Original Article

Periorbital botulinum toxin injection and lacrimal gland position

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ABSTRACT

Background: Botulinum toxin injection is the most widely performed nonsurgical procedure for upper facial rejuvenation and has an established safety profile. Because the lacrimal gland is anatomically supported by the surrounding periocular soft tissues, temporary muscle relaxation following periorbital botulinum toxin injection may alter the gland's configuration or spatial relationship within the lacrimal fossa. This prospective pilot study evaluated changes in ultrasonographically measured lacrimal gland dimensions following cosmetic periorbital botulinum toxin injection.

Methods: This prospective pilot study enrolled eligible adults undergoing cosmetic periorbital botulinum toxin type A injection at a tertiary ophthalmic center between January 2022 and September 2024. Participants underwent standardized ophthalmic and periorbital examinations before treatment. Lacrimal gland ultrasonography was performed at baseline and two weeks after injection by a blinded radiologist in both the supine and sitting positions. Maximum axial and anteroposterior dimensions of both lacrimal glands were measured bilaterally. These measurements represented ultrasonographic gland dimensions and did not directly quantify three-dimensional displacement or anatomical position. Changes from baseline, group comparisons, and associations with demographic and clinical characteristics were evaluated.

Results: Nineteen participants were included (10 [52.6%] women and 9 [47.4%] men; mean [standard deviation] age, 45.3 [9.0] years). Compared with baseline, lacrimal gland dimensions generally increased after periorbital botulinum toxin injection, except for a small, non-significant decrease in the axial diameter of the right lacrimal gland in the supine position ($P > 0.05$). Statistically significant increases in the axial and anteroposterior dimensions of both lacrimal glands were observed in the sitting position (all $P < 0.05$), with no statistically significant changes detected in the supine position (all $P > 0.05$). Changes in ultrasound parameters were not significantly associated with age, sex, previous upper-eyelid blepharoplasty, or number of crow's feet injection points (all $P \geq 0.05$).

Conclusions: This prospective pilot study showed that cosmetic periorbital botulinum toxin injection was associated with changes in ultrasonographically measured lacrimal gland dimensions, particularly in the sitting position. Although gland position was not directly quantified, these dimensional changes may indirectly reflect alterations in gland configuration or its spatial relationship with the surrounding periocular structures following temporary muscular relaxation. Larger prospective studies with longer follow-up, comprehensive functional assessments, and imaging methods that directly assess anatomical displacement are warranted to verify these preliminary findings and clarify their clinical significance.

KEYWORDS

clostridium botulinum toxins, botulinum toxin, skin wrinkling, lacrimal gland, medical sonography, ultrasonic imaging, supine positions, sitting positions, age factor

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INTRODUCTION

Botulinum toxin injection is the most widely performed nonsurgical procedure for upper facial rejuvenation. Since its introduction for the treatment of glabellar rhytids in the early 1990s, the cosmetic use of botulinum toxin has expanded substantially and has become a cornerstone of nonsurgical upper facial rejuvenation [1, 2]. Botulinum toxin has an established safety profile and is generally well tolerated, with most adverse effects being mild and self-limiting [1–3]. Nevertheless, the occurrence of complications is influenced largely by injection technique, anatomical knowledge, injection depth, and toxin diffusion. Therefore, a thorough understanding of upper facial anatomy and adherence to established safety zones are essential to minimize treatment-related complications [3, 4].

The lacrimal gland is located in the superolateral orbit within the shallow lacrimal fossa of the frontal bone [5, 6]. It measures approximately 20 × 12 × 5 mm and is divided into orbital and palpebral lobes by the lateral horn of the levator aponeurosis. The larger orbital lobe lies posterior to the orbital septum and preaponeurotic fat and anterior to the levator aponeurosis, the smaller palpebral lobe is situated inferior to the levator aponeurosis [5–7].

High-resolution ultrasonography has emerged as a practical, non-invasive imaging modality for evaluating the lacrimal gland because of its superficial anatomical location. Modern high-frequency linear transducers enable clear visualization of gland morphology and margins, allowing reliable, repeatable assessment without ionizing radiation [8–10]. Previous studies have demonstrated good reproducibility of lacrimal gland ultrasonography and its utility in detecting structural alterations, supporting its use as an accessible imaging technique for serial evaluation of anatomical changes in both clinical practice and research settings [8–10].

