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ORIGINAL PAPER

Efficacy and safety of botulinum toxin as a non-surgical option for upper eyelid retraction in active thyroid-associated ophthalmopathy: a prospective interventional study

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Abstract

Aim This study evaluates the efficacy and safety of botulinum toxin injection for the treatment of upper eyelid retraction in patients with active thyroid-associated ophthalmopathy (TAO).

Methods A prospective interventional study was conducted on 30 patients diagnosed with upper eyelid retraction secondary to active TAO. Patients received a single transcutaneous injection of botulinum toxin (7.5 units) into the levator palpebrae superioris muscle. Outcomes were assessed in terms of marginal reflex distance-1 (MRD-1), vertical palpebral fissure height, and subjective symptom improvement was assessed at 1,4, and 12 weeks post-injection. Adverse effects were also recorded.

Results The study demonstrated a significant reduction in MRD-1, with the peak effect observed between 2 and 4 weeks post-injection. The mean MRD 1 significantly reduced from 7.45 ± 1.76 mm at baseline to 4.43 ± 0.353 mm at 1 month ($p < 0.001$). Palpebral fissure height showed a similar trend. Improvement in ocular surface symptoms and photophobia was noted in 73.4% of patients. The effect began within 3–5 days post-injection, peaked by 1–2 weeks, and gradually waned over 2–3 months. The most common side effect was transient ptosis, which occurred in 13.3% of patients and resolved spontaneously. No serious adverse effects were observed.

Conclusion Botulinum toxin A offers a safe, effective, and minimally invasive option for temporarily correcting upper eyelid retraction during the active phase of TAO, providing symptomatic relief during the active inflammatory phase. Given the contradictions for surgery in the active phase, this minimally invasive intervention serves as a valuable bridge therapy until surgical correction becomes appropriate.

Keywords Botulinum toxin · Thyroid-associated ophthalmopathy · Eyelid retraction · Non-surgical treatment · Marginal reflex distance-1 (MRD-1) · Vertical palpebral fissure height (VPFH)

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Introduction

Thyroid-associated ophthalmopathy (TAO), also referred to as thyroid eye disease (TED), is an autoimmune orbital inflammatory disorder most commonly associated with Graves' disease, with variable clinical severity [1–3]. The condition is characterized by inflammation, extraocular muscle enlargement, and expansion of orbital fat, and often leads to a spectrum of ocular signs, including proptosis, diplopia, exposure keratopathy, and, most commonly, upper eyelid retraction [3–5]. Among the most frequent and distressing manifestations of TAO is upper eyelid retraction, which not only contributes to the characteristic staring appearance but also leads to ocular discomfort, photophobia, dry eye, and cosmetic disfigurement [6–8]. The etiopathogenesis of upper eyelid retraction in TAO is multifactorial. It includes increased sympathetic tone of Muller's muscle, fibrosis and inflammation of the levator palpebrae superioris muscle, and adhesions between the levator aponeurosis and surrounding orbital tissues. In some cases, secondary elevation due to proptosis further worsens eyelid retraction [9, 10].

Management of TAO depends heavily on the disease phase -active (inflammatory) versus inactive (fibrotic).In the active inflammatory phase, characterized by orbital congestion, pain, chemosis, and soft tissue involvement, the use of systemic corticosteroids and immunomodulators is the mainstay of therapy. Surgical interventions such as eyelid lengthening procedures, blepharotomy, or orbital decompression are typically reserved for the inactive phase when inflammation has subsided and the disease has stabilized for at least 6 months. Performing surgery during the active phase carries a risk of unpredictable outcomes and exacerbation of inflammation. However, patients frequently suffer significant discomfort during this phase due to eyelid retraction, and non-surgical symptomatic relief becomes essential [11–13].

There remains a clinical need for safe, effective, and reversible non-surgical interventions to manage upper eyelid retraction during the active phase of TAO, particularly for patients experiencing significant functional or aesthetic impairment. In this context, botulinum toxin type A (BoNT-A) has emerged as a valuable therapeutic option. BoNT-A is a neurotoxin produced by Clostridium botulinum that inhibits acetylcholine release at the neuromuscular junction, resulting in temporary paralysis of targeted muscles. When injected into the levator palpebrae superioris muscle, BoNT-A weakens its function, reducing eyelid elevation and thereby alleviating retraction. The effect typically begins within a few days, peaks at 1–2 weeks, and gradually wears off over 2–3 months. Importantly, BoNT-A provides a reversible and titratable approach, ideal for the fluctuating course of TAO [14–18].

