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REPORT

Lifting effect of onabotulinumtoxinA in patients treated for glabellar and crow's feet rhytids

Sarah Norman

Aesthetic Practitioner, Private Practice, Cheshire, UK

ABSTRACT

OnabotulinumtoxinA injection can enhance the appearance of the eyes. This study evaluated the lifting effect of onabotulinumtoxinA treatment of the eye area. A retrospective, single-center audit of patients treated for glabellar and crow's feet rhytids was undertaken. Standardized photographs taken before and 2–4 weeks after treatment were assessed. Computer-based measurements were made of the height of the visible superior tarsal plate (STP) and brow (measured from upper eyelid lash edge to eyebrow base) at rest and maximum frown. One hundred patients were included (96 females; mean age: 46.2 ± 8.8 years). Mean onabotulinumtoxinA doses were 14.95 ± 0.61 units (glabella) and 17.83 ± 2.74 units (crow's feet). There were significant post-treatment increases in mean STP height at rest (left side, 0.76 ± 0.99 mm, $p = .02$; right side, 0.79 ± 0.94 mm, $p = .01$) and maximum frown (left, 2.25 ± 1.52 mm, $p < .0001$; right, 1.87 ± 1.34 mm, $p < .0001$), and mean brow height at rest (left side, 1.54 ± 1.49 mm, $p = .0006$; right side, 1.47 ± 1.84 mm, $p = .0009$) and maximum frown (left, 4.37 ± 2.29 mm, $p < .0001$; right, 4.16 ± 1.88 mm, $p < .0001$). OnabotulinumtoxinA injection is effective for elevating brow position and increasing STP show.

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Superior tarsal plate; onabotulinumtoxinA; glabella; crow's feet; rhytids

Introduction

The eyes are a core element of human facial recognition and a key focus of interaction (1). They also play a significant part in the central facial triangle – composed of the eyes, nose, lips and cheek bones – that typically defines esthetic appeal (2). Indeed, the eyes may be the single most important aspect of the face in characterizing overall attractiveness (3). In a study of the relationship between facial features and the first impressions of viewers, four of the five traits that correlated most strongly with youthful attractiveness related to the eyes (4).

In general, it appears that larger eye features correlate with greater esthetic appeal (4,5). However, age-related changes can result in the eyes appearing smaller, and thus potentially less attractive. In particular, the upper third of the face starts to sag, the eyelids become loose, and the eyebrows descend (6). Causative factors may include loss of skin elasticity, decreased subcutaneous tissue, and reductions in bony volume. Furthermore, overactivity (hypertonicity and hyperkineticism) of the glabella complex and orbicularis oculi muscles – which have a depressor action – contribute to descent of the eyebrows (7), and thus a reduction in the visible height of the superior tarsal plate (STP). These depressor muscles tend to become stronger than the elevating frontalis muscle, resulting in a sad and tired appearance (8). All of these changes contribute to a worsening appearance of the eyes over time, and inversion of the youthful facial triangle.

Many techniques, both surgical and non-surgical, have been developed for the treatment of eyebrow descent and dermatochalasis. One non-surgical possibility is to use botulinum neurotoxin type A (BoNTA) to lift the eyelids and eyebrows. Several small studies have reported a lifting effect on the eyebrows following injection of BoNTA into the glabella and/or brow area (9–15). On the flipside, a study of BoNTA injection of the glabella, with or without treatment of the forehead and crow's feet, found little change in eyebrow position (16).

However, to the best of our knowledge, there are no reported studies demonstrating an increase in the height of both the brow and visible STP following BoNTA injection into the glabella and crow's feet. Anecdotally, in routine clinical practice, we have observed that the use of BoNTA in these two areas frequently results in a lifting effect on the brow and an increase in visible STP height. The present analysis was designed to evaluate whether there was a measurable lifting effect when a BoNTA product, onabotulinumtoxinA, was used to treat rhytids in the glabella and crow's feet.

