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Hybrid injection techniques in aesthetic medicine: Evaluating the clinical benefits of combining botulinum toxin and hyaluronic acid in upper face rejuvenation

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Abstract

The formation of wrinkles in the upper face, particularly in the glabella and frontalis regions, is a common concern that leads to facial stigmatization. Habitual facial expressions and the hyperdynamic activity of underlying muscles, combined with the normal aging process and external factors, contribute significantly to the development of hyperdynamic wrinkles. Botulinum toxin type A (BTXA) has become a widely used treatment for facial rejuvenation, while hyaluronic acid (HA) fillers are essential for enhancing skin hydration and elasticity. This study explores the efficacy and safety of combining BTXA with HA for upper face rejuvenation compared to BTXA monotherapy. To assess the clinical efficacy, duration of effect, and patient satisfaction of a combined therapy using botulinum toxin type A and hyaluronic acid fillers versus botulinum toxin alone. This case-control study was conducted at Ishtar Clinics for Dermatology, Aesthetic Medicine, and Laser in Basrah, Iraq. A total of 76 participants, aged 25 to 60 years, were enrolled, with 38 cases receiving the combination therapy and 38 controls receiving botulinum toxin monotherapy. The study spanned 12 weeks, with evaluations conducted at baseline and subsequent follow-ups at weeks 1, 2, 4, 8, and 12. Efficacy was assessed using the Investigator Global Assessment-Frown Wrinkle Severity (IGA-FWS) and Patient-Frown Wrinkle Severity (PFWS) scales, while safety was monitored through adverse event recording and physical examinations. The combination therapy group showed a significantly greater reduction in wrinkle severity across various facial regions, including glabellar lines, crow's feet, and forehead lines, compared to the monotherapy group. By week 4, 85% of the combination therapy group achieved at least a 2-point reduction in wrinkle severity scores, compared to 60% in the monotherapy group. The combined treatment also resulted in a longer duration of effect, with 70% maintaining improvement at 12 weeks versus 45% in the monotherapy group. Both groups had a low incidence of minor adverse effects, and patient satisfaction was notably higher in the combination therapy group. Combining botulinum toxin type A with hyaluronic acid fillers for upper face rejuvenation offers superior efficacy and patient satisfaction compared to botulinum toxin alone. This synergistic approach enhances treatment outcomes, prolongs the duration of effect, and maintains a favorable safety profile, making it a promising option for facial rejuvenation therapies.

Keywords: Botulinum toxin, Combination therapy, Facial rejuvenation, Hyaluronic acid, Hybrid botulinum toxin, Wrinkle reduction.

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1. Introduction

The formation of wrinkles in the upper face, specifically in the glabella and frontalis regions, is common and leads to facial stigmatization. The upper face is particularly prone to the influence of habitual facial expressions and the hyperdynamic activity of underlying muscles [1, 2]. Over time, the combined effect of the muscle contraction and the normal aging process that involves; decreased collagen production and skin elasticity, diminished fat cells, and skin dehydration, contribute to the development of hyperdynamic wrinkles. In addition, external factors such as sun exposure, air pollution, tobacco smoking, nutritional deficiencies, and stress also play a major role [3, 4]. Various treatment options have been developed to minimize facial lines, including dermal fillers, topical solutions, neuromodulators, and laser treatments [5].

Botulinum toxin type A (BTXA), formerly a life-threatening food poison [6] has evolved into a cosmetic treatment, ever since its FDA approval for aesthetic use in the glabellar region, in 2002 [7]. Currently, Botulinum toxin type A injections are the most commonly performed non-invasive procedure for face rejuvenation worldwide, and their efficacy have been extensively documented in the literature [8-10]. They are injected intramuscularly, resulting in reversible chemical paralysis of muscles by blocking the release of acetylcholine [11]. However, off-label intradermal BTXA injections are gaining popularity among medical professionals for facial rejuvenation [12]. Several studies suggest that intradermal injection of BTXA improves skin elasticity and surface roughness by enhancing collagen production and down-regulating its degradation in dermal fibroblasts [13]. It also has a role in lowering sebum production and facial pores size [14].

Hyaluronic acid (HA) is an essential naturally-occurring glycosaminoglycan in the extracellular matrix, contributing to tissue growth and development [15]. HA dermal fillers have now become a cornerstone of aesthetic medicine, due to their biocompatibility and safety. HA used in fillers are cross-linked by substances such as 1,4-butanediol diglycidyl ether and divinyl sulfone to prolong its half-life, by inhibiting endogenous enzymatic degradation [16]. HA reduces wrinkle formation and improves existing ones by promoting skin hydration, stimulating collagen and elastin synthesis, and enhancing cell regeneration through its antioxidant effects [17-19]. Moreover, HA has a myomodulation effect which is defined as regulation of muscular activity. When injected deep under the muscle, it augments the mechanical advantage and improves the muscular force, while superficial injection above the muscle reduces the muscular contraction without blocking it. This effect balances muscle action to improve facial appearance and structural defects [20, 21].