While BoNT-A is widely used in various ophthalmic and cosmetic indications, there are very few studies that have specifically demonstrated its usefulness in TAO-associated upper eyelid retraction, especially during the active inflammatory stage [19–22]. Given the paucity of data, further research is warranted to substantiate the role of BoNT-A in the management of eyelid retraction in active TAO. This study aims to evaluate the efficacy and safety of botulinum toxin type A as a non-surgical treatment for upper eyelid retraction in patients with active thyroid-associated ophthalmopathy, with a focus on clinical outcomes, complication rates, and patient-reported satisfaction. By providing more data on this therapeutic option, we hope to support its role as a useful adjunct or alternative in the early management of TAO-related eyelid changes. Furthermore, this study seeks to contribute to the growing but still limited body of literature on the non-surgical management of TAO during the active phase and establish practical guidance for ophthalmologists and oculoplastic surgeons.

Methodology

This was a prospective, interventional study conducted at the Department of Ophthalmology of a tertiary care center. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants. This study adhered to the tenets of the Declaration of Helsinki. The study was done for 03 months and all patients were followed up for 6 months.

A total of 30 patients (56 eyelids) diagnosed with active thyroid-associated ophthalmopathy (Clinical Activity Score ≥ 3) as recommended by the European Group on Graves' Orbitopathy (EUGOGO) and presenting with upper eyelid retraction were included in this study. Disease activity assessment included evaluation of classical inflammatory signs such as

pain, redness, and swelling, following the EUGOGO seven-point CAS system. Patients who were more than 18 years old, whose upper eyelid margin reflex distance was ≥ 5 mm, had no previous eyelid surgery or botulinum toxin treatment for eyelid retraction, and patients with euthyroid status were included in the study group. Patients with TAO in the inactive phase or significant proptosis requiring decompression, hypersensitivity to botulinum toxin, pregnant ladies and lactating mothers, patients with severe dry disease, corneal exposure, or lagophthalmos were excluded from the study. In all cases, detailed history was taken, and all of them underwent complete ocular examination.

All patients underwent a comprehensive ophthalmic assessment prior to treatment. This included recording of best-corrected visual acuity, intraocular pressure, and detailed slit-lamp and fundus examination. Upper eyelid position was evaluated by measuring the margin reflex distance 1 (MRD 1), and proptosis was assessed using Hertel exophthalmometry. The clinical activity of thyroid-associated ophthalmopathy was graded using the Clinical Activity score (CAS), with scores of 3 or higher considered indicative of active disease. The ocular surface evaluation included the Schirmer test and tear breakup time to assess baseline tear film status. Corneal integrity was assessed by fluorescein staining. Baseline thyroid function tests (T3, T4, TSH) were reviewed to correlate with systemic disease. All patients were confirmed to be biochemically euthyroid at the time of intervention. Thyroid function tests (TSH, free T3, and free T4) were within normal reference ranges, and patients had maintained a stable euthyroid state for at least 4 weeks prior to botulinum toxin injection. All patients were being treated with antithyroid medications (Tab. Carbimazole and Tab. Propranolol) to maintain euthyroid status. In accordance with EUGOGO treatment guidelines, all patients received weekly intravenous methylprednisolone (IVMP) infusions for a total of 12 weeks during the active phase. Botulinum toxin injection was administered during the treatment period, and no other immunosuppressive agents were used. Standardized clinical photographs of the ocular adnexa and eyelid position were taken at the initial presentation for comparison during follow-up visits. A history of previous treatments, including corticosteroids, radiation therapy, or surgical interventions for thyroid eye disease, was carefully documented.

Botulinum toxin type A (onabotulinum toxin A, Botox, Allergan) was used for all patients. A vial containing 50 units was reconstituted with 2 ml of preservative-free normal saline to achieve a concentration of 2.5 units per 0.1 ml.

Injection technique

The injections were given under strict aseptic precautions in a clinical setting. After instillation of topical anesthesia (proparacaine 0.5%), under protection using an eye shield, a single transcutaneous injection at the centrally superior tarsal border was administered into each eyelid, aiming at the complex of levator aponeurosis and Müller's muscle (Fig. 1).

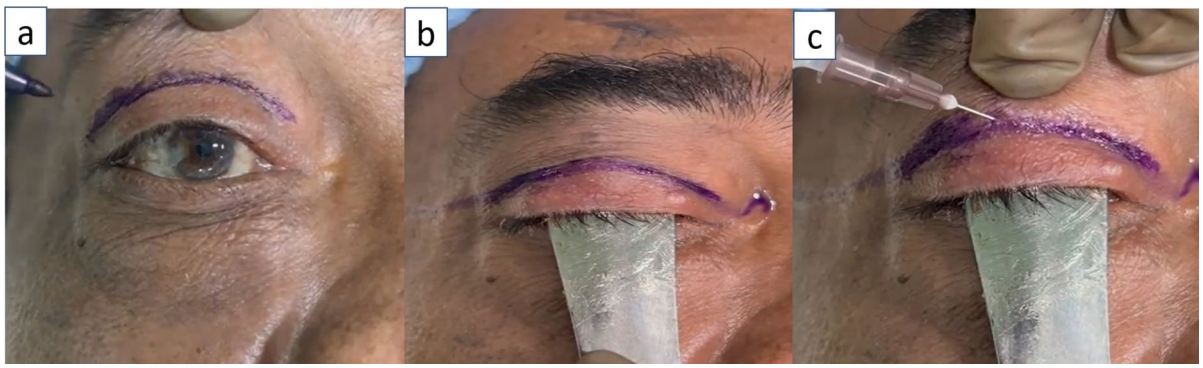

Fig. 1 (**a**, **b**, **c**) Clinical photograph showing transcutaneous administration of Injection Botox at the central superior tarsal border, with ocular protection provided by a lid guard

