

Management of nystagmus by surgery and botulinum toxin options: a review

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Abstract

Aim: To critically evaluate the literature in order to explore the success of botulinum toxin and extraocular muscle surgery in the management of acquired nystagmus.

Methods: A literature search was undertaken using the PubMed and Web of Knowledge databases. Only studies reported in English were included.

Results: The aim of using botulinum toxin is to alleviate the symptoms induced by acquired nystagmus. The major problematic symptoms are oscillopsia, reduced visual acuity and abnormal head posture. An injection of botulinum toxin into the retrobulbar space is beneficial if the acquired nystagmus has horizontal, vertical and torsional components, whereas if the nystagmus is purely horizontal an injection of botulinum toxin into the horizontal rectus muscles appears to be the better option. Surgery is aimed at alleviating the symptoms induced by acquired nystagmus. Extraocular muscle surgery is of value in the management of acquired nystagmus, particularly if the patient has developed an abnormal head posture.

Conclusion: It is difficult to come to any clear-cut conclusions due to the low numbers of patients that have been studied. It would, however, appear that botulinum toxin and surgery are of some value in the management of acquired nystagmus. Further research is required in this area.

Key words: Acquired nystagmus, Botulinum toxin, Oscillopsia, Surgery

Introduction

Acquired nystagmus is an involuntary repetitive oscillatory movement of one or both eyes that occurs secondary to a disruption of the normal mechanisms that maintain steady central fixation. This disruption could be either severely defective vision, or central nervous system damage. Nystagmus can be found in a horizontal,

vertical or rotary direction, and can be present in one to all of the nine positions of gaze.¹ Acquired nystagmus can be either jerk, which consists of a slow drift away from the object followed by a quick corrective movement, or pendular, which consists of sinusoidal slow-phase oscillations.² The most common causes are tumour, demyelination or degeneration, trauma, stroke, medications or toxins, and vestibular imbalance.³

The symptoms of acquired nystagmus usually consist of oscillopsia, which is the illusion of motion of the seen world, and a reduction in visual acuity. Both these symptoms are due to the excessive motion of images on the retina.² The severity of the symptoms will depend upon the amplitude, frequency and velocity of the nystagmus. The position of gaze where the nystagmus is present will also affect the severity. If the nystagmus is in primary position the patient is often aware of this and typically adopts an abnormal head posture to alleviate symptoms. Equally if nystagmus is in another position of gaze the patient will avoid looking in that direction of gaze along with adopting an abnormal head posture. The presence of oscillopsia is often used to aid the differential diagnosis of congenital or early-onset nystagmus versus acquired nystagmus. This is because oscillopsia is not frequently appreciated with congenital or early-onset nystagmus whereas it is frequently noticed in many forms of acquired nystagmus, particularly those types where nystagmus is present or encroaches on primary position. Hence in such cases the patient more readily appreciates oscillopsia.

The primary purpose of treatment of nystagmus is to investigate and treat, where possible, any underlying disorder such as vestibular or brain stem pathology that is causing the nystagmus. The aims of treatment for acquired nystagmus are to abolish or reduce the oscillopsia, to improve the vision and to reduce the abnormal head posture. In particular, adoption of an associated abnormal head posture to reduce the amplitude or frequency of nystagmus⁴ can cause the patient to have problematic torticollis. If this is the case then the management will be focused initially on reducing the abnormal head posture.