Materials and methods

Study design and participants

This was a retrospective audit of randomly selected, eligible adult patients treated for glabellar and crow's feet rhytids using onabotulinumtoxinA (Botox®, Allergan, Dublin, Ireland) at a single center between August 2014 and December 2018. The study was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent to undergo treatment.

Patients were excluded from the study if they: were also treated with BoNTA in other areas of the upper face (e.g.

CONTACT Sarah Norman sarah@drsarahnorman.co.uk Aesthetic Practitioner, Private Practice, BrightNewMe, 28 High Street, Altrincham, Cheshire WA14 1QP, United Kingdom.

forehead); received dermal fillers or other treatments in the upper face at the same time or during the follow-up period; or had inadequate photographic records (e.g. inconsistent or incomparable facial expressions, blinking, or hair covering their brows). Only one treatment episode per patient was included. For those with more than one round of treatment, data were used from the earliest treatment episode that met the eligibility criteria.

Procedures and assessments

All onabotulinumtoxinA treatments were administered using a dilution of 100 units into 1 mL of 0.9% bacteriostatic saline. Glabellar injections were intramuscular based on the standard injection pattern: two injections in each corrugator muscle and one in the procerus muscle. Crow's feet sites were injected intradermally using either 3 or 4 sites per side.

Data were retrospectively collated from practice clinical records, including baseline demographic information and patient photographs in the resting and frowning positions taken immediately before treatment and at a follow-up visit 2–4 weeks post-treatment. All photographs were taken by the principal investigator using the same camera and tripod and with patients sitting on the same chair.

Measurements of the visible STP (upper eyelid) height and of brow height (upper lash margin to the base of the eyebrow) were made by assessment of photographs on a computer (Figure 1). For every image used, ear height relative to the eyes and nose was checked to ensure that the head position was consistent (rather than the head tilting up or down). The scale of each photograph was adjusted to life size on the computer screen; 'life size' was benchmarked using the accepted standard human interpupillary distance of 60 mm measured between mid-pupil points (17). For each patient, four photographs were assessed: before and 2–4 weeks after treatment, both at rest and at maximum frown. For each of the four photographs, four measurements were made based on (a) the vertical height of the visible STP, and (b) the distance from the upper lash margin to the base of the eyebrow, for the left and right eye. Thus, a total of 16 measurements were made for each patient. In all instances, measurements were made on a vertical axis passing through the mid-point of the pupil. If the rim of the upper eyelid was visible at the edge of the tarsal plate below the lash line, this was not included in the measurement of the STP.

Images removed for patient privacy

Figure 1. Measurement of STP and brow heights. (**A**) Photographs were first adjusted to 'life size' on a computer screen, based on an interpupillary distance of 60 mm measured between the mid-pupil points. (**B**) All subsequent measurements were then made along the vertical mid-pupillary line. (**C**) The visible STP height was measured along the mid-pupillary line. (**D**) Brow height was measured as the distance from the upper lash margin to the base of the eyebrow along the mid-pupillary line. STP, superior tarsal plate.

Statistical analysis

Data were analyzed using SPSS software version 21 (IBM Inc., Chicago, IL, USA). Continuous data are presented as mean, standard deviation and range, and categorical data are given as frequency and percentage. Student's t test was used to compare continuous height variables between groups. A p value <.05 was considered to be statistically significant.

Results

A total of 100 patients were included in the analysis, of whom 96 were female and 4 were male. Ninety-five were Caucasian. The mean age was 46.2 ± 8.8 years (range: 27 to 71 years). All patients were treated with onabotulinumtoxinA in the glabella and crow's feet, based on mean doses of 14.95 ± 0.61 units (range: 12 to 17 units) and 17.83 ± 2.74 units (range: 12 to 30 units), respectively.