A 26-gauge needle attached to a 1 ml syringe was used to inject botulinum toxin. A dose of 5 units (0.2 ml) was injected at a central point; additional injections were placed medially or laterally depending on the distribution of eyelid retraction, with a total dose not exceeding 7.5 units per eyelid. After injection, gentle pressure was applied for 1–2 min to minimize bruising and diffusion. Patients were instructed to avoid massaging the injection site, strenuous activities, and lying flat for at least 2–3 h post-injection to reduce the risk of toxin spread. Follow-up visits were scheduled at 01 weeks, 01 month, and 03 months post-injection. At each follow-up visit, a comprehensive ophthalmic examination was performed. Standardized digital photographs in primary gaze were obtained for each patient at baseline, 1 month, and 3 months post-injection (Fig. 2). All photographs were taken under consistent lighting and patient positioning using the same camera settings. These images served to document eyelid changes and verify clinical measurements,

The outcome measures assessed in his study included both objective clinical parameters and subjective symptom relief following the administration of botulinum toxin. The primary outcome measures in the study were the change in upper eyelid position, objectively assessed by the reduction in margin reflex distance 1 (MRD 1) and vertical palpebral fissure height (VPFH) at follow-up intervals compared to baseline, which was measured in millimeter using a millimeter ruler under standardized lighting conditions. MRD1 was defined as the distance from the

