

Botulinum toxin injection for the treatment of epiphora in lacrimal outflow obstruction

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Abstract

Purpose: To describe our experience with the use of botulinum toxin (BoNTA) for the symptomatic treatment of lacrimal outflow obstruction.

Methods: We retrospectively reviewed the case notes of patients with epiphora due to lacrimal outflow obstruction who chose to have injections of botulinum toxin into the palpebral lobe of the lacrimal gland instead of surgery between 2009 and 2014. Epiphora was graded subjectively with Munk scores obtained before and after treatment as well as qualitative degree of improvement reported by the patients. Severity and duration of side effects were also noted.

Results: Seventeen patients (22 eyes, mean age 70.3, 4 males and 13 females) were identified. A mean of 3.5 (range; 1–10) injections of BoNTA (Botox, Allergan; 1.25–7.5 units) were given per eye. The mean interval between injections was 3.9 months (range 3–6). The mean Munk score (3.4, range 2–4) improved significantly after treatment to 1.6 (range: 0–3, $P = 0.0001$ paired two-tailed t -test). Epiphora completely resolved in a fifth, improved by up to 60–90% in a half and only 'a little better' in a further fifth. Temporary bruising and diplopia (lasting 2 weeks) was reported in 12% (2/17).

Conclusion: We report our outcomes for BoNTA to the palpebral lobe of the lacrimal gland in patients with lacrimal outflow obstruction epiphora seeking alternatives to surgery. This data provide further evidence for informed consent and for commissioning organisations considering the funding of this treatment.

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Introduction

Epiphora owing to lacrimal outflow obstruction affects a wide range of patients. It adversely

affects their quality of life by causing blurred vision, irritation of the eye and periocular tissue and social embarrassment. Its standard treatment is surgical in the form of DCR (dacryocystorhinostomy) and even Jones tube intubation depending upon the location and extent of obstruction. Jones tubes, however, have a high rate of displacement and the need for further procedures and patient satisfaction does not always correlate with the anatomical success.^{1–3} Surgery may not be the best option in all patients especially in the elderly population. It may also be medically inadvisable in those who have undergone excision of lacrimal apparatus for treatment of malignant lesions affecting the neighbouring anatomical structures.

The main and accessory lacrimal glands both significantly contribute to basal and reflex tear production.⁴ Injection of botulinum toxin A (BoNTA) in the lacrimal gland blocks the presynaptic release of acetylcholine, which is required for tear secretion.

BoNTA has been successfully used to treat excess tear production in the setting of gustatory hyperlacrimation owing to aberrant regeneration in proximal facial nerve injuries.^{5–9} To our knowledge, only two publications report its use in the treatment of either functional epiphora (14 patients patent to syringing)¹⁰ or lacrimal obstruction (27 patients).⁹

We report the outcomes of BoNTA injections in a group of patients with lacrimal outflow obstruction owing to a variety of pathologies.

Methods

We retrospectively reviewed the case notes of 17 patients with epiphora owing to lacrimal outflow obstruction who chose to have injections of BoNTA into the palpebral lobe of the lacrimal gland instead of surgery at a single centre

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between 2009–2014. IRB approval for this audit was obtained. Epiphora was graded subjectively with Munk scores before and after treatment.¹¹ Patients were also asked to report any improvement on a scale of zero to hundred per cent and to report if their symptoms were 'worse', 'no better', 'a little better', 'a lot better but not completely' or 'completely better' after the injection. The severity and duration of side effects were also noted.

BoNTA (Botox, Allergan) was reconstituted with sterile, preservative-free 0.9% sodium chloride solution diluted to a concentration of 50 units/1 ml. Each patient received topical Oxybuprocaine Hydrochloride 0.4% w/v (Bausch & Lomb, Kingston-upon-Thames, UK) before injection. The lateral upper eyelid was manually distracted away from the globe, while the patient looked down and to the opposite side to expose the palpebral lobe of the lacrimal gland. A transconjunctival injection of 1.25–7.5 units of BoNTA (the most common dose being 2.5 units) using a 27-gauge needle on a 1-ml syringe was given into the palpebral lobe.

Results

A total of 22 eyes of 17 patients were identified, 4 males, 13 females. The mean age was 70.3 (median = 72, range 36–93). Twelve eyes (10 patients) had canalicular or common canalicular obstruction, four eyes (3 patients) had nasolacrimal duct (NLD) obstruction and six eyes (4 patients) developed epiphora after punctal cautery. (Table 1) Sixteen patients had troublesome epiphora; one patient had bilateral blurred vision owing to a high tear meniscus encroaching upon the visual axis.

A total of 73 injections were given, 19 by a consultant and 54 by fellows. A mean of 3.5 injections (median = 3, range 1–10) were given per eye. Seven eyes (5 patients) had >3 injections.