There were significant increases in mean visible STP height on both the left and right side following treatment, whether assessed at rest or at maximum frown (Table 1; Figures 2–4). In the resting position, mean STP height increased from 3.41 ± 2.27 mm pre-treatment to 4.17 ± 2.42 mm post-treatment on the left side, and from 2.95 ± 2.04 mm to 3.74 ± 2.25 mm on the right side. Hence, the mean change from baseline was 0.76 ± 0.99 mm (p = .02) on the left and 0.79 ± 0.94 mm (p = .01) on the right. At maximum frown, mean STP height increased from 1.48 ± 1.92 mm to 3.73 ± 2.35 mm on the left side and from 1.17 ± 1.44 mm to

Table 1. Change in visible STP height with onabotulinumtoxinA injection in the glabella and crow's feet.

	At rest				At maximum frown			
	Before	After	Change	p	Before	After	Change	p
Left-side STP height (mm)	3.41 ± 2.27 (0 to 11)	4.17 ± 2.42 (0 to 11)	0.76 ± 0.99 (–2 to 4)	0.02	1.48 ± 1.92 (0 to 7)	3.73 ± 2.35 (0 to 11)	2.25 ± 1.52 (–1 to 7)	<0.0001
Right-side STP height (mm)	2.95 ± 2.04 (0 to 8)	3.74 ± 2.25 (0 to 9)	0.79 ± 0.94 (–2 to 4)	0.01	1.17 ± 1.44 (0 to 6)	3.04 ± 2.20 (0 to 10)	1.87 ± 1.34 (0 to 6)	<0.0001

N = 100. Data are mean ± standard deviation (range). Student's t test was used to compare between groups.
STP, superior tarsal plate.

Images removed for patient privacy

Figure 2. Lifting effect on the upper eyelid and eyebrow of combined onabotulinumtoxinA treatment for rhytids. A 40-year-old male before (left half – at rest and frowning) and 14 days after treatment (right half – at rest and frowning). He was injected with onabotulinumtoxinA in the glabella (15 units) and crow's feet (18 units). After treatment, changes from baseline were evident in visible STP height at rest (left eye, increased from 3 to 4 mm; right eye, no change, remained 5 mm) and while frowning (left eye, increased from 1 to 4 mm; right eye, increased from 2 to 3 mm). Changes from baseline were also evident in brow height at rest (left eye, increased from 10 to 11 mm; right eye, no change, remained 10 mm) and while frowning (left eye, increased from 7 to 10 mm; right eye, increased from 5 to 8 mm). STP, superior tarsal plate.

Images removed for patient privacy

Figure 3. Lifting effect on the upper eyelid and eyebrow of combined onabotulinumtoxinA treatment for rhytids. A 55-year-old female before (left half – at rest and frowning) and 14 days after treatment (right half – at rest and frowning). She was injected with onabotulinumtoxinA in the glabella (15 units) and crow's feet (16 units). After treatment, changes from baseline were evident in visible STP height at rest (left eye, increased from 4 to 5 mm; right eye, increased from 2 to 3 mm) and while frowning (left eye, increased from 0 to 3 mm; right eye, increased from 0 to 2 mm). Changes from baseline were also evident in brow height at rest (left eye, increased from 16 to 17 mm; right eye, no change, remained 13 mm) and while frowning (left eye, increased from 10 to 15 mm; right eye, increased from 8 to 14 mm). STP, superior tarsal plate.

3.04 ± 2.20 mm on the right side. The mean change from baseline was therefore 2.25 ± 1.52 mm ($p < .0001$) and 1.87 ± 1.34 mm ($p < .0001$), respectively.