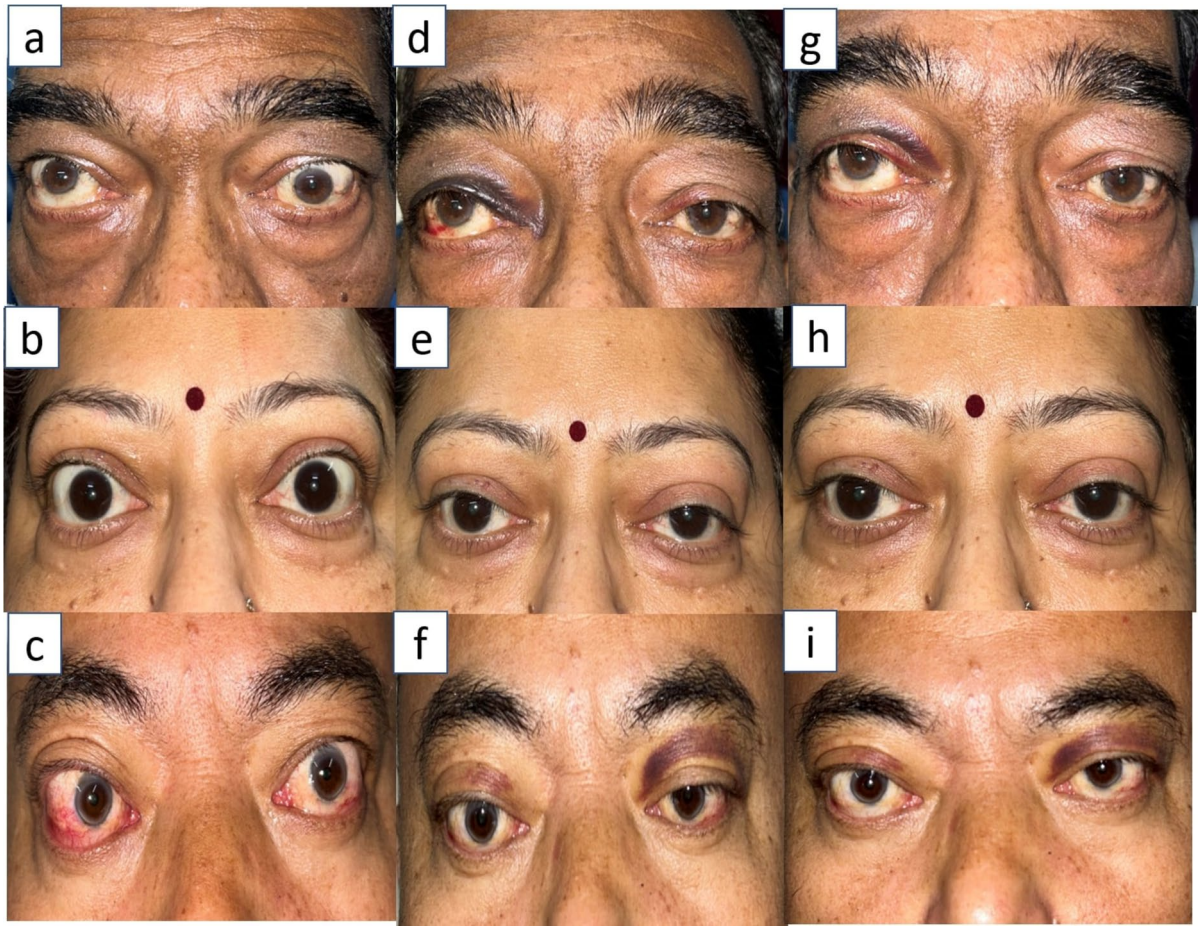

Fig. 2 (**a**, **b**, **c**): Pre-injection clinical photograph prior to Botox administration. (**d**, **e**, **f**): Post-injection clinical photograph at 1-month follow-up following transcutaneous administration of Botox (**g**, **h**, **i**): Post-injection clinical photograph at 3-month follow-up following transcutaneous Botox injection

central corneal light reflex to the upper eyelid margin in primary gaze (It is the reference for the upper eyelid position, which was reported to have a mean value of 3.5 mm and a standard deviation of 0.9 mm in normal population), and VPFH was measured as the vertical distance between the upper and lower eyelids margins at the mid-pupillary line. Measurements were recorded at baseline and at each follow-up visit. These parameters were chosen to evaluate the anatomical effectiveness of botulinum toxin in correcting upper eyelid retraction. All outcome measurements (MRD1 and VPFH) were performed by the same surgeon who administered the botulinum toxin injections. To reduce the risk of measurement bias, standardized high-resolution photographs were taken for each patient in primary gaze at baseline and at every follow-up visit using consistent lighting and positioning. These photographs were used to confirm and verify clinical measurements. Each parameter was measured twice, and the average value was recorded.

The secondary outcome measures included subjective symptom improvement was evaluated using a grading scale ranging from 0 to 3 (0 = no improvement, 1 = mild, 2 = moderate, 3 = marked improvement) for key patient-reported symptoms such as eyelid swelling, photophobia, and foreign body sensation. Additional secondary parameters included the safety profile of the intervention was evaluated based on the occurrence of adverse effects such as ptosis, lagophthalmos, dry eye symptoms, and diplopia, and the duration of therapeutic effect and need for repeat injections. These outcome measures, both objective and subjective parameters, allowed for a comprehensive assessment of the efficacy of botulinum toxin as a non-surgical intervention in the management of upper eyelid retraction in active thyroid-associated ophthalmopathy.

Statistical analysis

All collected data were entered into a Microsoft Excel spreadsheet and analyzed using statistical software (eg., SPSS version 25.0, IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic variables and baseline characteristics. Continuous variables such as margin reflex distance 1(MRD 1), and palpebral fissure height (PFH) were expressed as mean ± standard deviation (SD). Pre and post-treatment values of MRD 1 and VPFH were compared at 1 week, 1 month, and 3 months using the paired t-test to assess the short-term effects of botulinum toxin. Categorical variables, such as the incidence of complications and patient satisfaction scores, were expressed as frequencies and percentages. Additionally, for assessing change over time across the three post-injection time points, repeated measures ANOVA was used to determine the statistical significance between each interval. This combination of tests provided both pairwise and trend-level analysis of eyelid position changes. A p-value of less than 0.05 was considered statistically significant for all tests. A post hoc power analysis was performed based on the observed changes in both marginal reflex distance 1 (MRD 1) and vertical palpebral fissure height (VPFH) following botulinum toxin injection.

Results

A total of 30 patients (56 eyelids) with active thyroid-associated ophthalmopathy and upper eyelid retraction were included in the study. The cohort predominantly compromised female patients, in line with the higher incidence of thyroid-associated ophthalmopathy (TAO) among women. All patients enrolled in the study had moderate to severe Clinical Activity Score (CAS) at baseline (CAS ≥ 3), indicating active inflammatory disease. Additionally, bilateral upper eyelid retraction was noted in a maximum number of patients, further emphasizing the severity of the condition. Each patient had normal thyroid levels at the time of botulinum toxin injection, ensuring endocrine stability and minimizing systemic confounding factors. A small proportion of patients had a history of smoking, a known risk factor for worsening ophthalmic manifestations of thyroid disease. While the majority of patients had no systemic illnesses, a few had significant comorbidities such as hypertension and diabetes, which were well-controlled. The clinicodemographic details of the study population are shown in Table 1

All patients received a single session of botulinum toxin type A injection, with a dose adjusted between 5 and 7.5 units per eyelid, depending on the severity of retraction.

