




Original Article

Efficacy and Safety of Intradermal Botulinum Toxin Type A versus Normal Saline in Atrophic Post-Acne Facial Scars: A Single-Blind Split-Face Placebo-Controlled Study

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ABSTRACT

Background: Atrophic post-acne facial scars are cosmetically distressing and often difficult to treat. Botulinum toxin type A has been proposed as a potential therapeutic option through its effects on muscular tension and dermal remodelling.

Aim: To evaluate the efficacy and safety of intradermal botulinum toxin type A compared with normal saline in patients with atrophic post-acne facial scars.

Methods: This prospective, single-blind, split-face, placebo-controlled study included 30 patients with bilateral atrophic post-acne facial scars. One side of the face was randomized to receive intradermal botulinum toxin type A, while the contralateral side received normal saline. Injections were administered at baseline and repeated at 4 weeks. Outcomes were assessed at 8 weeks using the ECCA quantitative score, Goodman and Baron qualitative grading, patient self-assessment, independent observer photographic assessment, pain scores, and adverse-event monitoring.

Results: The mean ECCA score decreased from 199.50 to 195.33 on the botulinum toxin side and from 199.17 to 196.00 on the normal saline side. The reductions were not statistically significant, and no significant between-side difference was observed. Goodman and Baron grading improved significantly within both sides, but botulinum toxin did not show superiority over saline. Patient-reported improvement, observer assessment, and pain scores were comparable between groups. One patient developed transient angle-of-mouth asymmetry, which resolved without intervention.

Conclusion: Intradermal botulinum toxin type A produced mild improvement in atrophic post-acne facial scars but was not significantly superior to normal saline at 8 weeks.

Keywords: Acne scars; atrophic scars; botulinum toxin type A; ECCA score; split-face study.

INTRODUCTION

Acne vulgaris is a common inflammatory disorder of the pilosebaceous unit and may result in persistent scarring even after the active disease has subsided. Post-acne scarring is clinically important because it is often permanent, cosmetically distressing, and may affect self-esteem and social functioning; early clinical evaluation studies have shown that residual acne scarring is a frequent sequela among patients with acne [1]. Atrophic acne scars are the most common form of post-acne scarring and are believed to arise from dermal inflammation followed by disordered wound healing, extracellular matrix degradation, and inadequate collagen replacement, leading to visible depression of the skin surface [2].

Atrophic post-acne scars are commonly classified according to morphology into icepick, rolling, and boxcar scars. This distinction is clinically relevant because different scar types vary in depth, width, tethering, and response to treatment,

making careful baseline scar characterization essential before therapeutic intervention [3]. In addition to morphological classification, standardized severity assessment is necessary to objectively document treatment response. The Goodman and Baron qualitative grading system provides a simple global assessment of post-acne scarring severity and is useful for clinical categorization and communication [4]. The ECCA grading scale is a validated quantitative tool that assigns weighted scores according to scar type and number, allowing more structured measurement of scar burden and change over time [5].

Several treatment modalities have been used for atrophic acne scars, including chemical reconstruction, dermabrasion, microneedling, subcision, fractional lasers, radiofrequency devices, fillers, punch techniques, and combination procedures. However, no single modality is universally effective for all scar types, and treatment choice is often influenced by scar morphology, skin type, cost, availability, downtime, and risk of adverse effects. A Cochrane review concluded that the evidence base for many acne scar interventions remains limited by small sample sizes, heterogeneity of methods, and variable outcome measures, highlighting the need for well-designed controlled studies [6].

Botulinum toxin type A has traditionally been used for chemodenervation in aesthetic and therapeutic indications, but increasing attention has been given to its possible role in scar modulation. Proposed mechanisms include reduction of dynamic muscular tension across scars, modulation of fibroblast activity, and effects on collagen remodelling and wound-healing pathways [7]. In relation to post-acne and traumatic scarring, botulinum toxin has been explored as a primary or adjunctive treatment, but available evidence remains limited, and questions persist regarding optimal dose, route of administration, durability of response, and true treatment effect beyond placebo or needling-related improvement [8].