Similarly, there were significant increases in mean brow height (from the lash edge of the upper eyelid to the base of the eyebrow) at rest and at maximum frown (Table 2). In the resting position, mean brow height increased from 11.63 ± 3.06 mm pre-treatment to 13.17 ± 3.21 mm post-treatment on the left side, and from 11.60 ± 2.79 mm to 13.07 ± 3.36 mm on the right side. The mean change from baseline was 1.54 ± 1.49 mm ($p = .0006$) on the left and 1.47 ± 1.84 mm ($p = .0009$) on the right. At maximum frown, mean brow height increased from 8.50 ± 3.25 mm to 12.87 ± 3.26 mm on the left side and from 8.27 ± 3.18 mm to 12.43 ± 3.28 mm on the right side. The mean change from baseline was 4.37 ± 2.29 mm ($p < .0001$) and 4.16 ± 1.88 mm ($p < .0001$), respectively.

Overall response rates were high, with between 59 and 98 patients experiencing an increase in STP/brow height for each measurement (Table 3). Few patients experienced decreases in STP/brow height (between 0 and 6 patients for each measurement).

The intra-patient impact of treatment was also compared between the left and right eyes. There was no significant difference in the mean change in STP height between the two eyes at rest ($p = .83$) or at maximum frown ($p = .06$), or in the mean change in brow height between the two eyes at rest ($p = .77$) or at maximum frown ($p = .48$).

Discussion

This study demonstrated the lifting effect on the upper eyelid and eyebrow of combined BoNTA treatment for rhytids of the glabella and crow's feet. The observed effects were particularly pronounced at maximum frown; for example, mean visible STP height was more than doubled on both the right and left side after BoNTA injection.

Although surgical techniques are available for brow lifting (18), these are inevitably associated with increased complications, and hence minimally invasive alternatives are essential. A few previous small-scale studies have demonstrated the brow-lifting effects of BoNTA treatment (9–15). For example, in the largest of these studies, 79 women were treated in the glabella using various doses of onabotulinumtoxinA, with

Images removed for patient privacy

Figure 4. Lifting effect on the upper eyelid and eyebrow of combined onabotulinumtoxinA treatment for rhytids. A 56-year-old female before (left half – at rest and frowning) and 21 days after treatment (right half – at rest and frowning). She was injected with onabotulinumtoxinA in the glabella (15 units) and crow's feet (18 units). After treatment, changes from baseline were evident in visible STP height at rest (left eye, increased from 5 to 7 mm; right eye, increased from 4 to 5 mm) and while frowning (left eye, increased from 5 to 9 mm; right eye, increased from 4 to 7 mm). Changes from baseline were also evident in brow height at rest (left eye, increased from 13 to 16 mm; right eye, increased from 15 to 16 mm) and while frowning (left eye, increased from 10 to 18 mm; right eye, increased from 11 to 19 mm). STP, superior tarsal plate.

Table 2. Change in brow height from the upper lash margin with onabotulinumtoxinA injection in the glabella and crow's feet.

	At rest				At maximum frown			
	Before	After	Change	p	Before	After	Change	p
Left-side brow height (mm)	11.63 ± 3.06 (5 to 21)	13.17 ± 3.21 (5 to 22)	1.54 ± 1.49 (–2 to 6)	0.0006	8.50 ± 3.25 (3 to 20)	12.87 ± 3.26 (6 to 24)	4.37 ± 2.29 (0 to 9)	<0.0001
Right-side brow height (mm)	11.60 ± 2.79 (5 to 19)	13.07 ± 3.36 (1 to 21)	1.47 ± 1.84 (–8 to 7)	0.0009	8.27 ± 3.18 (1 to 19)	12.43 ± 3.28 (5 to 22)	4.16 ± 1.88 (0 to 9)	<0.0001

N = 100. Data are mean ± standard deviation (range). Student's t test was used to compare between groups.

resulting increases in eyebrow height (assessed laterally, centrally and medially) at doses of 20, 30 and 40 units (13).