We hypothesized that temporary relaxation of the periocular musculature following botulinum toxin injection might alter the configuration of the lacrimal gland or its spatial relationship within the lacrimal fossa, potentially resulting in detectable changes in its ultrasonographic dimensions. Therefore, this prospective pilot study investigated changes in the axial and anteroposterior dimensions of the lacrimal gland following cosmetic periorbital botulinum toxin injection.

METHODS

This prospective pilot feasibility study investigated changes in ultrasonographically measured lacrimal gland dimensions following periorbital botulinum toxin injection among eligible participants consecutively recruited between January 2022 and September 2024 at the Department of Oculofacial Plastic and Reconstructive Surgery, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran. As a pilot study, the sample size was determined by feasibility rather than a formal sample size calculation. The study was approved by the local Ethics Committee of Farabi Eye Hospital, Tehran University of Medical Sciences, and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment, including consent for the publication of anonymized clinical information.

Eligible participants were adults aged 20–70 years with a normal baseline ophthalmic and periorbital examination, including best-corrected visual acuity of 20/20 and intraocular pressure within the normal range (12–20 mmHg), and no history of periorbital surgery, lacrimal gland surgery, or periorbital trauma, except for previous upper-eyelid blepharoplasty. Exclusion criteria were a history of periorbital surgery other than upper-eyelid blepharoplasty, previous periorbital trauma, thyroid-associated orbitopathy, clinically apparent lacrimal gland enlargement or prolapse, and orbital pathology identified on computed tomography (CT).

All eligible participants underwent a standardized comprehensive ophthalmic and periorbital examination performed by an oculoplastic surgeon (MJT) before the procedure. Corrected distance visual acuity was assessed using a Snellen chart (Auto Chart Projector CP-670; Nidek Co., Ltd., Gamagori, Japan). Anterior-segment and dilated posterior-segment examinations were performed using a slit-lamp biomicroscope (Photo-Slit Lamp BX 900; Haag-Streit, Koeniz, Switzerland), and intraocular pressure was measured using a Goldmann applanation tonometer (Applanation Tonometer 900; Haag-Streit, Koeniz, Switzerland). The periorbital examination included external ocular and periocular inspection, lacrimal gland palpation, upper-eyelid examination after eyelid eversion, and the supine test to assess for lacrimal gland enlargement or prolapse. During the supine test [11], participants were examined in the supine position while looking downward and the eyebrow was gently elevated to eliminate eyelid dermatochalasis; any protrusion in the lateral upper eyelid was considered indicative of lacrimal gland prolapse. All baseline examination findings were normal.

Standardized facial photographs were obtained using a Nikon D5200 digital camera (Nikon Corporation, Tokyo, Japan). Orbital CT was performed using a SOMATOM Definition AS+ scanner (Siemens Healthineers, Forchheim, Germany) to rule out orbital pathology before study enrollment.

Following routine skin disinfection with an alcohol pad, the intended injection sites were marked with a sterile skin marker. Botulinum toxin type A (Dysport; Ipsen Ltd., Slough, Berkshire, UK) was administered by a single oculoplastic surgeon (MJT) to the frontalis, glabellar (corrugator supercilii, procerus, and depressor supercilii), and orbicularis oculi muscles, including the lateral crow's feet region, where one to three injection points were administered, and the inferior orbicularis region (jelly rolls). The injection pattern was individualized according to each participant's facial anatomy. During frontalis injections, the inferior 1–2 cm of the muscle above the orbital rim was avoided to reduce the risk of eyebrow ptosis.

For crow's feet treatment, injection points were maintained approximately 1 cm lateral to the orbital rim to minimize the risk of diplopia.

Participants were re-evaluated two weeks after the initial treatment, corresponding to the expected time of maximal clinical effect of botulinum toxin type A [12]. Lacrimal gland ultrasonography was performed before any additional touch-up injections were administered. Residual facial rhytids that had not completely resolved were treated with additional botulinum toxin injections when clinically indicated. Standardized facial photographs were obtained again following the touch-up treatment for documentation.