Combining both botulinum toxin type A (BTXA) and hyaluronic acid (HA) creates a synergistic effect, particularly beneficial in upper face rejuvenation [22]. Several studies showed that this combination is generally safe, leading to reduce required dosages of botulinum toxin; thus, reducing its side effects, reduced total dosage, longer duration of effect, and higher patient satisfaction, compared to single agent injection. Moreover, reduction in muscle contraction by BTXA decreases the absorption of HA fillers, prolonging its effect, while, HA can conceal the recovery of muscles from the BTXA effect, therefore, reducing the frequency of re-injection [22-24].

This study seeks to investigate the clinical efficacy, duration of effect, and patient satisfaction of combination therapy of botulinum toxin type A and hyaluronic acid fillers compared to monotherapy.

2. Patients and Methods

Study Design: This case-control study aims to compare the safety, efficacy, and best injection techniques of botulinum toxin alone versus a hybrid approach (botulinum toxin combined with cross-linked hyaluronic acid) for upper face rejuvenation. The study was conducted at Ishtar Clinics for Dermatology, Aesthetic Medicine, and Laser in Basrah, Iraq.

Setting and Duration: The research is set in a clinical environment specializing in dermatology and aesthetic medicine. The study spans six months, allowing for adequate follow-up and observation of treatment outcomes.

Population: The study includes a total of 38 cases and an equal number of controls. Participants are selected from individuals visiting Ishtar Clinics.

Inclusion Criteria: Male and female participants aged between 25 and 60 years.

Exclusion Criteria: Patients who received injections of botulinum toxin or hyaluronic acid in the upper face in the last six months, patients with autoimmune diseases, patients with a bleeding tendency, or blood disorders, patients with acute infections, inflammation, or cancer, and patients allergic to Botulinum Toxin (BTx) or Hyaluronic Acid (H.A).

Outcomes Measurement: The primary outcome is to measure the safety and efficacy of the treatments. Safety was assessed by recording any adverse effects or complications following the procedures. Efficacy was evaluated based on

clinical improvement in upper face rejuvenation, as judged by both clinicians and patients through standardized scales and photographic evidence.

Patient Evaluation: Participants underwent a thorough medical history and physical examination to ensure compliance with the inclusion and exclusion criteria. Baseline photographs and assessments of upper face aging will be conducted before the intervention.

Participants were evaluated for efficacy and safety over a period of 12 weeks. Assessments were carried out at baseline, followed by weeks 1, 2, 4, 8, and 12. The evaluation of treatment efficacy utilized the 4-point Investigator Global Assessment-Frown Wrinkle Severity (IGA-FWS) and Patient-Frown Wrinkle Severity (PFWS) scales [25]. The primary efficacy endpoint was established as the proportion of participants who achieved at least a 2-point reduction in both IGA-FWS and PFWS scores at maximum frown by week 4. Additionally, participants maintained diaries during the first 14 days post-treatment to record the onset and early response to the treatment. The study also measured the duration of the treatment's effectiveness and the participant's satisfaction with the outcomes, with satisfaction scores. For safety assessments, the study included monitoring for adverse events, performing physical examinations, and facial muscle strength.

2.1. Procedure:

2.1.1. Botulinum Toxin Type a Dilution and Storage

- Standard Vial Content: A typical vial contains 100 units of Botulinum Toxin Type A in a vacuum-dried form.
- Dilution Process: To prepare the BoNTA for injection, it is reconstituted with a saline solution. The amount of saline added will determine the concentration of the solution.
- Common Dilution Ratios: While the dilution can vary, one common approach is to add 2.5 ml of preservative-free saline to a 100-unit vial. This results in a concentration where 1 ml of the solution contains 40 units of BoNTA.
- Storage and Usage: Once reconstituted, BoNTA was used within 24-hour timeframe to maintain efficacy and safety.

2.2. Preparation of WMJ Mixture

The preparation of a WMJ Mixture using previously diluted Botulinum Toxin Type A (BONT-A) and cross-linked hyaluronic acid (HA) is a specialized procedure that combines the neuromodulating effects of BONT-A with the volumizing properties of HA.

2.3. Components

- BONT-A: Onabotulinum toxin A, which was already diluted as per standard clinical guidelines.
- Cross-Linked Hyaluronic Acid (HA): Concentration specified as 20 mg/dl.

The component we used was composed of cross-linked sodium hyaluronate (20 mg/ml) of non-animal origin and lidocaine hydrochloride (3 mg/ml) in a physiological phosphate buffer at pH 7. Its primary intended use is as an injectable biodegradable implant for the filling of fine lines, with lidocaine included to reduce local pain during the injection and enhance patient comfort. The product is designed for injection into the superficial to mid-dermis. The administration involves slow and controlled injection using a serial (micro) puncture technique, ensuring minimal pressure application and reducing the risk of complications.

2.4. Mixing Ratio: each 1 ml of the mixture contains.

- BONT-A: 0.72 ml.
- HA: 0.28 ml. without exceeding the amount of 0.0397 ml per single injection which can potentiate the supraorbital or supratrochlear artery occlusion [26].