Therefore, the present single-blind split-face placebo-controlled study was undertaken to evaluate the efficacy and safety of intradermal botulinum toxin type A compared with normal saline in patients with atrophic post-acne facial scars. By using each patient as his or her own control and assessing outcomes with ECCA quantitative scoring, Goodman and Baron qualitative grading, patient-reported improvement, independent observer photographic assessment, pain scores, and adverse-event monitoring, this study aimed to determine whether intradermal botulinum toxin provides clinically meaningful benefit over placebo injection

AIM

To evaluate the efficacy and safety of intradermal botulinum toxin type A compared with normal saline in patients with atrophic post-acne facial scars.

OBJECTIVES

- To compare the change in acne scar severity from baseline to 8 weeks on the botulinum toxin-treated and normal saline-treated sides using the ECCA quantitative score and Goodman and Baron qualitative grading.
- To compare patient-reported improvement and independent observer assessment of standardized clinical photographs between the botulinum toxin-treated and normal saline-treated sides.
- To evaluate tolerability and safety of intradermal botulinum toxin by assessing injection pain scores and treatment-emergent adverse events.

METHODS

Study design and setting

This prospective, single-blind, split-face, placebo-controlled study was conducted in the outpatient department of dermatology at a tertiary teaching institute between February 2012 and July 2013. The study was initiated after approval from the institutional ethics committee. Written informed consent was obtained from all participants before enrolment.

Study population

Thirty patients with atrophic post-acne facial scars involving the cheeks were included. Eligible participants were aged 18–40 years and were willing to participate in the study. Patients with active facial acne, a history of keloids, pregnancy or lactation, neuromuscular junction disorders such as myasthenia gravis, systemic aminoglycoside therapy, a history of radiotherapy or chemotherapy, haematological disorders, or known sensitivity to botulinum toxin were excluded.

Baseline assessment

At enrolment, demographic details, duration of acne and acne scars, treatment history, relevant medical history, and menstrual history in female participants were recorded. A general and neurological examination was performed to exclude clinically evident neuromuscular disease. Cutaneous examination of both cheeks included assessment of scar type, number and distribution. Atrophic scars were classified clinically as icepick, rolling or boxcar scars.

Clinical severity was assessed separately for each side of the face using the Goodman and Baron qualitative grading system and the ECCA quantitative acne scar grading system. In the Goodman and Baron system, scars were graded from

1 to 4, corresponding to macular, mild, moderate and severe scarring. For ECCA scoring, atrophic scars were categorized as V-shaped, U-shaped or M-shaped scars, with additional assessment for superficial elastolysis. A weighted score was calculated for each side according to the number and morphology of scars.

Standardised clinical photography

Standardised clinical photographs were obtained at baseline and at 8 weeks using a Canon PowerShot SX40 camera mounted on a stereotactic photographic device. The device provided a fixed chin rest and a rotating camera arm to maintain uniform patient positioning, camera distance and angle. Frontal and lateral views were recorded under comparable conditions at each visit.

Randomisation, blinding and intervention

Each participant served as his or her own control. The side of the face assigned to receive botulinum toxin type A was determined by lottery method; the contralateral side received normal saline placebo. Participants were blinded to the side allocation.

Botulinum toxin type A was reconstituted with 2.5 mL of normal saline per 100-unit vial. The dose administered was based on the clinical severity of scarring: 10 units for mild scarring and 15–20 units for moderate to severe scarring. In areas dominated by icepick scars, aliquots were distributed intradermally at approximately 1-cm staggered intervals to cover the scarred cheek area. For larger rolling or boxcar scars, 1 unit was injected into the scar; when several larger scars were present in close proximity, 1 unit was injected into the comparatively larger scar.

Injections were administered intradermally with the needle held at approximately 30 degrees to the skin surface, producing a subepidermal wheal. An equal volume of normal saline was injected intradermally into corresponding scars on the opposite side using the same technique. Injections were administered at baseline and repeated after 4 weeks. After each procedure, participants were advised not to rub the face and to avoid heavy physical activity for the next 2 days.