None of the patients had previously undergone eyelid surgery or received botulinum toxin injections.

Table 1 Clinicodemographic profile of the study population (n = 30)

Features	No of patients (n)	Percentage (%)
Age (Years)		
Range	30 – 56 years	
Mean ± SD	47 ± 8.18 years	
Gender		
Male	09	30
Female	21	70
Laterality		
Unilateral	4	13.3
Bilateral	26	86.6
Mean duration of the disease	10 ± 3.2 months	
Mean clinical activity score (CAS)	4 ± 0.7	
Smoking status		
Smoker	06	20
Non-smoker	24	80
Comorbidities		
Diabetes mellitus	04	13.3
Hypertension	05	16.6
Both	03	10
Thyroid status		
Euthyroid	30	100

The mean baseline MRD1 was 7.45 ± 1.76 mm, and the mean palpebral fissure height was 16.8 ± 3.18 mm. Both MRD 1 and vertical fissure height showed a marked reduction from baseline at the 1 -1-month follow-up, indicating the early effectiveness of the intervention. However, by the 3-month follow-up, a gradual decline in the effectiveness of the injection was observed in nearly all patients, with partial recurrence of eyelid retraction and associated symptoms. Statistical analysis using paired t-tests confirmed significant differences between the baseline and each follow-up point (Table 2). Repeat injection was advised in all patients after 03 months to maintain the therapeutic effect. Furthermore, repeated measures ANOVA revealed a significant time-dependent effect on both MRD1 (Fig. 3) and VPFH (Fig. 4), supporting the consistent and measurable impact of botulinum toxin over the short-term follow-up period.

For MRD 1, the mean reduction was from 7.45 ± 1.76 to 4.32 ± 0.35 mm, yielding an effect size (Cohen's d) of 2.47. For VPFH, the mean reduction was from 16.8 ± 3.18 to 8.11 ± 0.84 mm, with an effect size of 3.74. With a sample size of 30 and a significance level of 0.05, the calculated post hoc power was 100% for both outcomes. These results indicate that the study was statistically well-powered to detect

Table 2 Analysis of MRD1 and VPFH changes using paired t-tests at baseline and subsequent follow-up visits (n = 30)

n Number of Participants, *MRD 1* Marginal Reflex Distance, *VPFH* Vertical Palpebral Fissure Height, *p*-value < .05 was considered statistically significant

Parameter	Time point	(Mean ± SD, mm)	Mean difference	T-value	*p*-value
MRD 1	Baseline	7.45 ± 1.76	–	–	–
	1 Week	4.32 ± 0.353	− 3.13	10.84	< 0.0001
	1 Month	4.43 ± 0.353	− 3.02	10.45	< 0.0001
	3 Months	6.2 ± 1.06	− 1.25	4.62	< 0.0001
VPFH	Baseline	16.8 ± 3.18	–	–	–
	1 Week	8.11 ± 0.84	− 8.69	14.32	< 0.0001
	1 Month	8.2 ± 0.85	− 8.60	14.05	< 0.0001
	3 Months	10.9 ± 1.32	− 5.90	9.82	< 0.0001

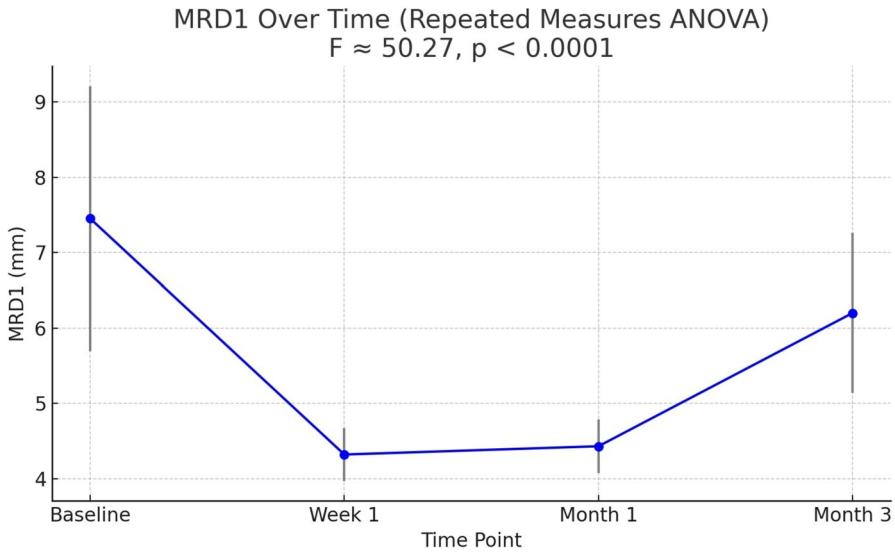

Fig. 3 MRD 1 Over time (Repeated measures ANOVA)