2.5. Preparation Process

The two substances (BONT-A and HA) are drawn into separate syringes. A special syringe connector is used to link the two syringes. The contents are then re-infused between the syringes approximately 20 times to ensure thorough mixing

This study utilized the Cohesive Polydensified Matrix (CPM) technology to enhance the performance of our hyaluronic acid (HA) filler. This advanced technique involved creating a gel that combines high and low-density cross-linked HA zones within a cohesive structure. By incorporating CPM technology, we ensured that the HA gel maintained a high degree of cohesiveness, allowing for smooth and even distribution when injected. This approach not only provided structural support and flexibility but also mimicked the natural variations in skin tissues, leading to superior integration and longer-lasting results. The filler, designed for correcting fine lines, wrinkles, and volume loss, was administered using the blanching technique. This method ensured precise placement of the filler with minimal pressure application, reducing the risk of complications and resulting in natural-looking and enduring outcomes.

This hybrid formulation aims to leverage the muscle-relaxing effect of BONT-A and the skin-rejuvenation effect of HA.

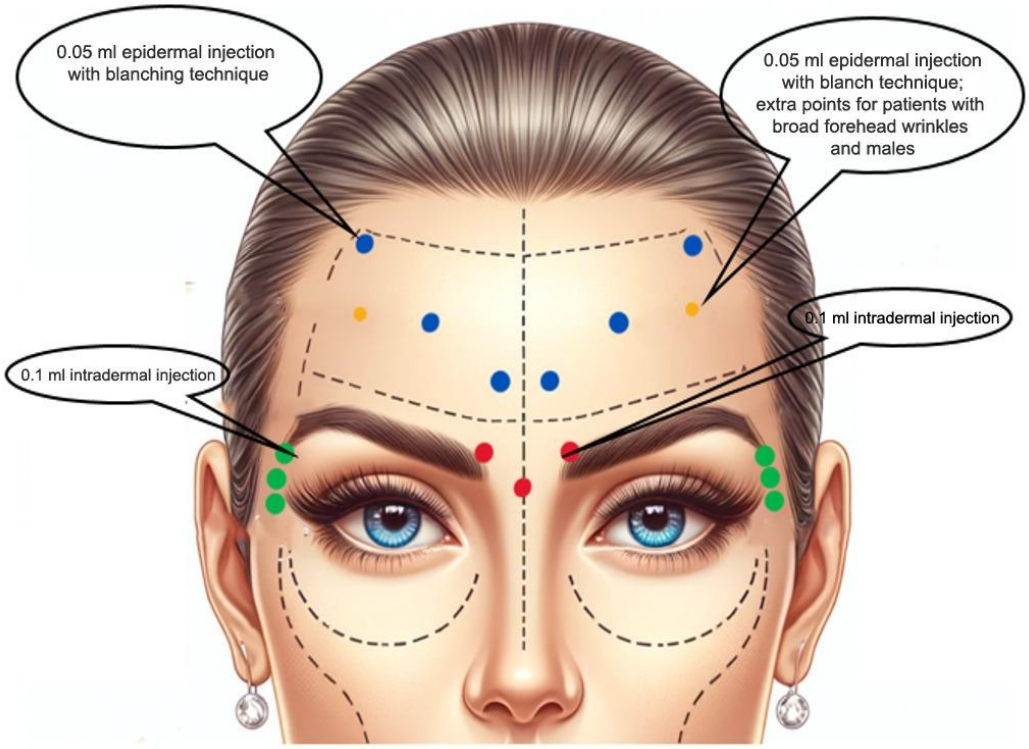


Figure 1.
Illustration showing the site and amount of the mixture injection at the upper part of the face.

Data Collection: Data were collected on patient demographics, specific details of the injection techniques used (dose, sites, depth), and any immediate reactions to the treatment. Follow-up data included assessments of rejuvenation effects and any delayed adverse reactions.

Ethical Approval: The study was conducted following the Declaration of Basrah Health Directorate's approval (No. 9787 dated 17/12/2022). Informed consent was obtained from all participants, ensuring they were aware of the nature of the study, the treatments involved, and their rights as participants.

2.6. Statistical Analysis

In our methodology, we used the chi-square test to examine associations between categorical variables, setting a significance threshold at $p < 0.05$. We applied a 95% confidence interval (CI) to ensure reliability, indicating a 95% certainty that the true effect size lies within the specified range. Data accuracy was rigorously verified, and the assumptions of the chi-square test were checked to maintain the robustness of our findings.