Outcome measures

The primary efficacy outcome was change in ECCA quantitative score from baseline to 8 weeks on the botulinum toxin-treated side compared with the normal saline-treated side. Secondary efficacy outcomes included change in Goodman and Baron qualitative grade, patient self-assessment, and independent observer assessment of clinical photographs.

Patient self-assessment was recorded separately for each side of the face using a 3-point scale: 0, not satisfied; 1, slightly or somewhat satisfied; and 2, highly satisfied. Independent observer assessment was performed using baseline and 8-week clinical photographs and was graded on a 5-point scale: 0, no improvement; 1, poor improvement (<25%); 2, mild improvement (25–50%); 3, moderate improvement (51–75%); and 4, excellent improvement (>75%).

Tolerability was assessed by recording injection-related pain separately for the botulinum toxin and normal saline sides after each treatment session using a 0–10 numerical pain scale. The mean pain score of the two treatment sessions was used for analysis. Safety was assessed by documenting adverse events during follow-up and by instructing participants to report earlier if any treatment-related symptoms occurred.

Statistical analysis

Data were analysed using SPSS version 15. Continuous variables were summarised as mean, standard deviation and range, while categorical variables were expressed as frequencies and percentages. Paired within-side comparisons between baseline and 8-week scores were performed using the Wilcoxon signed-rank test. Paired comparisons between the botulinum toxin and normal saline sides were performed for efficacy and tolerability outcomes. A p value of less than 0.05 was considered statistically significant.

Assessment schedule

| Assessment | Baseline | 4 weeks | 8 weeks |
|--|----------|-----------|---------|
| Clinical examination and scar classification | Yes | Follow-up | Yes |
| Goodman and Baron qualitative grading | Yes | — | Yes |
| ECCA quantitative grading | Yes | — | Yes |
| Standardised photography | Yes | — | Yes |
| Botulinum toxin/normal saline injection | Yes | Yes | — |
| Patient self-assessment | — | — | Yes |
| Independent observer assessment | — | — | Yes |
| Pain and adverse-event assessment | Yes | Yes | Yes |

RESULTS

Study population

Thirty patients with atrophic post-acne facial scars were included in the study. The age of the patients ranged from 18 to 36 years, with a mean age of 24 years. Twenty-one patients (70.0%) were male and nine (30.0%) were female, giving a male-to-female ratio of 2.33:1. The majority of patients were in the 21–30-year age group (23/30, 76.7%).

The duration of acne scarring ranged from 0.5 to 10 years, with a mean duration of 3.87 ± 2.80 years. Twenty patients (66.7%) had acne scars for 4 years or less.

Table 1. Baseline demographic and disease characteristics

| Characteristic | Value |
|------------------------------|-------------------------|
| Number of patients | 30 |
| Age range | 18–36 years |
| Mean age | 24 years |
| Male sex | 21 (70.0%) |
| Female sex | 9 (30.0%) |
| Male:female ratio | 2.33:1 |
| Most common age group | 21–30 years: 23 (76.7%) |
| Duration of acne scars | 0.5–10 years |
| Mean duration of acne scars | 3.87 ± 2.80 years |
| Scar duration ≤ 4 years | 20 (66.7%) |

Baseline scar characteristics

At baseline, icepick scars were the predominant morphological type, followed by rolling scars and boxcar scars. The mean number of icepick scars was 113 on the right side and 121 on the left side. The corresponding mean counts for rolling scars were 38 and 37, and for boxcar scars were 33 and 37, respectively.

Baseline ECCA scores were comparable between treatment sides. The mean baseline ECCA score was 199.50 on the botulinum toxin side and 199.17 on the normal saline side. By Goodman and Baron qualitative grading, 24 patients (80.0%) had grade 3 or 4 scarring on each side at baseline.