Nonetheless, the present analysis expands on previous findings in at least three important ways. First, a total of 100 patients were included, which is more than any of the earlier studies (some of which analyzed only a handful of individuals). Second, earlier studies were based primarily on assessment of eyebrow height and none measured visible STP height; thus, this appears to be the first demonstration of increased eyelid show with BoNTA. Third, the present study is the first specifically to assess the impact of combination treatment of the glabella and crow's feet, both of which are licensed indications for onabotulinumtoxinA (19). There is a clear mechanistic rationale for expecting an additive lifting effect. The corrugator and procerus muscles in the glabella act as medial brow depressors, and orbicularis oculi performs a similar role laterally (9,13,15,20), and weakening these depressors with BoNTA thus facilitates the brow-elevating effects of the frontalis muscle.

In the present study, combined treatment of both the glabella and crow's feet was associated with high patient response rates – particularly in brow height, which was increased in around three-quarters of individuals at rest and in almost all cases at maximum frown. Most previous studies did not report responder data, but Frankel & Kamer

Table 3. Patient response after onabotulinumtoxinA injection in the glabella and crow's feet.

	At rest			At maximum frown		
	Increased	No change	Decreased	Increased	No change	Decreased
Left-side STP height	59	35	6	89	10	1
Right-side STP height	60	36	4	86	14	0
Left-side brow height	77	18	5	96	4	0
Right-side brow height	71	25	4	98	2	0

N = 100. Data indicate the number of patients with measurable increases or decreases in STP and brow heights after treatment.
STP, superior tarsal plate.

observed elevations in central brow position in 48% of patients following injection of 20 units of BoNTA in the glabella (9). Thus, our response rate appears to be favorable.

These effects were achieved despite the use of relatively low mean doses of onabotulinumtoxinA – around 15 units in the glabella and 18 units in the crow's feet – which were below the standard recommended doses of 20 and 24 units, respectively. This was because the audit used data from each patient's first treatment visit, and my normal practice is to start with a low dose for a subtle effect and then to increase the dose as required at repeat visits. In a previous multi-dose study, injection of 10 units of BoNTA into the glabella led to mean reductions rather than elevations in brow height, and increases were only observed at doses ≥ 20 units (13). Thus, it is possible that greater elevations in visible STP and brow height would have been observed had I used the standard licensed doses of onabotulinumtoxinA, although this remains to be demonstrated.

It should be noted that a small number of patients experienced reductions rather than increases in visible STP and/or brow height after onabotulinumtoxinA injection. Negative changes in brow position following BoNTA treatment have also been reported elsewhere in a minority of patients (9,13). As well as BoNTA dose, this may be related to specific patient characteristics. In the present study, several older patients had substantial laxity and this adversely affected results, such that they experienced decreased lift.

The limitations of the present analysis should be acknowledged. First, it was a retrospective audit of patient photographs from a single center with no control group. A prospective, multicenter study comparing the impact of BoNTA versus an appropriate comparator would of course be valuable. Second, no assessments were made that might correlate increases in STP and brow height with esthetic outcomes such as perception of age or attractiveness. To the best of my knowledge, no such work has yet been published, although anecdotally patients reported increased satisfaction. Third, some patients appeared to experience greater lift at either end of the STP, and additional medial and lateral measurements might therefore have been valuable. Fourth, although photographs were pre-assessed to ensure that the head was not in a tilted position, minor differences could have gone unnoticed, resulting in small variations in measured distances; the use of chin and/or forehead rests would have helped to mitigate this effect. Finally, almost all patients were Caucasian and it may not be possible to extrapolate the brow-lifting impact of BoNTA treatment to patients from different ethnic groups.

Conclusions

Relatively low doses of onabotulinumtoxinA injected into the glabella and crow's feet for the treatment of rhytids led to significant improvements in visible STP height and in the distance from the lash edge of the upper eyelid to the base of the eyebrow. Thus, onabotulinumtoxinA appears to be an effective, safe and minimally invasive method for enhancing the eyes – a core aspect of attractiveness – and addressing a common problem of aging.

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Disclosure statement

The author(s) reports no conflicts of interest.

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