The treatment of acquired nystagmus can be separated into invasive management options and non-invasive management options. Non-invasive management options include the use of spectacles, contact lenses and prisms. It is essential that an up-to-date spectacles prescription is

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Table 1. Botulinum toxin dose

Authors	Date	Type of botulinum toxin	Single injection dose	Retrobulbar injection dose
Leigh <i>et al.</i> ²²	1992	Botox	2.5–3 units	
Ruben <i>et al.</i> ¹⁰	1993	Botox	2.5 units	10–25 units
Kosmin <i>et al.</i> ¹²	1996	Botox	1–2.5 units (2.5 units recommended)	5–20 units (15–20 units recommended)
Lennerstrand <i>et al.</i> ¹⁵	1998	Botox	1–2.5 units	20–25 units
Helveston and Pogrebniak ¹³	1988	Botox	3 units	
Ruben <i>et al.</i> ¹¹	1994	Botox		20 units
Repka <i>et al.</i> ¹⁷	1994	Botox		25–30 units
Tomsak <i>et al.</i> ¹⁹	1995	Botox		10–25 units
Mathai <i>et al.</i> ²¹	1996	Botox		25 units
Menon and Thaller ¹³	2002	Dysport		40 units
Devogelaere <i>et al.</i> ¹⁸	2006	Botox		20–25 units
Dawson <i>et al.</i> ¹⁴	2007	Dysport		25 units

Poulton¹⁶ (2007) did not state the dose used.

being worn so that the patient can achieve their best level of vision. The spectacles should be single focal lenses, as this will allow the patient to adopt an abnormal head position to use a position of gaze where oscillopsia is at its least.⁴ Contact lenses can be used to manage acquired nystagmus because a contact lens can move with the oscillating eye. This means that the patient may benefit from more prolonged foveation periods than that achieved with spectacles.⁵ Prisms have also been used to relieve the symptoms of acquired nystagmus, by deviating images and thus moving the eyes away from the position of gaze where the nystagmus is at its greatest.¹ This use of prisms simulates the effect of the abnormal head posture and thus is used diagnostically to assess the effect of reducing the abnormal head posture prior to undertaking extraocular muscle surgery. Base-out prisms can be used to induce a convergence dampening effect on nystagmus in selected cases of idiopathic nystagmus that are straight-eyed with good fusional vergence.

Surgical procedures for congenital nystagmus have been well documented in the ophthalmic literature over the past 50 years. This has been since Kestenbaum⁶ and Anderson⁷ independently described surgical treatment for the management of associated face turns that arise due to patients trying to keep their eyes in the position of the null point, i.e. the position of gaze where nystagmus is at its least. It is only more recently that similar surgery has been undertaken in order to correct abnormal head postures in types of acquired nystagmus.⁸ The literature also describes the use of other surgical procedures to improve either abnormal head postures or the amplitude and frequency of the nystagmoid movements, thereby alleviating the associated symptoms of torticollis, reduced visual acuity and oscillopsia.

This literature review addresses the invasive management options of botulinum toxin and surgery. The review was undertaken by the use of online (PubMed, Web of Knowledge) and non-Medlined (orthoptic journal and conference transactions) databases followed by checking of the reference sections of selected papers. Search terms included 'nystagmus', 'oscillopsia', 'strabismus surgery', 'surgery', 'botulinum toxin', 'Botox', 'Dysport', 'treatment', 'management' and 'head posture' as the main search terms. The time period was from 1939 to 2008.

Botulinum toxin

Botulinum toxin is considered to be the most potent biological toxin in nature.⁹ It works by binding to receptor sites on the cholinergic nerve terminal. This causes the blockage of quantal acetylcholine release, which in turn decreases skeletal muscle power, therefore paralysing the muscle. Muscle function will only return when new motor end plates are formed.^{10–12} It has been used to treat a number of conditions within ophthalmology, which include strabismus, blepharospasm and ocular motility restrictions.^{12,13} Additionally botulinum toxin type A has been used in the treatment of acquired nystagmus.¹⁴

Botulinum toxin A can be injected directly into extraocular muscles, or it can be injected into the retrobulbar space behind the globe of the eye. This will paralyse either a specific or all of the extraocular muscles, in order to damp down the nystagmoid movements.^{13,14}