3. Results

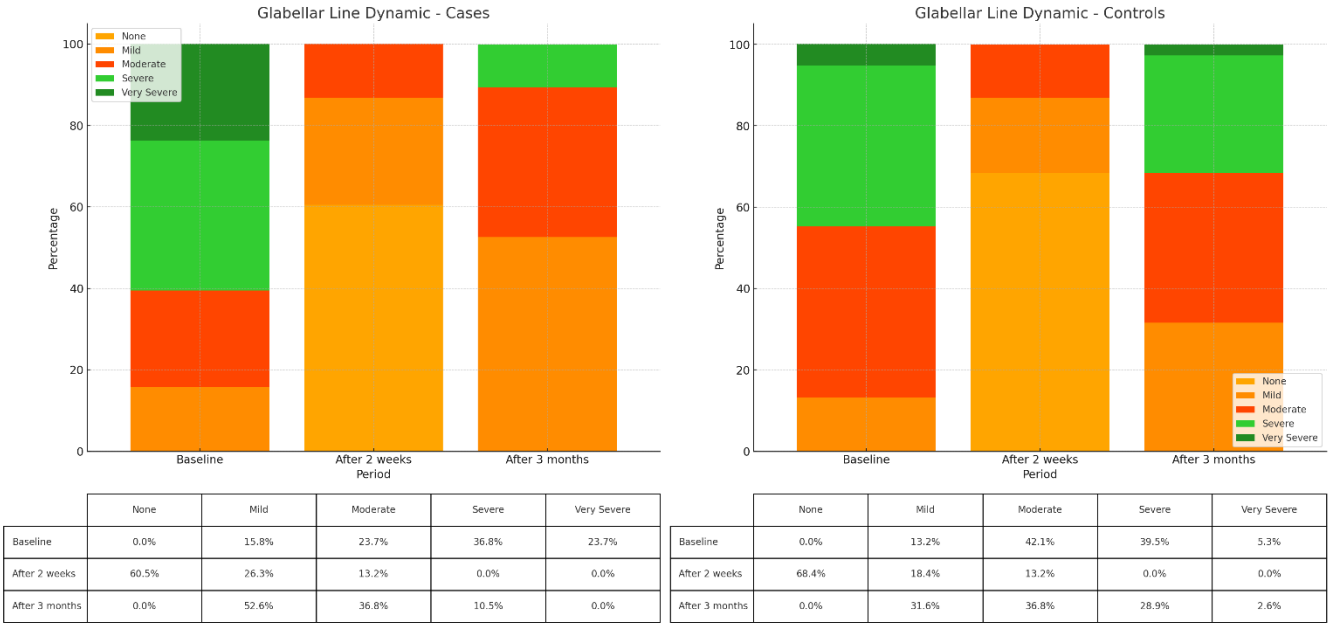
The demographical data presented in Table 1 reveals several significant and non-significant differences between the cases and controls across various variables. Age distribution between cases (mean 41.39±12.83 years) and controls (mean 41.74±12.28 years) shows no significant difference (P=0.906), indicating age homogeneity in both groups. However, a notable difference exists in the sex distribution, with males comprising 21.1% of cases compared to only 5.3% of controls (P=0.042), suggesting a higher prevalence of the condition under study among males in the case group. The usage of food supplements and cosmetics, as well as the use of sunblock, did not show significant differences between cases and controls, with P values of 0.454, 0.818, and 0.642 respectively.

Regarding skin phototypes, there is a predominance of phototype 4 in both groups, with 89.5% in cases and 81.6% in controls, but this difference is not statistically significant (P=0.556). Smoking habits show a significant difference; 39.5% of cases are smokers compared to 21.1% of controls (P=0.015), suggesting a possible association between smoking and the condition. The other categories of smoking (ex-smoker and non-smoker) also exhibit notable distribution patterns, with a higher percentage of non-smokers in the control group (71.1%) compared to cases (50.0%).

Table 1.
Demographical data distribution among the studied patients.

Variables		Cases	Controls	P value
Age (mean± SD) years		**41.39± 12.83**	**41.74± 12.28**	**0.906**
Sex	Male	8 (21.1%)	2 (5.3%)	0.042
	Female	30 (78.9%)	36 (94.7	
Food supplement	Yes	10 (26.3%)	13 (34.2%)	0.454
	No	28 (73.7%)	25 (65.8%)	
Skin phototypes	2	1 (2.6%)	1 (2.6%)	0.556
	3	3 (7.9%)	6 (15.8%)	
	4	34 (89.5%)	31 (81.6%)	
Use of sunblock	Yes	21 (55.3%)	23 (60.5%)	0.642
	No	17 (44.7%)	15 (39.5%)	
Use of cosmetics	Yes	21 (55.3%)	20 (52.6%)	0.818
	No	17 (44.7%)	18 (47.4%)	
Smoking	Smoker	15 (39.5%)	8 (21.1%)	0.015
	Ex-smoker	4 (10.5%)	3 (7.9%)	
	None	19 (50.0%)	27 (71.1%)	

This figure examines the dynamic glabellar lines in both cases and controls over three time periods: baseline, after 2 weeks, and after 3 months. At baseline, both groups are likely to have similar scores, indicating the initial severity of the lines. After 2 weeks, cases should show a significant reduction in scores compared to controls, reflecting the treatment's early effectiveness. At the 3-month mark, the scores for cases should further decrease or stabilize, while the controls may show less pronounced improvement or a return to baseline. This indicates that the treatment is effective in reducing dynamic glabellar lines in the short term and maintaining these effects over a longer period.

