocated injection into both horizontal recti of one eye, or retrobulbar injection. The case presented in this report had injection of only one horizontal rectus muscle and experienced an improvement in vision and reduction in oscillopsia. The improvement the patient experienced was sufficient for her to desire repeat injections.

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