Types of nystagmus

Botulinum toxin has been injected into the medial rectus and lateral rectus muscles for the treatment of acquired pendular nystagmus.^{2,10,12,13,15,16} Helveston and Pogrebniak injected all four rectus muscles of the left eye in one patient who had bilateral vertical, horizontal and rotary pendular nystagmus.¹³ In one case Lennerstrand *et al.* injected the inferior oblique to treat vertical nystagmus.¹⁵

More commonly botulinum toxin is injected into the retrobulbar space. Retrobulbar injection was used to treat acquired pendular nystagmus which had horizontal, vertical and rotary components,^{10–13,15,17–20} upbeat nystagmus,¹⁷ downbeat nystagmus^{11,12} and acquired horizontal periodic alternating nystagmus.²¹ Retrobulbar injection is usually undertaken unilaterally although bilateral injection has been reported.^{10,11,17,18} However, retrobulbar injection often induces diplopia and ptosis. Hence unilateral injection is more commonly utilized than bilateral. Dosage of botulinum toxin varies considerably along with the type of botulinum toxin used. Reported dosages are outlined in Table 1.

Outcome

In all the studies reviewed where botulinum toxin was

Table 2. Visual acuity before and after botulinum toxin injection into the extraocular muscles

Authors	Date	Injected eye	Visual acuity before	Visual acuity after
Helveston and Pogrebniak ¹³ Kosmin <i>et al.</i> ¹²	1988	LE	20/160	No subjective improvement
	1996	LE	6/18	6/18
Leigh <i>et al.</i> ²²	1992	RE	6/12	6/4
		RE	20/40 + 2	20/25-3
Poulton ¹⁶ Ruben <i>et al.</i> ¹⁰	2007 1993	RE	10/40 + 2	10/40 + 2
		LE	6/75	6/48-2
		LE	CF	1/24
		LE	6/36	6/24
		LE	6/60	6/18

injected directly into extraocular muscles, vision was found either to improve in the eye that was injected or to remain at the same level. Most patients had improved visual acuity ranging from one to four lines of acuity.^{10,12,16,22} Table 2 shows the changes in visual acuity.

In the main, it appears that injecting botulinum toxin A into either one or both horizontal rectus muscles of one eye will only aid the patient if their nystagmus has only a purely horizontal component. In patients with purely horizontal pendular nystagmus^{12,16} this treatment showed subjective improvement of oscillopsia. Patients with combined nystagmus components found that by abolishing the horizontal motion, the vertical and torsional nystagmus was unmasked, and consequently they reported that their oscillopsia was worse.^{10,22}

Retrolbulbar injection of botulinum toxin was reported by Dutton and Fowler to result in improved visual acuity in up to 66% of patients.⁹ Unilateral injection of botulinum toxin was reported to improve the vision in the treated eye^{11,12,17,20} and in two reports vision was improved in the treated eye in up to 70% of patients.^{10,14} Bilateral injection of botulinum toxin was reported to improve visual acuity in both eyes.^{10,11,17,18} Improvement in acuity varied from subjective reports to documented improvement in visual acuity by formal acuity measures.^{17,18} However, there were also reports of lack of improvement in the level of acuity.^{10,21} Table 3 outlines the visual acuity changes

There was a subjective improvement in oscillopsia found in all patients where this symptom was reported.^{11,14,17,19,21} This ranged from abolition of the symptom to subjective improvement of the symptom.^{11,19,21}

Complications

Complications from injection of botulinum toxin into individual extraocular muscles when undertaken for strabismus and other ocular motility disorders commonly include ptosis. However, this was infrequently reported when the injection was undertaken for nystagmus treatment and was typically mild.^{10,15,22}

Induced vertical or horizontal strabismus was reported to be due to the spread of botulinum toxin into adjacent extraocular muscles. This occurred infrequently in patients treated with botulinum toxin for nystagmus.^{15,16,22,23} Induced intermittent or constant diplopia has been reported, which was treated in the main by occlusion until resolution occurred^{12,22} or with an abnormal head posture.^{12,16}