Lacrimal gland ultrasonography was performed at baseline and two weeks after the initial botulinum toxin injection, corresponding to the expected time of maximal clinical effect [12]. A qualified radiologist (SSK.), blinded to all clinical information, performed all examinations using an HD15 ultrasound system (Philips Ultrasound, Bothell, WA, USA). Participants underwent ultrasonography in both the supine and sitting positions with their eyelids gently closed. A high-frequency linear transducer (7–10 MHz) was placed obliquely over the lacrimal fossa, parallel to the anterior orbital rim, using the globe as an acoustic window to visualize the lacrimal gland [8–10]. The participants' heads were maintained in a neutral position aligned with the body throughout the examination. A 5-cm transducer was applied with minimal pressure to avoid skin indentation, and sufficient coupling gel was used to eliminate air interference. The frontal bony ridge of the eyebrow served as a stabilizing point for the probe, minimizing operator variability in probe pressure and positioning. The scanning site was identified at the intersection of virtual lines passing through the superior and supratemporal orbital rims. The probe was positioned horizontally to obtain axial measurements and vertically to obtain anteroposterior measurements, and the maximum dimensions of both lacrimal glands were measured bilaterally in millimeters. For all analyses, changes in ultrasound parameters were calculated as the post-injection value minus the pre-injection value (post-pre). Positive values indicated an increase, whereas negative values indicated a decrease in lacrimal gland dimensions following botulinum toxin injection

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, continuous variables were summarized as mean (standard deviation [SD]) and median (range), as appropriate. Normality of continuous variables was assessed using the Kolmogorov–Smirnov test and visual inspection of Q–Q plots. Changes from baseline were evaluated using the Wilcoxon signed-rank test. In addition, 95% confidence intervals (CIs) were calculated for the mean paired differences. Because the *P*-values and CIs were derived using different statistical approaches, minor discrepancies between statistical significance and CI interpretation may occur. Associations between changes in ultrasound parameters and a history of upper-eyelid blepharoplasty were assessed using the Mann–Whitney U test. Associations between changes in ultrasound parameters and both age and the number of crow's feet injection points were assessed using Spearman's rank correlation coefficient. Differences in changes in ultrasound parameters between men and women were assessed using the Mann–Whitney U test. A two-sided P-value < 0.05 was considered statistically significant.

RESULTS

Nineteen participants—(10 women [52.6%] and 9 men [47.4%]) with a mean (SD) age of 45.3 (9.0) years—were included in the study. Mean (SD) age was 44.8 (10.7) years (range 25–66 years) for women and 45.9 (10.3) years (range 24–65 years) for men. Two men (22.2%) and two women (20.0%) had previously undergone bilateral upper-eyelid blepharoplasty. The number of crow's feet injection points and other demographic characteristics of the study participants are summarized in Table 1.

Table 2 summarizes the ultrasound measurements of the maximum axial and anteroposterior diameters of the lacrimal glands obtained in the supine and sitting positions before and after periorbital botulinum toxin injection. Compared with baseline, post-injection lacrimal gland dimensions generally increased, except for the axial diameter of the right lacrimal gland in the supine position, which showed a small, non-significant decrease ($P > 0.05$). Statistically significant increases were observed in both the axial and anteroposterior diameters of the right and left lacrimal glands in the sitting position (all $P < 0.05$), with no significant changes detected in the supine position (all $P > 0.05$). In the sitting position, the mean (SD) change in the right lacrimal gland was 0.6 (2.2) mm (95% CI, −0.5 to 1.6; $P < 0.05$) for the axial diameter and 1.2 (3.2) mm (95% CI, −0.4 to 2.7; $P < 0.05$) for the anteroposterior diameter. Corresponding changes in the left lacrimal gland were 0.5 (1.0) mm (95% CI, 0.1 to 1.1; $P < 0.05$) and 1.7 (2.4) mm (95% CI, 0.5 to 2.9; $P < 0.05$), respectively (Table 2).

Table 3 summarizes the associations between changes in ultrasound parameters and a history of upper-eyelid blepharoplasty, as well as the number of crow's feet injection points. No statistically significant associations were observed between changes in ultrasound parameters and either a history of upper-eyelid blepharoplasty (all $P > 0.05$) or number of crow's feet injection points (all $P > 0.05$).

Table 4 summarizes the associations between age and changes in ultrasound parameters, as well as comparisons according to sex. No statistically significant associations were observed between age and changes in ultrasound parameters (all $P > 0.05$), and no statistically significant differences in changes in ultrasound parameters were found between men and women (all $P \geq 0.05$) (Table 4).