Table 2. Baseline scar characteristics

| Variable | Botulinum toxin side | Normal saline side |
|---|----------------------|--------------------|
| Mean baseline ECCA score | 199.50 | 199.17 |
| Goodman and Baron grade 1/2 at baseline | 6 (20.0%) | 6 (20.0%) |
| Goodman and Baron grade 3/4 at baseline | 24 (80.0%) | 24 (80.0%) |
| Predominant scar morphology | Icepick scars | Icepick scars |

Treatment allocation and dose

Botulinum toxin was injected on the right side in 21 patients (70.0%) and on the left side in nine patients (30.0%); the contralateral side received normal saline. The dose of botulinum toxin was selected according to scar severity. Eight patients (26.7%) received 10 units, 16 patients (53.3%) received 15 units, and six patients (20.0%) received 20 units.

Table 3. Treatment allocation and botulinum toxin dose

| Variable | Number of patients (%) |
|---|------------------------|
| Right side treated with botulinum toxin | 21 (70.0%) |
| Left side treated with botulinum toxin | 9 (30.0%) |
| Botulinum toxin dose: 10 units | 8 (26.7%) |
| Botulinum toxin dose: 15 units | 16 (53.3%) |
| Botulinum toxin dose: 20 units | 6 (20.0%) |

Clinical efficacy outcomes

At 8 weeks, the mean ECCA score decreased from 199.50 to 195.33 on the botulinum toxin side, corresponding to a mean reduction of 4.17 points; this change did not reach statistical significance ($p=0.063$). On the normal saline side, the mean ECCA score decreased from 199.17 to 196.00, corresponding to a mean reduction of 3.17 points; this change was also not statistically significant ($p=0.066$). The magnitude of reduction in ECCA score was not significantly different between the two sides. The trend in mean ECCA score over time is shown in Figure 1.

Table 4. Change in ECCA score from baseline to 8 weeks

| Outcome | Botulinum toxin side | Normal saline side |
|-----------------------------|---|------------------------|
| Baseline mean ECCA score | 199.50 | 199.17 |
| 8-week mean ECCA score | 195.33 | 196.00 |
| Mean reduction | 4.17 | 3.17 |
| Within-side p value | 0.063 | 0.066 |
| Between-side interpretation | No significant superiority over normal saline | Reference/control side |

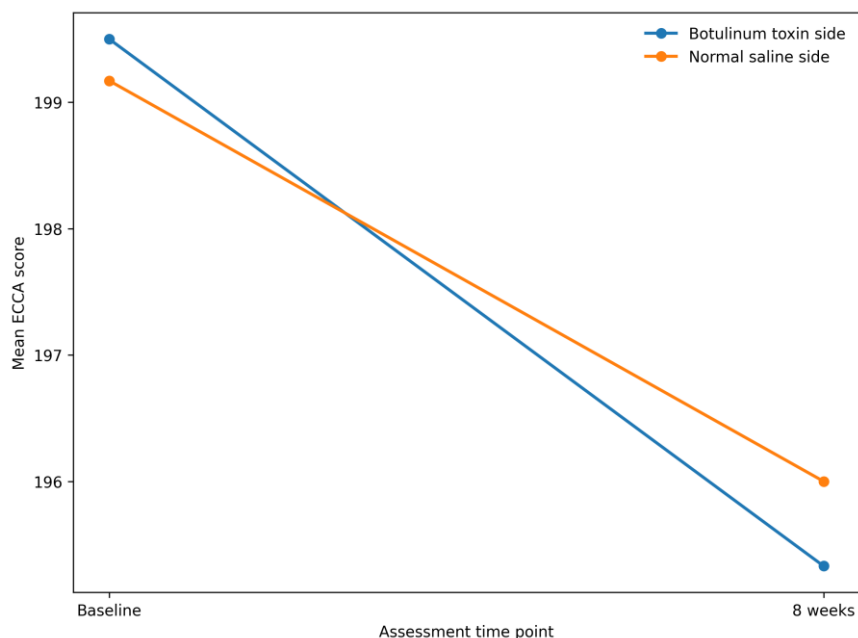


Figure 1. Change in mean ECCA score from baseline to 8 weeks on the botulinum toxin and normal saline sides.