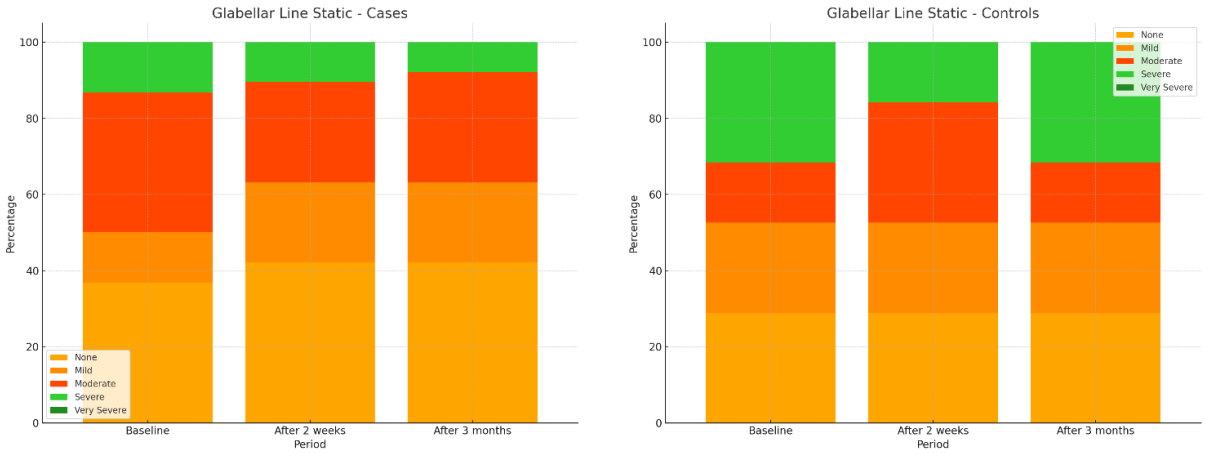


	None	Mild	Moderate	Severe	Very Severe
Baseline	0.0%	15.8%	23.7%	36.8%	23.7%
After 2 weeks	60.5%	26.3%	13.2%	0.0%	0.0%
After 3 months	0.0%	52.6%	36.8%	10.5%	0.0%

	None	Mild	Moderate	Severe	Very Severe
Baseline	0.0%	13.2%	42.1%	39.5%	5.3%
After 2 weeks	68.4%	18.4%	13.2%	0.0%	0.0%
After 3 months	0.0%	31.6%	36.8%	28.9%	2.6%

Figure 2.
Merz scale of Glabellar line dynamic at 3 periods (baseline, after 2 weeks, and after 3 months).

Static glabellar lines present a more persistent challenge. Baseline scores for both groups would initially be high. After 2 weeks, cases should exhibit a notable reduction in static line scores, whereas controls might show minimal change. By the 3-month evaluation, cases should maintain or further improve their scores, demonstrating sustained treatment efficacy. In contrast, controls are expected to show little to no significant change, highlighting the treatment's role in reducing static glabellar lines effectively over time.

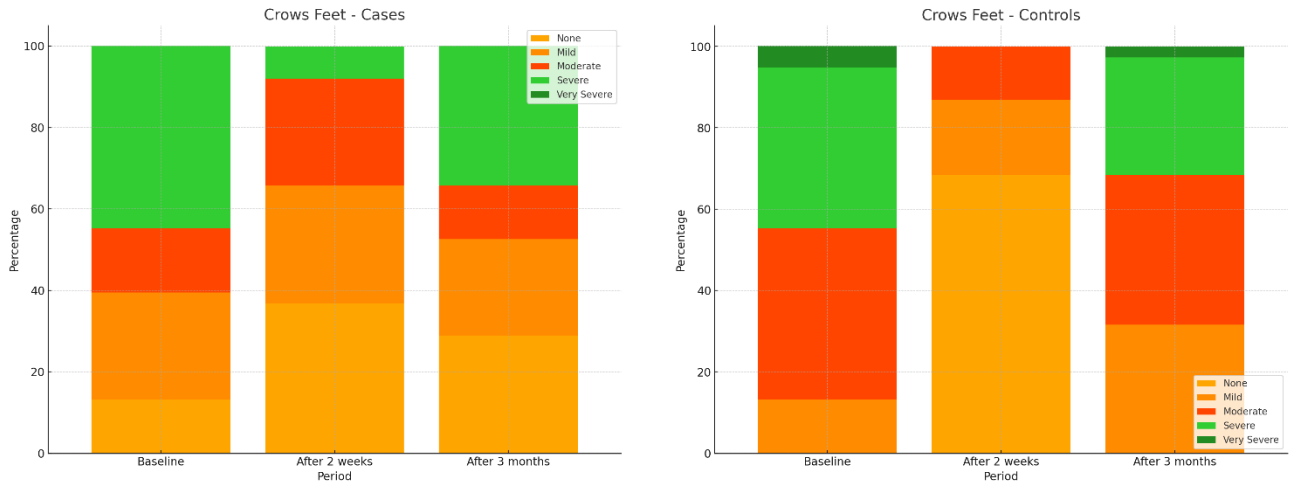


	None	Mild	Moderate	Severe	Very Severe
Baseline	36.8%	13.2%	36.8%	13.2%	0.0%
After 2 weeks	42.1%	21.1%	26.3%	10.5%	0.0%
After 3 months	42.1%	21.1%	28.9%	7.9%	0.0%

	None	Mild	Moderate	Severe	Very Severe
Baseline	28.9%	23.7%	15.8%	31.6%	0.0%
After 2 weeks	28.9%	23.7%	31.6%	15.8%	0.0%
After 3 months	28.9%	23.7%	15.8%	31.6%	0.0%

Figure 3.
Merz scale of Glabellar line static at 3 periods (baseline, after 2 weeks, and after 3 months).