The median duration of effectiveness was 10 weeks (range 3–24 weeks). The mean indoors Munk score (3.4, range 2–4) improved significantly after treatment to 1.6 (range 0–4, $P=0.00001$, paired two-tailed *t*-test). The mean outdoors Munk score (3.8, range 3–4) improved significantly after treatment to 1.7 (range 0–3, $P=0.0001$; Table 2).

Three patients (18%, 3 eyes) reported their epiphora completely resolved, 53% (9/17, 12 eyes) patients reported their epiphora was a lot better but not completely resolved (60–90% improvement). Three (18%, 5 eyes) were 'a little better' (30–50% improvement), one patient (1 eye) did not report any subjective improvement after two treatments and one patient (1 eye) deteriorated after one injection (further described below). Five patients received bilateral treatment of similar dose and they reported similar outcomes of the two sides (Table 3).

The mean interval between injections was 3.9 months (range 3–6). One patient developed a lacrimal gland and upper eyelid haematoma following injection that lasted 2 weeks. Another patient had horizontal diplopia that prevented her from driving for 2 weeks. (Table 2)

Sixteen eyes (13 patients) received 2.5 units at every treatment. Four eyes (3 patients) received 5–7.5 units. One patient had 1.25 units bilaterally at her first treatment that was later increased to 2.5 units. Early on, during our learning curve, three patients received 5–7.5 units. One patient with canalicular stenosis received 7.5 units at her first treatment with 80% improvement. She was given 5 and then 2.5 units in her subsequent treatments with similar degree of effectiveness and duration. Two other patients also received 5 units with 60–90% improvement. None experienced any side effects. Therefore, we recommend a starting dose of 2.5 units.

One patient had four-lid punctal cautery for dry eyes syndrome (reduced Schirmer's with anaesthetic of 2–3 mm after 5 min) and despite improvement in the ocular surface with a reduction in corneal punctate staining and no objective evidence of tear overflow, had symptomatic epiphora. She underwent three BoNTA (1.25, 2.5 and 2.5 units) treatments over the course of a year with little (30%) subjective improvement. This patient went on to have punctal retrieval surgery with anatomical success but minimal subjective improvement. One patient with Sjögren's syndrome, who had undergone 4-eyelid punctal cautery, had subsequent symptomatic epiphora in one eye, despite Schirmer's with anaesthetic of 2 mm. She requested treatment for this and her epiphora improved after one injection of 2.5 units. She chose not to have repeat treatment as her dry eye symptoms worsened.

Discussion

Patients with epiphora with canalicular obstruction, those who are elderly or medically frail and those with previous malignancy involving the lacrimal system are particularly challenging. Surgery in the latter group is often a relative contraindication for fear of facilitating tumour spread into the adjacent nose and sinuses. Pharmacologic treatment of this group is a useful adjunct in the evolving armamentarium for symptomatic improvement. It may be cheaper, safer and less invasive than surgery.

This study adds to the scarce evidence in the literature supporting the value of BoNTA in the non-surgical treatment of patients with lacrimal outflow obstruction.

There are only two case series reporting on the application of BoNTA in non-crocodile tear epiphora. Wojno⁹ has provided the only existing evidence on the value of BoNTA in 27 patients with lacrimal outflow obstruction. Sixty-three per cent of this group mostly or