Goodman and Baron qualitative grading showed significant within-side improvement on both sides. On the botulinum toxin side, grade 3/4 scarring decreased from 24 patients (80.0%) at baseline to 21 patients (70.0%) at 8 weeks, with three patients improving from grade 3/4 to grade 1/2 (p=0.034). On the normal saline side, grade 3/4 scarring decreased from 24 patients (80.0%) to 19 patients (63.3%), with five patients improving from grade 3/4 to grade 1/2 (p=0.014). The between-side comparison did not demonstrate a statistically significant advantage for botulinum toxin. The distribution of Goodman and Baron grades at baseline and 8 weeks is presented in Figure 2.

Table 5. Goodman and Baron qualitative grade distribution at baseline and 8 weeks

| Grade | BT baseline | BT 8 weeks | NS baseline | NS 8 weeks |
|---------------------|-------------|------------|-------------|------------|
| Grade 1 | 0 (0.0%) | 1 (3.3%) | 1 (3.3%) | 3 (10.0%) |
| Grade 2 | 6 (20.0%) | 8 (26.7%) | 5 (16.7%) | 8 (26.7%) |
| Grade 3 | 5 (16.7%) | 4 (13.3%) | 7 (23.3%) | 4 (13.3%) |
| Grade 4 | 19 (63.3%) | 17 (56.7%) | 17 (56.7%) | 15 (50.0%) |
| Grade 3/4 total | 24 (80.0%) | 21 (70.0%) | 24 (80.0%) | 19 (63.3%) |
| Within-side p value | — | 0.034 | — | 0.014 |

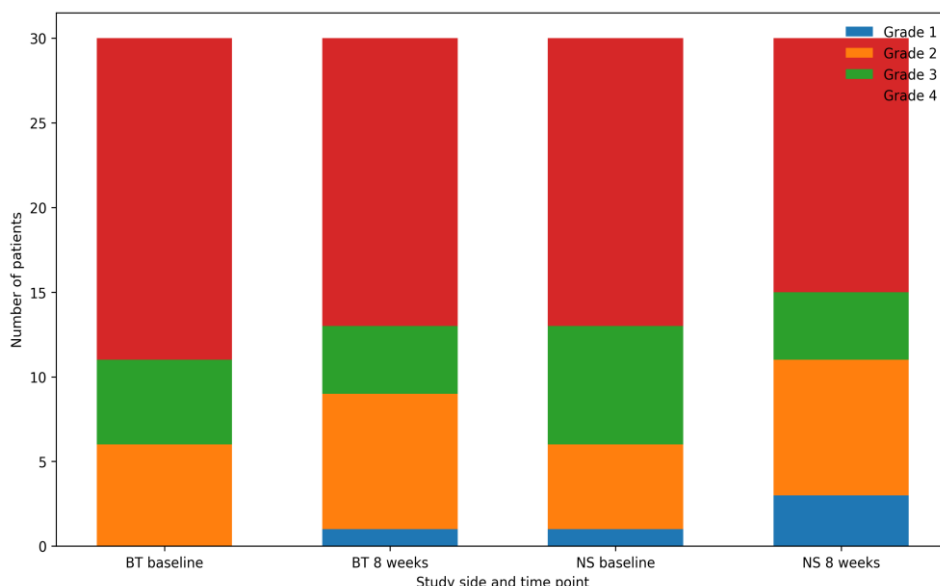


Figure 2. Distribution of Goodman and Baron qualitative grades at baseline and 8 weeks on the botulinum toxin and normal saline sides.

Patient and observer assessments

On patient self-assessment, 24 patients (80.0%) reported slight or some improvement on the botulinum toxin side, while six patients (20.0%) were not satisfied. On the normal saline side, 22 patients (73.3%) reported slight or some improvement and eight patients (26.7%) were not satisfied. No patient reported high satisfaction on either side. The difference in patient-reported improvement between the two sides was not statistically significant.