For crow's feet, the baseline scores should be comparable between cases and controls, reflecting the initial condition of the fine lines. After 2 weeks, cases should show a significant reduction in scores, indicating a quick response to the treatment, while controls may exhibit minor changes. At the 3-month follow-up, cases are likely to maintain lower scores or improve further, whereas controls could see little change or a slight increase, underscoring the treatment's sustained impact on crow's feet reduction.

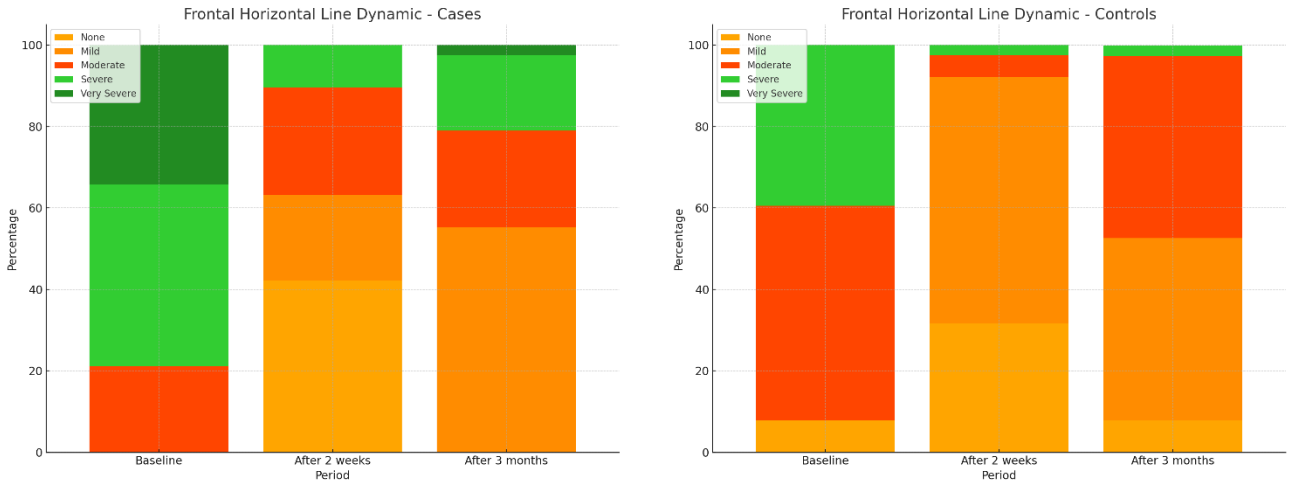


	None	Mild	Moderate	Severe	Very Severe
Baseline	13.2%	26.3%	15.8%	44.7%	0.0%
After 2 weeks	36.8%	28.9%	26.3%	7.9%	0.0%
After 3 months	28.9%	23.7%	13.2%	34.2%	0.0%

	None	Mild	Moderate	Severe	Very Severe
Baseline	0.0%	13.2%	42.1%	39.5%	5.3%
After 2 weeks	68.4%	18.4%	13.2%	0.0%	0.0%
After 3 months	0.0%	31.6%	36.8%	28.9%	2.6%

Figure 4.
Merz scale of Crows feet at 3 periods (baseline, after 2 weeks, and after 3 months).

Dynamic horizontal lines on the forehead are assessed in both groups. At baseline, scores should be similar for cases and controls. Following 2 weeks of treatment, cases are expected to show a marked reduction in scores, whereas controls might experience only slight changes. By 3 months, cases should exhibit continued improvement or stability in scores, demonstrating long-term benefits, while controls are unlikely to show significant reductions, highlighting the efficacy of the treatment in smoothing dynamic forehead lines.