Potential complications that could occur due to an injection into the retrobulbar space of the eye included retrobulbar haemorrhage, orbital cellulitis, penetration of the globe, and trauma to the optic nerve.^{13,14,17,18,20}

The side effects after injecting botulinum toxin A into the retrobulbar space of one or both eyes appear to be more severe than when the botulinum toxin is injected into extraocular muscles. Devogelaere *et al.* reported that ptosis was more common following retrobulbar injection than with injection to individual extraocular muscles.¹⁸ It was suggested that by using a lower dose of botulinum toxin the ptosis was reduced without any lessening of the visual improvement.^{14,20}

Diplopia was also found to be quite a common symptom.^{10-12,14,17,19,21} Kosmin *et al.* reported the symptom of diplopia after injection of all their patients requiring occlusion or the use of an abnormal head posture.¹²

Although it was not mentioned as a specific complication in any of the cases that were reviewed, many of the studies discussed the effect of impairing the vestibular ocular reflex. This was caused by injecting the botulinum toxin into the retrobulbar space of the eye.^{10,12,14,19} It occurs because this procedure effectively causes the patient to have ophthalmoplegia in order to stop the nystagmoid movements. It was therefore suggested that this treatment is more beneficial to non-ambulant patients,^{12,14} because the impairment of the vestibular ocular reflex causes oscillopsia and blurred vision whenever the head is moved.¹⁹ Patients in wheelchairs are able to keep their heads much steadier and therefore this is not so much of a problem.²⁴

Further treatment

For many patients reported in the literature botulinum toxin appeared an effective, albeit temporary, treatment option. Treatment typically included repeat injections, ranging from 1 to 31 injections across studies.^{10,12} Lennerstrand *et al.* reported that some patients underwent extraocular muscle surgery on the basis of the outcome of the botulinum toxin treatment.¹⁵

Summary

Many of the studies concluded that the use of botulinum toxin A in the management of acquired nystagmus can be very valuable in selected cases. From the literature, it could be suggested that if the nystagmus has a purely horizontal component the best method would appear to be injection of botulinum toxin A into the horizontal rectus muscles. However, if the nystagmus has hori-

Table 3. Visual acuity before and after botulinum toxin injection into the retrobulbar space

Authors	Date	Injected eye of one patient	Visual acuity before	Visual acuity after
Dawson <i>et al.</i> ¹⁴	2007	RE	6/24	6/24
		RE	6/18	6/12
		LE	6/36	6/12
		LE	6/36	6/24
		RE	6/60	6/24
		RE	6/36	6/18
		LE	6/36	6/36
		LE	6/9	6/9
		RE	6/36	6/12
		RE	6/24	6/18
		RE	6/24	6/12
		RE	6/24	6/18
		LE	0.5/60	2/60
		LE	6/60	6/60
		RE	6/12	6/9
		LE	6/60	6/12
		Helveston and Pogrebnik ¹³	1988	RE
LE	20/80			20/40
Kosmin <i>et al.</i> ¹²	1996	RE	6/60	6/18
		LE	1/60	6/18
		LE	6/18	6/12
		RE	6/36	6/18
Mathai <i>et al.</i> ²¹	1996	RE and LE	6/6 and 6/6	6/6 and 6/6
Menon and Thaller ²⁰	2002	RE	6/36	6/12
Repka <i>et al.</i> ¹⁷	1994	RE	20/80	20/40
		RE and LE	20/40 and 20/40	20/40 and 20/40
		RE and LE	20/200 and 20/200	20/200 and 20/200
		RE	20/200	20/200
Ruben <i>et al.</i> ¹⁰	1993	RE	20/200	20/80
		RE	6/9	6/9
		RE	1/60	5/60
		RE and LE	NPL and NPL	NPL and NPL
		LE	6/24	6/12
		RE and LE	6/18 and 6/18	6/9
		LE	3/60	6/36
		RE	5/60	5/60
		RE	6/60	6/60
Ruben <i>et al.</i> ¹¹	1994	RE	3/60	6/60
		LE	6/24	6/12 + 1
		RE and LE	6/18 and 6/18	6/9 and 6/9