Table 1. Demographic and treatment characteristics of the study participants

Variable	Subgroup	Value	
Age (y), Mean ± SD	Male	45.9 ± 10.3	
	Female	44.8 ± 10.7	
Sex, n (%)	Male	9 (47.4)	
	Female	10 (52.6)	
Blepharoplasty, n (%)	Male	2/9 (22.2)	
	Female	2/10 (20.0)	
Number of crow's feet injection, n (%)	Male	1	0/9 (0.0)
		2	4/9 (44.4)
		3	5/9 (55.6)
	Female	1	2/10 (20.0)
		2	4/10 (40.0)
		3	4/10 (40.0)

Abbreviations: y, years; SD, standard deviation; n, number of participants; %, percentage.

Table 2. Changes in the maximum axial and anteroposterior diameters of the lacrimal glands measured by ultrasonography in the supine and sitting positions before and after periorbital botulinum toxin injection.

Parameter	Pre Injection	Post Injection	Change	95 % CI	*P*-value
Rt Sup AX (mm), Mean ± SD, Median (Range)	5.0 ± 1.2, 4.9 (3.5 to 8.6)	4.7 ± 0.6, 4.8 (3.8 to 6.1)	-0.3 ± 1.2, -0.2 (-2.9 to 2.5)	-0.9–0.3	0.150
Rt Sup AP (mm), Mean ± SD, Median (Range)	10.3 ± 2.9, 10.0 (6.4 to 14.9)	11.3 ± 2.5, 11.0 (7.5 to 16.5)	1.0 ± 3.7, 0.3 (-7.2 to 8.4)	-0.8–2.8	0.240
Rt Sit AX (mm), Mean ± SD, Median (Range)	4.9 ± 1.5, 4.6 (2.5 to 8.8)	5.4 ± 1.4, 5.1 (3.9 to 9.8)	0.6 ± 2.2, 0.0 (-1.9 to 7.3)	-0.5–1.6	**0.030**
Rt Sit AP (mm), Mean ± SD, Median (Range)	11.5 ± 2.7, 11.5 (7.2 to 15.5)	12.7 ± 2.7, 10.4 (7.4 to 17.1)	1.2 ± 3.2, 0.0 (-5 to 9.3)	-0.4–2.7	**0.020**
Lt Sup AX (mm), Mean ± SD, Median (Range)	4.7 ± 1.2, 4.3 (3.1 to 7.9)	5.4 ± 2.6, 4.9 (3.2 to 15.4)	0.7 ± 2.6, 0.2 (-1.3 to 11.1)	-0.5–2.0	0.250
Lt Sup AP (mm), Mean ± SD, Median (Range)	10.3 ± 2.4, 10.3 (6.5 to 16.5)	11.4 ± 2.7, 10.9 (6.3 to 17.2)	1.0 ± 3.3, 0.6 (-6.1 to 7.5)	-0.6–2.7	0.180
Lt Sit AX (mm), Mean ± SD, Median (Range)	4.5 ± 0.9, 4.4 (3.4 to 7.5)	5.1 ± 0.9, 5.1 (3.5 to 6.9)	0.5 ± 1.0, 0.5 (-1.9 to 2)	0.1–1.1	**0.030**
Lt Sit AP (mm), Mean ± SD, Median (Range)	10.5 ± 2.7, 9.7 (6.8 to 16.6)	12.2 ± 2.9, 12 (6.9 to 16.6)	1.7 ± 2.4, 1.0 (-1.7 to 6.4)	0.5–2.9	**0.010**

Abbreviations: CI, confidence interval; Rt, right; Sup, supine; AX, axial, mm, millimeters; SD, standard deviation; AP, anteroposterior; Lt, left; Sit, sitting. Note: *P*-values < 0.05 are shown in bold.

Table 3. Associations between changes in maximum axial and anteroposterior lacrimal gland diameters and a history of upper-eyelid blepharoplasty or number of crow's feet injection points.