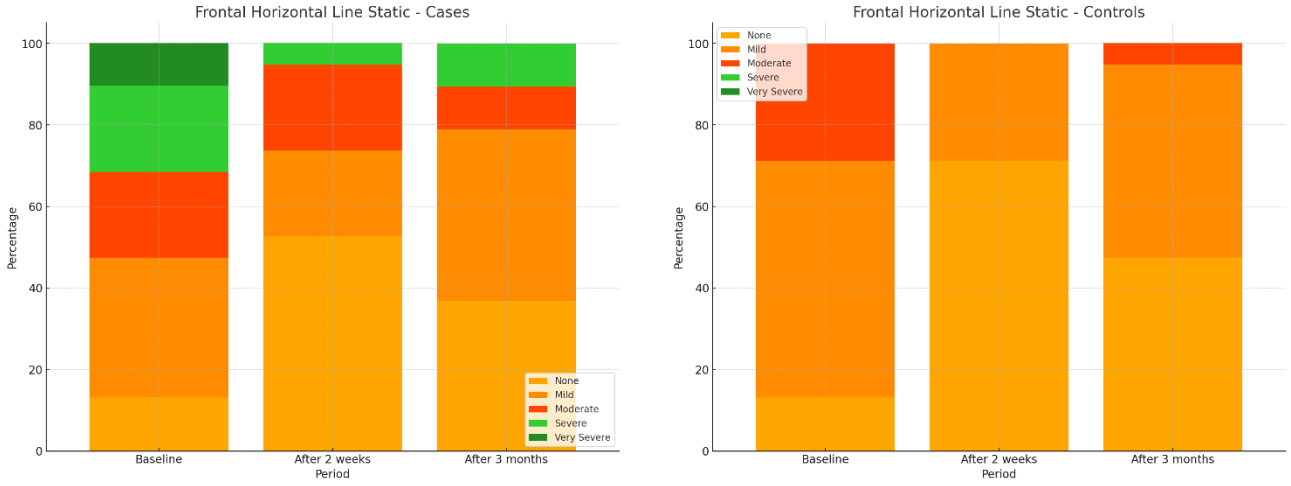


	None	Mild	Moderate	Severe	Very Severe
Baseline	0.0%	0.0%	21.1%	44.7%	34.2%
After 2 weeks	42.1%	21.1%	26.3%	10.5%	0.0%
After 3 months	0.0%	55.3%	23.7%	18.4%	2.6%

	None	Mild	Moderate	Severe	Very Severe
Baseline	7.9%	0.0%	52.6%	39.5%	0.0%
After 2 weeks	31.6%	60.5%	5.3%	2.6%	0.0%
After 3 months	7.9%	44.7%	44.7%	2.6%	0.0%

Figure 5.
Merz scale of Frontal horizontal line dyanmic at 3 periods (baseline, after 2 weeks, and after 3 months).

Static horizontal forehead lines, persistent even without facial movement, show initial high scores in both groups. After 2 weeks, cases should display significant score reductions, indicating early treatment effectiveness, while controls may show little change. At the 3-month mark, cases are expected to maintain lower scores or show further improvement, while controls might not exhibit significant differences from their baseline scores. This comparison underscores the treatment's effectiveness in reducing even the most persistent static lines over time.



	None	Mild	Moderate	Severe	Very Severe
Baseline	13.2%	34.2%	21.1%	21.1%	10.5%
After 2 weeks	52.6%	21.1%	21.1%	5.3%	0.0%
After 3 months	36.8%	42.1%	10.5%	10.5%	0.0%

	None	Mild	Moderate	Severe	Very Severe
Baseline	13.2%	57.9%	28.9%	0.0%	0.0%
After 2 weeks	71.1%	28.9%	0.0%	0.0%	0.0%
After 3 months	47.4%	47.4%	5.3%	0.0%	0.0%

Figure 6.
Merz scale of Frontal horizontal line static at 3 periods (baseline, after 2 weeks, and after 3 months).

Table 2 examines the complications among cases and controls, highlighting the incidence of minor adverse effects. Bruises at the injection site occurred in 2.6% of cases and 5.3% of controls, which is not statistically significant (P=0.210). Eyebrow asymmetry and mild erythema were observed at identical rates in both groups (2.6% in cases and 5.3% in controls), while eyebrow ptosis was reported in 2.6% of controls and none of the cases. Mild local swelling was more common in cases (5.3%) compared to controls (0.0%), indicating a slightly higher complication rate in the cases, although these differences are not statistically significant.

Table 2.
Complications among cases and controls.

Variables	Cases	Controls	P value
Bruises at the site of injection	**1 (2.6%)**	**2 (5.3%)**	0.210
Eyebrow asymmetry	1 (2.6**%**)	2 (5.3**%**)	
Eyebrow ptosis	0 (0.0**%**)	1 (2.6**%**)	
Mild erythema	1 (2.6**%**)	2 (5.3**%**)	
Mild local swelling	2 (5.3**%**)	0 (0.0**%**)	

Patient satisfaction data in Table 3 reveals a stark contrast between cases and controls. Among cases, 18.4% were satisfied, and a significant majority (81.6%) were very satisfied. In contrast, the control group had 57.9% satisfied and 42.1% very satisfied. This difference is highly significant (P<0.001), indicating a higher level of satisfaction among the cases, which could imply a better outcome or perceived effectiveness of the treatment under study for this group.

Table 3.
Patient satisfaction among cases and controls.