Devogelaere *et al.*¹⁸ (2006), Lennerstrand *et al.*¹⁵ (1998) and Tomsak *et al.*¹⁹ (1995) did not state the values of visual acuity.

zontal, vertical and torsional components, it would seem that injecting the botulinum toxin into the retrobulbar space is the better option. It also appears that acquired pendular nystagmus responds better than jerk nystagmus to treatment with botulinum toxin, with the exception of one patient with periodic alternating nystagmus who reported that his symptoms were greatly improved.²¹ It was particularly stated that when the botulinum toxin was injected into the retrobulbar space it was a simple, safe and worthwhile treatment to improve vision and oscillopsia.^{10,11,14,17,20}

Surgery

Types of nystagmus

The majority of the literature describes surgery for vertical jerk or pendular acquired nystagmus.^{8,25-33} Other types of acquired nystagmus that were reviewed were periodic alternating nystagmus (4 cases), horizontal uniocular acquired pendular nystagmus (1 case) and acquired pendular nystagmus with both a horizontal and a vertical component (1 case).^{32,34-36}

Indications

Most patients requiring surgery underwent surgery to

correct an associated abnormal head posture. For patients with a chin depression, the nystagmus described was mainly downbeat nystagmus. This was frequently reported with a null point of nystagmus in up gaze.^{8,27,28,31,32} For patients with a chin elevation the nystagmus described was always upbeat nystagmus, with the null point being found in down gaze.^{8,27,29,31} Yang *et al.* reported that an abnormal head posture might be adopted in cases of acquired nystagmus to improve binocular single vision, and not because of any null point.³¹

Occasional cases were reported which display the reverse of Alexander's law.²⁵⁻³⁰ Pedersen *et al.*²⁵ described a patient with acquired downbeat nystagmus in whom the nystagmus was at its worst in up gaze. Depalo *et al.*³⁰ described a patient with acquired upbeat nystagmus that was worse in down gaze. Therefore this patient had a chin depression as the null point was in elevation. However, regardless of the direction of the nystagmus, the position of the head according to the adopted abnormal head posture was the main factor considered when planning surgery.

The amount of chin depression or elevation pre-operatively was not always reported in a quantitative format.^{28-30,32,33} It is therefore quite difficult to assess the largest and smallest chin depressions that were

operated upon. The limited quantitative data found in the literature reported chin depression of 10–35 degrees and chin elevation of 10–30 degrees.^{8,27,31} Associated torticollis due to chin elevation was occasionally reported.^{27,31}

Oscillopsia is the main symptom of acquired nystagmus and was recorded as a subjective symptom in the majority of the reports.^{25,30–33,36} Other symptoms included blurred or reduced vision, nausea and vomiting.^{25,27,31}

Surgical options

Various surgical procedures have been described. For patients with an abnormal chin-down head posture, the most frequently reported procedure was bilateral superior rectus recessions, which were usually symmetrical.^{8,27,30,31,33} Some of these studies reported additional extraocular muscle surgery along with the superior rectus recessions. This surgery consisted of bilateral superior oblique tenectomies and bilateral inferior oblique myectomies, bilateral inferior oblique anterior transpositions and bilateral inferior rectus tenotomies.^{27,30,33} It has been reported that the superior rectus recessions are to eliminate the chin depression, whereas adjuvant surgery alleviates the nystagmoid movements. Dell'Osso and Wang³² carried out only bilateral inferior rectus tenotomies in their patient who had acquired downbeat nystagmus whereas Buckley and Elston²⁸ undertook bilateral surgical disinsertion and extirpation of both the superior and inferior rectus muscles.