Parameter	History of blepharoplasty		*P*	Number of crow's feet injection points			Spearman's ϱ	*P*
	No	Yes		1	2	3		
Change Rt Sup AX (mm), Mean ± SD, Median (Range)	-0.3 ± 1.3, -0.2 (-2.9 to 2.5)	-0.4 ± 0.6, -0.4 (-1 to 0.2)	>0.99	-0.7 ± 3.0, -0.7 (-2.9 to 1.4)	-0.7 ± 0.6, -0.9 (-1.4 to 0.3)	0.1 ± 1.1, -0.1 (-1.6 to 2.5)	0.30	0.210
Change Rt Sup AP (mm), Mean ± SD, Median (Range)	1.3 ± 4.0, 0.4 (-7.2 to 8.4)	0.0 ± 2.3, 0.0 (-2.8 to 2.8)	0.420	-0.7 ± 0.9, -0.7 (-1.4 to -0.1)	0.9 ± 2.4, 0.3 (-2.8 to 5.3)	1.5 ± 4.9, 1.6 (-7.2 to 8.4)	-0.20	0.440
Change Rt Sit AX (mm), Mean ± SD, Median (Range)	0.5 ± 2.5, 0.0 (-1.9 to 7.3)	0.8 ± 0.6, 0.9 (0 to 1.5)	0.340	0.9 ± 3.9, 0.9 (-1.8 to 3.7)	0.3 ± 1.5, 0.4 (-1.9 to 2.7)	0.7 ± 2.7, 0.0 (-1.9 to 7.3)	0.00	0.940
Change Rt Sit AP (mm), Mean ± SD, Median (Range)	1.3 ± 3.5, 0.0 (-5 to 9.3)	0.6 ± 0.9, 0.6 (-0.4 to 1.7)	0.880	0.5 ± 1.1, 0.5 (–0.3 to 1.3)	0.3 ± 2.0, -0.8 (-3.5 to 2.7)	2.0 ± 4.1, 0.0 (-5 to 9.3)	-0.20	0.500
Change Lt Sup AX (mm), Mean ± SD, Median (Range)	0.2 ± 0.9, 0.2 (-1.3 to 1.7)	2.7 ± 5.7, 0.3 (-1.1 to 11.1)	0.800	-0.4 ± 0.8, -0.4 (-1.0 to 0.2)	1.8 ± 3.8, 0.6 (-0.9 to 11.1)	0.0 ± 0.9, 0.0 (-1.3 to 1.7)	0.20	0.480
Change Lt Sup AP (mm), Mean ± SD, Median (Range)	1.1 ± 3.7, 0.6 (-6.1 to 7.5)	0.9 ± 1.0, 0.7 (0.0 to 2.3)	0.840	0.1 ± 1.5, 0.1 (-0.9 to 1.2)	1.2 ± 1.2, 1.3 (-0.5 to 2.4)	1.1 ± 4.8, 0.0 (-6.1 to 7.5)	0.10	0.700
Change Lt Sit AX (mm), Mean ± SD, Median (Range)	0.5 ± 1.1, 0.9 (-1.9 to 1.9)	0.7 ± 0.9, 0.4 (0.0 to 2.0)	0.760	-1.3 ± 0.8, -1.3 (-1.9 to -0.7)	1.0 ± 0.7, 0.9 (0.0 to 2)	0.6 ± 0.9, 0.3 (-0.9 to 1.8)	-0.10	0.690
Change Lt Sit AP (mm), Mean ± SD, Median (Range)	2.0 ± 2.6, 1.4 (-1.7 to 6.4)	0.5 ± 1.3, 0.0 (-0.5 to 2.5)	0.250	1.9 ± 1.3, 1.9 (1.0 to 2.9)	1.8 ± 2.0, 1.9 (-0.5 to 5.4)	1.6 ± 3.1, 0.1, (-1.7 to 6.4)	0.10	0.640

Abbreviations: *P*, *P*-value; Rt, right; Sup, supine; AX, axial, mm, millimeters; SD, standard deviation; AP, anteroposterior; Lt, left; Sit, sitting.