Independent observer assessment of standardized clinical photographs showed poor improvement in 15 patients (50.0%), mild improvement in 12 patients (40.0%), and moderate improvement in three patients (10.0%) on the botulinum toxin side. On the normal saline side, poor improvement was observed in 16 patients (53.3%), mild improvement in 12 patients (40.0%), and moderate improvement in two patients (6.7%). No patient showed excellent improvement on either side. The difference between treatment sides was not statistically significant ($p=0.367$).

Table 6. Patient-reported and independent observer assessments at 8 weeks

| Assessment | Botulinum toxin side | Normal saline side |
|---|----------------------|--------------------|
| Patient not satisfied | 6 (20.0%) | 8 (26.7%) |
| Patient slightly/somewhat satisfied | 24 (80.0%) | 22 (73.3%) |
| Patient highly satisfied | 0 (0.0%) | 0 (0.0%) |
| Observer: no improvement | 0 (0.0%) | 0 (0.0%) |
| Observer: poor improvement (<25%) | 15 (50.0%) | 16 (53.3%) |
| Observer: mild improvement (25–50%) | 12 (40.0%) | 12 (40.0%) |
| Observer: moderate improvement (51–75%) | 3 (10.0%) | 2 (6.7%) |
| Observer: excellent improvement (>75%) | 0 (0.0%) | 0 (0.0%) |
| Observer assessment p value | 0.367 | 0.367 |

Tolerability and safety

The mean injection pain score was 4.69 ± 0.57 on the botulinum toxin side and 4.53 ± 0.64 on the normal saline side. The difference in pain scores between the two sides was not statistically significant.

One patient (3.3%) developed asymmetry of the angle of the mouth, which became evident six days after the baseline injection and was more prominent during smiling. The event was attributed to possible diffusion of botulinum toxin into the intramuscular plane, with partial involvement of the orbicularis oris muscle. The asymmetry improved over one month without active intervention, and the second injection was delayed by 15 days. No other treatment-emergent adverse event was reported.

Table 7. Tolerability and adverse events

| Variable | Botulinum toxin side | Normal saline side |
|----------|----------------------|--------------------|
|----------|----------------------|--------------------|

| | | |
|----------------------------------|------------------------------------|-------------------------------|
| Mean pain score | 4.69 ± 0.57 | 4.53 ± 0.64 |
| Pain score range | 3.5–5.5 | 3.5–5.5 |
| Pain-score comparison | Not statistically significant | Not statistically significant |
| Treatment-emergent adverse event | 1 (3.3%) | 0 (0.0%) |
| Type of adverse event | Transient angle-of-mouth asymmetry | None |

Summary of results

In this single-blind split-face placebo-controlled study, intradermal botulinum toxin type A produced mild improvement in atrophic post-acne facial scars; however, the magnitude of improvement was not significantly greater than that observed after normal saline injection. ECCA score reduction was small and not statistically significant on either side. Goodman and Baron grading improved significantly within both sides, but the normal saline side showed a numerically greater shift from grade 3/4 to grade 1/2 scarring. Patient-reported improvement, independent observer assessment, and pain scores did not differ significantly between treatment sides. Botulinum toxin was generally well tolerated, with one transient adverse event.

DISCUSSION

In this single-blind split-face placebo-controlled study, intradermal botulinum toxin type A produced only mild improvement in atrophic post-acne facial scars and was not significantly superior to normal saline. The mean ECCA score decreased from 199.50 to 195.33 on the botulinum toxin side and from 199.17 to 196.00 on the saline side at 8 weeks, with no significant between-side difference. Although Goodman and Baron grading improved significantly within both sides, the improvement was not greater with botulinum toxin. Patient satisfaction, independent observer assessment, and pain scores were also comparable between treatment sides. Thus, the observed benefit appears modest and may partly reflect the effect of repeated intradermal needling and injection rather than a specific pharmacological effect of botulinum toxin.

The comparable response on the saline side is consistent with the findings of Gandhi and Makhecha, who compared intralesional platelet-rich plasma with normal saline in a split-face study of acne scars. They observed significant improvement on both sides, but no significant intergroup difference, suggesting that mechanical effects of injection, including dermal stimulation and subcision-like separation, may contribute to clinical improvement independent of the injected agent [9]. This is relevant to the present study because both sides received repeated intradermal injections, which may have induced minor collagen remodelling or scar release.