The surgical treatment performed on patients with acquired upbeat nystagmus with a chin elevation most commonly involved bilateral recessions of the inferior rectus muscles, varying in size from 7 mm to 10 mm.^{8,29,31} A variation on this involved bilateral inferior rectus recessions with bilateral superior rectus resections.²⁷

For patients with acquired horizontal pendular nystagmus two different procedures have been described to alleviate or ameliorate their symptoms. Bilateral retro-equatorial recessions of all four horizontal rectus muscles were undertaken as one option.³⁴ The second option involved tenotomies of all four horizontal rectus muscles or tenotomies on the horizontal rectus muscles of the affected eye.^{32,36} In each case the procedure aimed to eliminate the horizontal component of the nystagmus.

Outcome

The follow-up periods for the surgical cases reported in the literature range from 5 weeks to 8 years.^{28,29,31–34} The results from the studies that had longer follow-up appointments are considered more reliable as an increase or reduction in the original improvements is possible with the passage of time following surgery.

Although the amplitude of nystagmus was reported as reduced in all cases, this was difficult to quantify.^{28,32} Dell'Osso and Wang³² used a computer program (NAFX), which showed a reduction in amplitude of nystagmus. Coexistent patient reports showed oscillopsia had also reduced.³² Oscillopsia was subjectively found to improve post-operatively in other

studies,^{25,28,30,31,33,36} with occasional reports of elimination of the symptom.^{25,29} Where pre-operative visual acuity measures were reduced these were reported to improve post-operatively.^{27,30,32,34–36}

In studies assessing vertical acquired nystagmus, the post-surgical results were mainly focused on the improvement of any abnormal head posture. Post-operatively the reported improvements in abnormal head posture ranged from slight residual head posture to complete elimination of the head posture.^{27,29,31–33} In the studies where abnormal head posture was quantified, residual head postures were reported of 10–15 degrees.^{8,27,28,30,31}

Complications

Complications reported following surgery on extraocular muscles for nystagmus related to the induced limitation of ocular motility post-operatively. Surgery for chin depression was reported to induce marked bilateral elevation deficit.^{27,31} Jain *et al.* reported one patient with mild transient diplopia.²⁹

Post-surgical treatment

Of the surgical cases reviewed for this paper, none underwent further surgery, although this was considered for some cases.^{32,36} Treatment with botulinum toxin was undertaken for patients with downbeat nystagmus to further improve their oscillopsia.²⁸ Other patients opted for a trial of the drug memantine, which was reported to improve the level of visual acuity and amplitude of nystagmus when formally measured.^{32,36}

Summary

Lee³⁷ states that unless the causal lesion can be removed, little can generally be done surgically for patients with acquired nystagmus. However, for certain types of nystagmus surgery can reduce oscillopsia and improve vision. There seems to be particular success with surgery when there is a null point causing the patient to have an abnormal head posture. The major difficulty in reviewing this literature has been the small numbers of patients that have been reported in the research, as the majority of the literature consists of single case studies. Thus it is difficult to reach a consensus on the type of surgical procedure most beneficial in treating certain types of nystagmus.

Conclusion

It is very difficult to form any definite conclusions from the literature because of the limited numbers of patients that have been reported. Many studies included different types of acquired nystagmus, which affected the judgement of treatment effect for each type. Separating types of nystagmus could be considered in future studies for further investigation into the invasive treatment of nystagmus, in order to guide clinicians in offering the correct management options to each specific patient.

From the literature it can be seen that botulinum toxin can alleviate the symptoms of acquired nystagmus in some patients. It would appear that patients with acquired pendular nystagmus respond particularly well

to botulinum toxin injections. Surgery could be used in cases of vertical jerk nystagmus, especially if the patient has a chin depression or elevation. This method of management requires further research as, from the literature that has been reviewed, there is a good reported level of success without any major side effects.

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