Table 4. Associations between age and changes in ultrasound parameters and comparisons according to sex

Parameters (mm)		Change Rt Sup AX	Change Rt Sup AP	Change Rt Sit AX	Change Rt Sit AP	Change Lt Sup AX	Change Lt Sup AP	Change Lt Sit AX	Change Lt Sit AP
Age	Spearman's ϱ	-0.3	-0.2	-0.2	-0.4	0.1	-0.2	-0.1	-0.2
	P-values	0.270	0.320	0.460	0.130	0.680	0.330	0.730	0.450
Sex comparison (*P*-value)		0.350	0.580	0.460	0.900	0.130	0.500	0.050	0.450

Abbreviations: mm, millimeters; Rt, right; Sup, supine; AX, axial, mm, millimeters; AP, anteroposterior; Lt, left; Sit, sitting.

DISCUSSION

To the best of our knowledge, this is among the first studies to investigate changes in ultrasonographically measured lacrimal gland dimensions following cosmetic periorbital botulinum toxin injection. The principal finding was that significant changes in lacrimal gland dimensions were detected in the sitting position, whereas the corresponding changes in the supine position were not statistically significant and generally followed the same direction, except for a small decrease in the axial diameter of the right lacrimal gland. Although the anatomical position of the gland was not directly quantified, these dimensional changes may indirectly reflect alterations in gland configuration or its spatial relationship with the surrounding periocular structures. Furthermore, changes in the ultrasonographic measurements were not significantly associated with age, sex, previous upper-eyelid blepharoplasty, or number of crow's feet injection points.

The lacrimal gland is anatomically related to the levator palpebrae superioris aponeurosis, which divides the gland into orbital and palpebral lobes and contributes to its anatomical support within the lacrimal fossa [13]. Previous studies investigating periocular botulinum toxin injections have primarily focused on tear secretion, tear film stability, dry eye symptoms, ocular surface changes, and extraocular muscular dysfunction [14–17] rather than alterations in lacrimal gland position. For example, Ho et al. [15] demonstrated that botulinum toxin injection for lateral canthal rhytids significantly reduced tear film stability within one week after treatment, with the effect persisting for up to three months, while tear production gradually recovered during follow-up [15]. However, to the best of our knowledge no previous clinical study has evaluated changes in lacrimal gland position following cosmetic periorbital botulinum toxin injection using ultrasonography.

Lacrimal gland prolapse is generally considered an involutional age-related change of the upper orbit. Clinical studies have reported lacrimal gland prolapse in approximately 15% of patients undergoing upper blepharoplasty, whereas intraoperative exploration suggests that its true prevalence may be considerably higher, reaching approximately 60% in older patients [18, 19]. In addition to age-related involutional changes, lacrimal gland prolapse has also been reported in association with congenital ptosis, craniofacial abnormalities, orbital trauma, inflammatory disorders, and thyroid-associated orbitopathy [20–24]. Gao et al. [24] evidenced that, in patients with thyroid-associated orbitopathy, the degree of lacrimal gland prolapse measured on orbital magnetic resonance imaging was positively associated with Clinical Activity Score, proptosis, and extraocular muscle volume [24]. In the absence of these conditions, age-related attenuation of the orbital septum, Whitnall's ligament, and other connective tissue attachments is considered the principal mechanism responsible for anterior and inferior displacement of the lacrimal gland [18, 19]. Based on these anatomical relationships, transient relaxation of the periocular musculature induced by botulinum toxin may reduce the dynamic support provided by the surrounding muscular and connective tissue structures, potentially contributing to subtle changes in lacrimal gland configuration or its spatial relationship within the lacrimal fossa.

One possible explanation for the observed dimensional changes is the close anatomical relationship between the lacrimal gland and the surrounding periocular soft tissues. Although none of the participants developed clinically evident eyelid ptosis, subtle diffusion of botulinum toxin [25] may have transiently influenced the functional support provided by the levator palpebrae superioris muscle and its aponeurosis. In addition, botulinum toxin-induced relaxation of the orbicularis oculi muscle, particularly in the lateral periocular region [26], may reduce the dynamic support normally provided by the surrounding muscular structures. These effects could modify the configuration or orientation of the lacrimal gland relative to the ultrasound beam, thereby affecting the dimensions visualized in a two-dimensional ultrasonographic plane. However, because no fixed anatomical landmark, gland centroid, displacement vector, or three-dimensional imaging measurement was used, this proposed positional mechanism remains hypothetical.