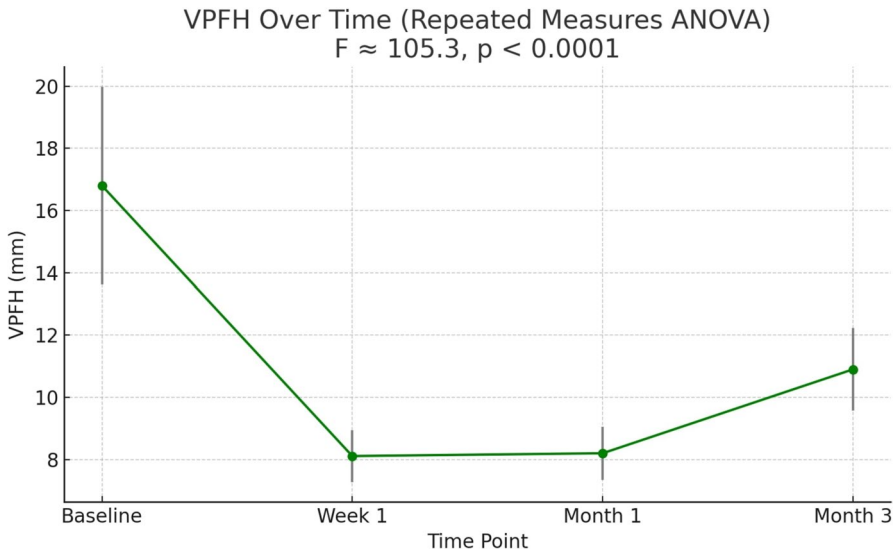

Fig. 4 VPFH Over time (Repeated measures ANOVA)

the observed clinical improvements, despite the limited sample size.

Subjective symptom improvement was assessed using a scale from 0 (no improvement) to 3 (marked improvement) across the three common symptoms: eyelid swelling, foreign body sensation, and cosmetic dissatisfaction. At the 1-month follow-up, the majority of patients reported moderate to marked improvement in these symptoms, with many experiencing relief in daily activities and improved cosmetic satisfaction. But by the 3-month follow-up, a noticeable reduction in symptom relief was observed, with several patients reporting a recurrence of mild eyelid

Table 3 Subjective symptom scores over time (n = 30)

Symptom	1 Week (Mean ± SD)	1 Month (Mean ± SD)	3 Months (Mean ± SD)
Eyelid discomfort	2.1 ± 0.5	2.5 ± 0.4	1.7 ± 0.6
Foreign body sensation	2.0 ± 0.6	2.4 ± 0.5	1.6 ± 0.6
Cosmetic dissatisfaction	1.9 ± 0.5	2.6 ± 0.4	1.8 ± 0.5

n Number of Participants, Scoring: *0* = No Improvement, *1* = Mild, *2* = Moderate, *3* = Maximum Improvement

heaviness and discomfort (Table 3). This trend mirrored the objective findings and emphasized the need for repeat injections around the 3-month mark to sustain patient-reported benefits.

Adverse events

Botulinum toxin injections were generally safe and well tolerated, with no serious or long-term complications observed. The most common side effect was mild ptosis, observed in 4 eyes (13.3%). Ptosis was transient, resolving spontaneously by 8 weeks in both cases. Bruising at the injection site was reported in 3 patients (10%), which subsided within a week without intervention. Diplopia was observed in 1 patient (3.3%) (Fig. 5). All adverse effects resolved spontaneously within 4–6 weeks. There were no reports of dry eye symptoms, local infection, hypersensitivity reactions, or systemic side effects. Overall, the treatment demonstrated a favourable safety profile.

A subset analysis revealed that patients with severe baseline retraction (> 3 mm) showed a slightly greater absolute reduction in MRD 1 compared to those with milder retraction (< 3 mm), although this did not reach statistical significance. The mean duration of clinically significant improvement was 10–12 weeks, after which re-injection was considered based on patient preference and recurrence of symptoms. Improvement in eyelid retraction was observed as early as 1 week post-injection and peaked around 3 to 4 weeks. The effect gradually waned over the following 3 months in most cases.

Discussion

Thyroid-associated ophthalmopathy (TAO), an autoimmune condition associated with Graves' disease, manifests prominently with upper eyelid retraction—a distressing symptom for both functional and aesthetic reasons [23–25]. The active inflammatory phase of TAO is characterized by fluctuating symptoms and ongoing tissue remodelling, during which surgical intervention is typically deferred. In this context, the use of botulinum toxin type A (BoNT-A) has emerged as a valuable non-surgical modality to manage upper eyelid retraction, offering temporary yet effective relief during the active phase of the disease [26–28].