Variables		Cases	Controls	P value
Satisfaction	Satisfied	7 (18.4	22 (57.9	<0.001
	Very satisfied	31 (81.6	16 (42.1	

4. Discussion

4.1. Demographic and Baseline Characteristics

Evidence-based medicine suggests that an ideal study would examine all treated patients in a consecutive fashion, and a no-exclusion criterion may lead to a higher response [27]. In a practical environment, however, providing no patient exclusion can lead to confounding factors that interfere with the results including autoimmune diseases, bleeding tendency, infection, inflammation, cancer, and previous procedures in the last 6 months. Evaluation of outcomes was done on a course of 12 weeks. Any longer follow-up may risk having lower response rates due to a lack of motivation to stay in longer studies among patients [28, 29] especially when treatment alternatives are continuously being introduced to the market, mostly directing the age group enrolled in this study.

The results exhibited an association between smoking and the need for facial rejuvenation. This might be attributed to the idea that smoking contributes to an older appearance, especially when associated with other factors including general health. This has been reported previously with an establishment of an association between the number of years of smoking and the cumulative increase in perceived age [30]. Skin aging caused by smoking is primarily driven by oxidative stress and impaired cellular functions [31]. Smoking promotes the expression of matrix metalloproteinase-1 (MMP1), an enzyme that degrades collagen, further contributing to wrinkle formation. Consequently, smokers often exhibit pronounced facial wrinkles, particularly around the mouth and eyes, and altered skin hue and radiance, signs of accelerated skin aging [3].

A note must be taken regarding the validity of patient satisfaction score as it can be limited by patients' expectations and perceptions of the treatment. Fluctuations in patient response may also result from the timing of score recording [32]. For future investigations, a better interpretation of results can be achieved by evaluating psychological factors prior to any intervention

4.2. Treatment Efficacy

The youthful convexity of the forehead can be altered by two main mechanisms, as reported in the literature. Firstly, skin thinning and repetitive muscle movements (frontal muscle and glabellar complex) play a major role in the emergence of lines and thin wrinkles which are then augmented by volume reduction happening due to bone reabsorption, and loss or thinning of fat compartments [33]. Although the use of botulinum toxin has long-established efficacy in the treatment of dynamic and static glabellar lines, there is still a need for volume replacement to restore the area's natural look, which is accounted by the use of Hyaluronic acid, as stated by Sadick et al. in their study on the role of the adipose system in facial aging and approaches to volume restoration [34].

The superior efficacy of the hybrid treatment was highlighted by the more pronounced and sustained reduction in scores of the treated group, mostly due to the addition of Hyaluronic acid. Studies have established that Hyaluronic acid can potentially cause an increase in the production of collagen and elastic fiber, which subsequently leads to restoring the extracellular matrix through directly stimulating and/or mechanically stretching fibroblasts [35, 36]. This can explain the early treatment effectiveness and may lead to prolongation of treatment effects beyond the 3-month mark.

Botulinum toxin A alone is established as a good treatment option for patients having only dynamic lines. Static lines emerge as a challenging condition and require the use of hyaluronic acid to fill the lines thoroughly, making them visually appealing or even absent. Moreover, according to a study by Nanda et al., fillers can stay longer in combined with botulinum toxin A injections, as there is minimal muscle movement [37]. This can consequently prolong the treatment outcomes and reduce injection frequency.

Crow's feet affect patient satisfaction greatly especially among females, as it affects facial appearance making it look angry, sad, or unattractive [38]. As for the hybrid treatment, the improvement pattern was similar to that of glabellar lines. In the studies by Carruthers et al. and Beer et al., similar results were reported with maximum improvement in 1 month and

persistent results up to 6 months [38, 39]. Similarly, effectiveness is also established in the case of horizontal forehead lines.

In the past, doctors administered hyaluronic acid and Botox injections separately, never combining them in a single syringe. This was considered best practice due to concerns about potential interactions and the different injection techniques required for each product. For instance, HA fillers are typically injected deeper into the dermis to provide volume and support, whereas Botox is injected superficially into the muscles to achieve muscle relaxation [40]. In a parallel study on neck rejuvenation, by Pecora [41] researchers investigated the combined use of botulinum toxin and hyaluronic acid, which were diluted in a single syringe and injected into the same layer. Their findings indicated faster results, enhanced final outcomes, increased patient satisfaction, and improved ease of the procedure for both patients and clinicians [42]. This aligns with the findings of the present study. Furthermore, combining hyaluronic acid (HA) and Botox in a single syringe and administering them intradermally offers several advantages. It allows for targeted delivery, effectively weakening superficial muscle fibers attached to the dermis. This approach helps smooth skin creases and enhances skin texture[43]. In addition, a single injection offers several benefits. It minimizes patient discomfort by reducing the number of needle pricks required. For clinicians, it streamlines the procedure, saving time and improving overall efficiency in the clinic [44].

5. Conclusion

The demand for facial rejuvenation is increasing, in all age groups. At the same session, Botulinum toxin type A administration was successfully combined with Hyaluronic acid filler for facial rejuvenation. This study found that when hyaluronic acid and Botox are combined in the precise concentrations mentioned in this study, and injected intradermally, showed greater potential as an anti-aging therapy compared to using Botulinum toxin alone. This was evidenced by increased patient satisfaction, improved efficacy, enhanced safety, and minimal side effects. However, improper concentrations and levels of injection could potentially result in unsafe or ineffective outcomes.

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