Table 1 Outlines the demographics and aetiologies of all treated patients

	<i>Patient</i>	<i>Age</i>	<i>Sex</i>	<i>Side</i>	<i>Symptoms</i>	<i>Aetiology</i>	<i>Indication for choosing BoNTA over surgery</i>	<i>Ocular disease/surgery</i>
Punctal occlusion	1	72	F	Left	Epiphora	Upper and lower punctal cautery	Dry eye	Dry eye, blink lagophthalmos
	2	72	F	Right	Epiphora	Upper and lower punctal cautery	Dry eye	Dry eyes, blink lagophthalmos
	3	70	F	Left	Epiphora	Bilateral upper and lower punctal cautery, only left had epiphora	Sjögren's syndrome	Sjögren's syndrome
Canalicular or common canalicular stenosis	4	65	F	Left	Epiphora	Bilateral upper and lower punctal cautery, only left had epiphora	Dry eye	Dry eye
	5	77	F	Right	Epiphora	Upper and lower punctal cautery	Dry eye	Blepharospasm/bilateral orbicucleotomy
	6	89	F	Left	Epiphora	Upper and lower punctal cautery	Dry eye	Blepharospasm/bilateral orbicucleotomy
	7	79	F	Left	Epiphora	Canaliculi sacrifice after medial canthal SCC	Medial canthal SCC	
	8	63	F	Right	Epiphora	Bilateral common canalicular stenosis after collagen intracanalicular plug	Rejected Jones tube	Anophthalmic following childhood infection
	9	79	F	Left	Epiphora	Common canalicular blockage	Unwell with Leukaemia	Old keratitis
	10	45	M	Left	Epiphora	Upper and lower canalicular stenosis after herpetic infection	Rejected Jones tube	
	11	66	F	Right	Epiphora	Upper and lower canalicular stenosis after herpetic infection	Rejected Jones tube	
	12	85	F	Right	Epiphora	Upper and lower canalicular stenosis	Rejected surgery due to back problems	
	13	36	M	Right	Epiphora	Common canalicular stenosis	Disturbed nasal anatomy	Fibrous Dysplasia/previous maxillectomy
	14	57	M	Right	Epiphora	Canalicular blockage after BCC excision	Medial canthal BCC	
	15	59	F	Left	Epiphora	Common canalicular stenosis	Previously failed DCR, rejected Jones tube	Previously failed bilateral DCR and proximal cut down
	16	93	F	Right	Epiphora	Common canalicular stenosis	Previously failed DCR, rejected Jones tube	
	17	88	M	Right	Epiphora	Loss of canaliculi after conjunctival SCC excision	Previously failed DCR, rejected Jones tube	
						Loss of canaliculi after conjunctival SCC excision	Conjunctival SCC	Blink lagophthalmos
						conjunctional SCC excision	Conjunctival SCC	
						Surgery and radiotherapy for nose and sinus melanoma	Melanoma of nose and sinus	Dry eyes secondary to radiotherapy
						NLD obstruction	Old age	
						NLD obstruction	Old age	
						NLD obstruction	Rejected DCR	Recurrence of cicatricial medial ectropion

Abbreviations: BoNTA, botulinum toxin A; BCC, basal cell carcinoma; DCR, dacryocystorhinostomy; F, female; M, male; NLD, nasolacrimal duct; SCC, squamous cell carcinoma.

Table 2 Outlines the Munk scores before and after injections

	Patient	Indoors Munk score before treatment	Indoors Munk score after treatment	Outdoors Munk score before treatment	Outdoors Munk score after treatment	
Punctal occlusion	1	4	3	4	3	
	—	4	3	4	3	
	2	3	0	4	0	
	3	3	0	4	0	
	4	4	3	4	3	
	—	4	2	4	2	
Canalicular/common canalicular stenosis	5	4	1	4	1	
	6	4	4	4	4	
	7	3	(1,1,1) 1	3	2	
	8	4	(2,1,2,2,1) 1.6	4	NA	
	—	4	(2,1,2,2,1) 1.6	4	NA	
	9	3	1	4	1	
	10	4	(3,1,1) 1.6	4	NA	
	11	NA	NA	NA	NA	
	12	3	1	3	1	
	—	2	1	3	1	
	13	3	1	NA	NA	
	14	3	1	—	—	
	NLD stenosis	15	4	0	4	1
		16	NA	—	—	—
—		NA	—	—	—	
17		2	3	3	3	

Abbreviations: NA, not available; NLD, nasolacrimal duct.

completely improved with 2.5 units of BoNTA. This improved to 71% with an additional 2.5 units to those with less than maximal improvement. He did not elaborate on the underlying pathology in these patients. Whittaker *et al*¹⁰ investigated the usefulness of BoNTA in patients with functional epiphora and achieved symptomatic relief in 8 of 11 patients with transconjunctival injections of 2.5–5 units of BoNTA in the palpebral lobe of the lacrimal gland, causing transient ptosis and diplopia in two patients.

Our results are consistent with the existing evidence with 70% of patients achieving >60% improvement in their symptoms with significant improvement in Munk scores and median duration of effectiveness of 10 weeks. The majority of patients in our series who benefited from this treatment were elderly, a mean 10 years older than those in the series by Wojno. Advanced age, frailty and co-existing morbidities often make attending clinic appointments difficult for this group let alone surgical intervention. Therefore BoNTA is a useful alternative in this group for whom little else may be available.

We found BoNTA beneficial in patients with previous malignancy involving the lacrimal apparatus. Five patients (age range 36–77) had canalicular or NLD obstruction following excision of the carcinoma of their eyelid or conjunctiva and melanoma of the nose and sinus. All reported a significant improvement in their symptoms.

That patients in our series who were initially given doses >2.5 units with no complications and subsequently achieved the same improvement with 2.5 unit injections suggests that doses >2.5 units may not produce superior outcomes. Although we did not observe any side effects with the higher dose, symptoms in one patient with NLD obstruction and recurrent cicatricial ectropion deteriorated after 2.5 units. This patient improved after ectropion repair, suggesting that eyelid malposition should be addressed first in patients being considered for this option.