The present study explored the therapeutic potential of botulinum toxin in patients with moderate-to-severe active TAO presenting with upper eyelid retraction. Our findings demonstrated that a single transcutaneous injection of BoNT-A into the upper eyelid effectively reduced upper eyelid retraction in patients with active TAO, as evidenced by a significant and measurable decrease in marginal reflex distance 1 (MRD 1) and vertical fissure height. The

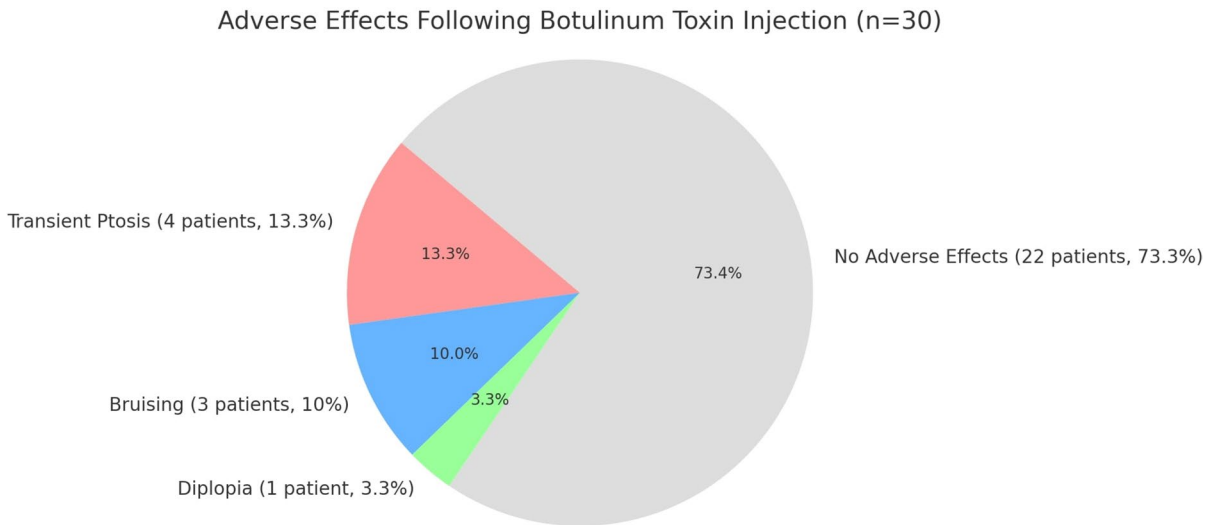

Fig. 5 Adverse effects following Botulinum toxin injection

value of botulinum toxin lies not merely in its capacity to lower the eyelid but in the broader therapeutic benefits that stem from improved eyelid closure, such as enhanced corneal protection and mitigation of exposure-related symptoms. In active TAO, the corneal surface is particularly vulnerable due to proptosis, lid lag, and retraction, leading to discomfort and potential complications like keratitis. A reduction in upper eyelid retraction, even by a few millimeters, can significantly alter the ocular surface environment, reducing evaporative loss and mechanical irritation. From a patient-centered perspective, this improvement in ocular comfort often translates into a better quality of life, particularly in individuals experiencing photophobia, tearing, and foreign body sensations. The temporary nature of botulinum toxin's effect is often considered a limitation, but in the context of active TAO, where reversibility is often preferable to permanence, it becomes an asset. This temporality allows clinicians to adjust treatment as the disease evolves or resolves, avoiding the risks associated with premature or irreversible interventions.

Botulinum toxin stands out among non-surgical interventions for upper eyelid retraction in active thyroid-associated ophthalmopathy due to its targeted mechanism and direct impact on eyelid position.. While topical lubricants and eyelid tapping serve a supportive role by managing symptoms of exposure keratopathy, such as dryness, irritation, and photophobia. They do not address the underlying muscular cause of lid retraction and offer only temporary symptomatic relief without influencing the structural position of the eyelid. Local corticosteroids, on the other hand, aim to reduce orbital inflammation and tissue oedema during the active inflammatory phase. However, their effect on eyelid retraction is indirect and inconsistent, as they do not act specifically on the levator palpebrae superioris muscle. Additionally, corticosteroids carry potential risks including elevated intraocular pressure, fat atrophy, and globe perforation with improper technique [18, 29]. Botulinum toxin uniquely provides a reversible and minimally invasive option that acts directly on levator muscle by temporarily blocking acetylcholine release at the neuromuscular junction. This results in a controlled lowering of the upper eyelid, offering both and cosmetic improvement. Thus, unlike other non-surgical measures that offer either symptomatic relief or indirect benefit, botulinum toxin directly targets the pathophysiology of eyelid retraction with greater precision and reliability [30, 31].