The observation that statistically significant dimensional changes were detected in the sitting but not the supine position raises the hypothesis that gravitational loading may influence the ultrasonographic appearance or configuration of the lacrimal gland following periocular muscular relaxation. The lacrimal gland occupies the superolateral aspect of the orbit within the lacrimal fossa of the frontal bone and is closely related to the levator aponeurosis, Whitnall's ligament, and surrounding periocular soft tissues [27, 28]. In the sitting position, gravitational forces may exert a greater downward influence on these supporting structures [29], potentially making subtle changes in gland configuration or its spatial relationship within the lacrimal fossa more apparent on ultrasonography. In contrast, the altered gravitational vector in the supine position may reduce the visibility of such changes. However, because changes in the sitting and supine positions

were not compared directly, these findings do not establish that the effect of botulinum toxin differed significantly between the two positions.

The present study has several limitations. First, the small sample size and pilot nature of the study limited statistical power, particularly for subgroup analyses; therefore, the findings should be interpreted with caution. Second, the short follow-up period precluded evaluation of whether the observed ultrasonographic changes persisted or resolved after the effects of botulinum toxin had completely subsided. Serial assessments extending beyond the duration of toxin activity would help determine the temporal course and reversibility of these dimensional changes. Third, this study measured the maximum axial and anteroposterior dimensions of the lacrimal gland rather than its anatomical position directly. No measurements relative to fixed orbital landmarks, displacement coordinates, gland-centroid location, or three-dimensional volumetric assessments were obtained. Consequently, the observed dimensional changes cannot be considered direct evidence of lacrimal gland displacement, although they may indirectly reflect changes in gland configuration, orientation, or spatial relationship with the surrounding structures. Ultrasonography is also inherently operator-dependent, and differences in the imaging plane, probe positioning, probe pressure, or measurement variability cannot be excluded. Furthermore, the use of a relatively large linear transducer may have limited gland visualization, particularly in individuals with deep-set orbits. Smaller curved transducers or advanced imaging modalities, such as magnetic resonance imaging or three-dimensional ultrasonography, may allow more accurate assessment of gland configuration and displacement relative to fixed orbital landmarks. Finally, botulinum toxin injections were administered as a combined cosmetic treatment involving the frontalis, glabellar, and crow's feet regions according to the participants' aesthetic goals. Consequently, the independent contribution of individual injection sites to the observed dimensional changes could not be determined. Despite these limitations, this study has several important strengths. To our knowledge, it is among the first prospective studies to evaluate ultrasonographic dimensional changes of the lacrimal gland following cosmetic periorbital botulinum toxin injection. Additional strengths include the prospective pre–post design, standardized ophthalmic and ultrasonographic assessments, evaluation of both lacrimal glands in the sitting and supine positions, blinded image acquisition, and assessment at a predefined time point corresponding to the expected peak clinical effect of botulinum toxin. By quantifying both axial and anteroposterior dimensions, the study provides preliminary evidence that combined periorbital botulinum toxin injection may affect the ultrasonographic configuration of the lacrimal gland, potentially reflecting subtle changes in its spatial relationship with the surrounding structures. Future multicenter studies with larger cohorts, longer follow-up, repeated imaging after complete resolution of botulinum toxin activity, direct measurements relative to fixed orbital landmarks, and comparisons between isolated crow's feet injections and combined upper facial injection patterns are warranted to confirm these preliminary findings and further elucidate the underlying mechanisms.

CONCLUSIONS

Cosmetic periorbital botulinum toxin injection was associated with changes in the ultrasonographically measured axial and anteroposterior dimensions of the lacrimal glands, particularly in the sitting position. These findings do not directly demonstrate anatomical displacement but may indirectly reflect changes in gland configuration or its spatial relationship with the surrounding periocular structures following temporary muscular relaxation. Given the small sample size, short follow-up period, pilot design, and absence of direct positional or three-dimensional measurements, the findings should be considered preliminary and hypothesis-generating. Larger prospective studies with longer follow-up, repeated imaging after resolution of botulinum toxin activity, comprehensive functional assessments, and advanced imaging methods referenced to fixed anatomical landmarks are warranted to confirm these findings, elucidate the underlying mechanisms, and determine their clinical significance.

ETHICAL DECLARATIONS

Ethical approval: The study was approved by the local Ethics Committee of Farabi Eye Hospital, Tehran University of Medical Sciences, and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment, including consent for the publication of anonymized clinical information.

Conflict of interests: None.

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