We treated two patients with dry eye syndrome and symptomatic epiphora following punctal cautery. One patient experienced a deterioration of dry eye symptoms and the other reported minimal improvement despite punctal retrieval. This emphasises the importance of counselling patients with severe dry eye against interventions to improve epiphora.

BoNTA has been used safely for decades with no long-term side effects. Demetriades *et al*¹² reported no evidence of histological changes in the lacrimal gland of rabbit following injection of 1.25 and 2.5 units of BoNTA. This is similar to previous reports confirming the absence of orbicularis histological changes following BoNTA injection for blepharospasm.¹³

In conclusion, our results show favourable outcomes for non-surgical BoNTA treatment of lacrimal outflow obstruction in the elderly patients or those for whom

Table 3 Outlines the treatments, grade of surgeons and outcomes of all patients

Patient	Indication for choosing BoNTA over surgery	Number of injections	Dose (frequency)	Grade of surgeon	Subjective improvement	Percentage of improvement	Complications	
Punctal occlusion	1 Dry eye	3	1.25, 2.5(2)	All by fellows	A little better	All 30%	None	
	2 Dry eye	3	1.25, 2.5(2)	All by fellows	A little better	All 30%	None	
	3 Sjögren's syndrome	1	2.5	Fellow	Completely better	100%	Very dry eye	
	4 Dry eye	6	2.5	All by fellows	Completely better	90%, 90%, 95%, 95%, 90%, 95%	Haematoma after last injection	
Canalicular or common canalicular stenosis	4 Dry eye	4	5, 2.5(3)	All by consultant	A lot better but not completely	All about 60%	Diplopia after last injection	
	5 Dry eye	4	5, 2.5(3)	All by consultant	A lot better but not completely	All about 60%	—	
	5 Medial canthal SCC	3	2.5	All by fellows	A lot better but not completely	90%, 80%, 80%	None	
	6 Rejected Jones tube	2	2.5	All by fellows	No better	No better	None	
	7 Unwell with Leukaemia	3	5	First by consultant, all the rest by fellows	A lot better but not completely	90%, 90%, 90%	none	
	8 Rejected Jones tube	7	2.5	All by fellows	A lot better but not completely	First 50%, all rest 80–90%	None	
	8 Rejected Jones tube	7	2.5	All by fellows	A lot better but not completely	First 50%, all rest 80–90%	None	
	9 Rejected surgery due to back problems	10	7.5, 2.5, 5(2), 2.5(6)	Three by consultant, seven by fellows	A lot better but not completely	First 6 treatment 80%, the rest not available	None	
	10 Disturbed nasal anatomy	3	2.5	All by fellows	A lot better but not completely	First 50% and the rest 80%	None	
	11 Medial canthal BCC	2	2.5	All by fellows	A little better	< 50%	None	
	12 Previously failed DCR, rejected Jones tube	2	2.5	All by consultant	A lot better but not completely	Both 75%	None	
	12 Previously failed DCR, rejected Jones tube	2	2.5	All by consultant	A lot better but not completely	Both 75%	None	
	13 Conjunctival SCC	2	2.5	All by fellows	A lot better but not completely	Both 80%	None	
	14 Conjunctival SCC	1	2.5	Consultant	A lot better but not completely	60%	None	
	NLD stenosis	15 Melanoma of nose and sinus	5	2.5	All by fellows	Completely better	All 90–98%	None
		16 Old age	1	2.5	Consultant	A little better	30%	None
		16 Old age	1	2.5	Consultant	A little better	30%	None
17 Rejected DCR		1	2.5	Fellow	Worse	Worse	Epiphora got worse	

Abbreviations: BoNTA, botulinum toxin A; DCR, dacryocystorhinostomy; NLD, Nasolacrimal duct; SCC, squamous cell carcinoma.

surgery may be contraindicated. Epiphora completely resolved in a fifth, improved by up to 60–90% in a half and only ‘a little better’ in a further fifth. This information may be of value for informed consent and for commissioning organisations considering funding this therapeutic option.

Summary

What was known before

- Surgery for lacrimal outflow obstruction may not be the best option in all patients especially in the elderly and medically frail patients and after excision of lacrimal apparatus for treatment of malignant lesions affecting the neighbouring anatomical structures.
- Botulinum toxin has been successfully used to treat gustatory hyperlacrimation owing to an aberrant regeneration in proximal facial nerve injuries.
- There is scarce evidence in the literature showing the usefulness of BoNTA in patients with functional epiphora and lacrimal outflow obstruction.

What this study adds

- We report favourable outcomes for non-surgical BoNTA treatment of lacrimal outflow obstruction.
- Epiphora completely resolved in a fifth, improved by up to 60–90% in a half and only ‘a little better’ in a further fifth.

Conflict of interest

The authors declare no conflict of interest.

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