In interpreting our findings, it is essential to contextualize them within the existing body of literature. A few studies have evaluated botulinum toxin in TAO, and while methodologies and populations vary, there is a consistent pattern of moderate eyelid lowering, symptom relief, and an acceptable safety profile. The therapeutic effect of botulinum toxin in TAO-related lid retraction was first described by Ebner et al. in 1993 [14]. In their cohort of 07 patients, a 2.5–7.5 unit dose of BoNT-A was injected, leading to noticeable improvement in eyelid position, although the response duration was brief. Subsequent studies refined this approach by optimizing the dose and injection rate. Shih et al. (2004) conducted a prospective study that demonstrated a statistically significant reduction in MRD 1 and VFH at 2 and 6 weeks post-injection [24]. The therapeutic effect persisted for a minimum of four months. Their results also confirmed a similar profile, with ptosis reported in 22% of patients.

In 2009. Costa et al. conducted a prospective study involving 24 patients with upper eyelid retraction due to TAO [16]. The patients were divided into two groups based on disease stage: 12 in the congestive stage and 12 in the fibrotic stage. They administered a single transcutaneous injection of 5 units of BTX-A into the upper eyelid. They reported a mean reduction in eyelid retraction in both groups. The therapeutic effect lasted longer in the fibrotic group, with significant improvements observed up to three months post-injection. Our study findings support this approach, as we observed reliable results with minimal invasiveness and patient discomfort. In another relevant study, Zhiqing Huang et al. (2025) demonstrated that BoNT- A, when used alongside corticosteroid therapy, yielded greater reductions in eyelid retraction than either therapy alone, suggesting a potential synergistic role [32]. Although our study did not incorporate combination therapy, the favourable response to BTX-A monotherapy suggests that it remains a valid standalone intervention, particularly in cases where steroids are contraindicated or poorly tolerated [32].

A distinctive contribution of our work lies in its exclusive focus on patients in the active phase of the disease, which enhances the clinical relevance of the findings, as these patients are often ineligible for surgical correction due to ongoing inflammation. Many

prior studies have combined cohorts of active and inactive cases, potentially confounding the response to treatment, potentially confounding the response to treatment given the differing tissue characteristics and inflammatory status. By limiting our study population to active TAO, we provided a clearer assessment of botulinum toxin's role in this challenging clinical window, where few interventions are both effective and safe. This distinction is critical because active TAO presents not only with retraction but also with fluctuating oedema, fibrosis, and inflammation, all of which may influence treatment outcomes. The ability of botulinum toxin to deliver meaningful symptomatic and cosmetic improvements in this setting underscores its relevance as a temporizing measure before the disease stabilizes.

The study has certain limitations that must be acknowledged. The relatively small sample size limits the generalizability of the findings and reduces the ability to detect rare adverse events or variations in response among different subgroups. Additionally, the absence of a control or comparison group, such as a placebo, alternative conservative therapies, or other minimally invasive interventions (e.g. taping or eyelid weights), restricts the ability to draw comparative conclusions. While the observed improvements were substantial, it remains possible that a placebo effect or natural fluctuation in disease activity may have contributed to the results. Furthermore, the follow-up duration in this study was limited to 12 weeks, corresponding to the known clinical duration of action of a single botulinum toxin injection in periorbital tissues. As the therapeutic effect typically wanes after this period, the study was designed to assess short-term efficacy and safety. Consequently, the long-term outcomes and the effects of repeated injections could not be evaluated. Future studies with extended follow-up are necessary to assess sustained benefits and safety over time.

Despite these limitations, the findings contribute meaningfully to the current understanding of non-surgical management strategies for eyelid retraction in TAO. As treatment paradigms continue to evolve, especially with increasing interest in biologics and targeted immunomodulators, the role of supportive symptomatic therapies like BTX-A remains highly relevant. It offers patients a bridge between the active and inactive phases of the disease, allowing functional and psychological relief during a period otherwise marked by clinical uncertainty and visual discomfort.

Conclusion

Botulinum toxin injection offers a safe, effective, and minimally invasive strategy for managing upper eyelid retraction in the active phase of thyroid-associated ophthalmopathy. Its utility lies in its ability to provide symptomatic relief, cosmetic improvement, and corneal protection during a phase of disease in which other options are limited. The treatment's temporary and reversible nature aligns well with the unpredictable trajectory of active TAO, offering clinicians a flexible tool to address patient concerns while awaiting disease stabilisation. The current study supports the incorporation of BoNT-A into the therapeutic armamentarium for managing TAO in its active phase. While short-term outcomes were favourable, longer-term studies with larger cohorts and repeated injections are necessary to further validate its efficacy and safety.

Author contributions Conceptualization: [SVK,VK,NVK]; methodology: [SVK,AS]; formal analysis [SVK,SKM]; writing- original draft preparation;[SVK,VK,NVK]; writing-review and editing:[SVK,SKM,AS];supervision; [SKM].

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (Command Hospital Eastern Command, Kolkata) and with the 1964 Helsinki Declaration and its amendments or comparable ethical standards. This manuscript did not involve any kind of animal research. All the authors consent to the publication of this manuscript in International Ophthalmology.

Informed consent Informed consent was obtained from all individual participants included in the study.

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