Our findings differ from those of Ebrahim et al., who reported better outcomes when botulinum toxin was applied topically after microneedling. In their split-face study, microneedling followed by botulinum toxin produced 70% overall improvement, whereas the saline side showed only mild improvement in 50% of patients [10]. The stronger response in that study may be attributable to the combined effect of microneedling-induced dermal remodelling and enhanced transcutaneous delivery of botulinum toxin through microchannels. In contrast, the present study evaluated intradermal botulinum toxin alone, and most patients had predominantly icepick scars, which are structurally deep and less likely to respond to neuromodulation or superficial dermal relaxation.

Scar morphology probably influenced the limited efficacy observed in this study. Icepick scars were the predominant scar type, and these scars often require focal reconstructive procedures rather than diffuse intradermal therapy. In a study of 100% trichloroacetic acid CROSS for icepick acne scars, Khunger et al. reported excellent improvement in 73.3% and good improvement in 20% of patients after four sessions [11]. In comparison, observer assessment in the present study showed only poor improvement in 50%, mild improvement in 40%, and moderate improvement in 10% on the botulinum toxin side, with no excellent responses. This suggests that botulinum toxin is unlikely to be an optimal monotherapy for icepick-predominant scarring.

Compared with established collagen-induction procedures, the effect size in the present study was also smaller. Alam et al. conducted a randomized split-face trial of microneedling and reported a significant reduction in acne scar scores at 6 months, with participants perceiving a mean 41% improvement and no adverse events [12]. Chandrashekar et al. evaluated microneedling fractional radiofrequency in grade 3 and 4 acne scars and found that 80.64% of patients improved by two qualitative grades, while 19.35% improved by one grade [13]. These outcomes are more substantial than the small ECCA reduction and limited grade shift observed in the present study, indicating that procedures producing controlled dermal injury and neocollagenesis may be more effective than botulinum toxin injection alone.

The present results are also less marked than those reported with subcision and fractional laser resurfacing. Alam et al. reported improvement in 90% of patients treated with subcision, with a mean overall improvement of 51% among responders [14]. Vaishnani similarly reported 40–80% improvement in rolling acne scars treated with needle subcision [15]. Fractional laser studies have also shown higher response rates; Alajlan and Alsuwaidan reported more than 50%

improvement in 35% of patients treated with non-ablative fractional 1550-nm laser and 37% treated with ablative fractional CO₂ laser, although transient post-inflammatory hyperpigmentation occurred in 17% and 14%, respectively [16]. In contrast, botulinum toxin in the present study had minimal downtime but produced only mild clinical improvement.

Botulinum toxin was generally well tolerated. Pain scores were similar on the botulinum toxin and saline sides, indicating that injection-related discomfort was mainly procedure dependent. One patient developed transient asymmetry of the angle of the mouth, probably due to diffusion of botulinum toxin into deeper muscular planes. The event resolved without intervention, but it highlights the need for very superficial intradermal placement, small aliquots, and caution near the perioral region.

The strengths of this study include its split-face placebo-controlled design, side-wise assessment, standardized photography, and use of both ECCA and Goodman and Baron grading systems. Limitations include the small sample size, short follow-up of 8 weeks, single-blind design, predominance of icepick scars, and absence of objective imaging or histological assessment of dermal remodelling. Longer follow-up may be required to assess delayed collagen changes, and future studies should evaluate botulinum toxin according to scar subtype and in combination with modalities such as microneedling, subcision, radiofrequency, or laser resurfacing.

In conclusion, intradermal botulinum toxin type A produced mild improvement in atrophic post-acne facial scars but did not show significant superiority over normal saline at 8 weeks. The findings suggest that botulinum toxin should not be considered a stand-alone treatment for atrophic acne scars, particularly when icepick scars predominate. Its potential role may be better explored as an adjunctive treatment in selected patients, especially when combined with procedures that directly stimulate dermal remodelling.

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