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ORIGINAL ARTICLE NON-SURGICAL AESTHETIC

# The Efficacy and Safety of Early Postoperative Botulinum Toxin A Injection for Facial Scars

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**Abstract**
*Background* Scars widen when the underlying musculature pulls apart suture lines, and scars oriented against relaxed skin tension lines are especially susceptible to these distraction forces. Because botulinum toxin A (BTA) induces complete muscle paralysis, the purpose of the current study was to evaluate the effects of BTA using both observer-dependent qualitative assessments and quantitative measurements to verify its beneficial effects on facial scarring.
*Methods* Patients with vertical forehead lacerations, treated by primary closure, were randomly assigned to two groups: one ($n = 15$) received BTA injections within 5 days of primary closure and the other ($n = 15$) received no further treatment. Vancouver scar scale (VSS) scores and wound width were determined at the 1-month and 6-month follow-up visits. Quantitative color differences between the scar and surrounding normal skin, using the Commission International d'Eclairage *L*a*b** color coordinates, were measured and compared by analyzing photographs.
*Result* Improved VSS scores, less increase in wound width, and less scar discoloration were noted among patients treated with BTA injections compared with the control group. These differences were observed at the 6-month visit, but not at the 1-month visit.
*Conclusion* BTA injection improves scar quality when injected during the early postoperative days.

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**Keywords** Botulinum toxin A · Facial scarring · Scar hyperpigmentation · Wound healing · Scar maturation

## Introduction

Skin damaged by either trauma or surgical intervention inevitably results in scar formation. Disfiguring scars may have a major negative effect on an individual's psychological well-being, especially when they are on the face and widen over time. Because it is impossible to completely hide a scar, the major goal of repairing skin damage has been to minimize scar widening.

Scars widen when opposing forces that tend to pull apart the suture lines are applied to newly formed collagen before it reaches final maturity, a process that can take several months before completion [1]. Tension exacerbates inflammation and leads to increased collagen synthesis and deposition of glycosaminoglycans, while prolonging erythema [2–5]. The increased local metabolic activity can intensify hypertrophic scars. Mechanical influences, such as nearby muscular contraction and elasticity of the cutaneous skin, comprise the main distracting tensile force. This concept relates to relaxed skin tension lines (RSTL), which lie perpendicular to the tension vector of the muscle contraction: scars aligned with RSTL are subject to reduced tension and heal well, whereas scars oriented against RSTL are subject to repetitive tension and result in scar hypertrophy [4].

Surgical techniques, carefully executed to best align incisions with RSTL, are routinely applied in facial plastic surgery. However, such techniques reduce, rather than eliminate, the muscle tension that acts on the healing wound. Because a major mechanical influence of tensile force involves the underlying musculature, paralysis of muscles under a facial wound can be reliably achieved by injection of botulinum toxin A (BTA). BTA irreversibly blocks acetylcholine release at the neuromuscular junction to achieve muscle paralysis [6]. This method has been shown to produce cosmetically more favorable scars in a controlled primate model [7]. Human case reports also suggest that chemoimmobilization of cutaneous facial wounds results in favorable healing [2].

The purpose of the current study was to evaluate the effectiveness of BTA using both observer-dependent qualitative assessments and quantitative measurements to verify its positive effects on facial scarring.

## Methods

### Patient Selection

This study was conducted on 36 patients with a Fitzpatrick skin type ranging between III and V, who suffered from traumatic forehead lacerations and presented to our emergency department from March 2014 to May 2016. All lacerations were vertical, aligned perpendicular to the RSTL. Patients aged 18 years or above, who had lacerations comprising more than one-third of the vertical forehead height, were selected. The following exclusion criteria were applied: (1) underlying neuromuscular disorder, (2) previous surgical or non-surgical intervention that may have influenced the tensile force of the underlying forehead muscles, or (3) pregnancy or breast-feeding. Patients with follow-up for at least 6 months were included. To reduce bias, the patients were randomly assigned to one of the two groups consisting of 18 patients each: one group received BTA injections, whereas the other group received no injections. This study was carried out in compliance with the Declaration of Helsinki.

On the day of the presentation to the emergency department, a plastic surgeon (S.H.L) blinded to the experimental conditions performed all primary repairs under local anesthesia. All layered suture procedures were performed with 5-0 vicryl (Ailee Co., Busan, Korea) and 6-0 nylon (Ailee Co., Busan, Korea). The patients were then asked to visit the outpatient clinic for wound management and assessment every other day for a week. All sutures were removed on postoperative day 5, and all patients were asked to wear sunblock. For patients in the BTA injection group, the injections were performed within the first 5 postoperative days at the clinic by a single surgeon (Y.W.C). The entire forehead area, including the underlying musculature of the repaired wound, was injected. To prevent lid ptosis, the supraorbital rim was spared. BTA (Nabota®; Daewoong Pharmaceutical, Seoul, Korea) was prepared by mixing 4 mL of 0.9% saline with 100 U of BTA (25 U/mL). In general, 30 U of BTA was prepared, and an additional 10–20 U was injected when complete muscle paralysis was not observed within 5 days of the initial injections. All patients were asked to return for follow-up visits at 1-month intervals for at least 6 months; photographs and possible adverse effect documentation were obtained at these visits. Digital photographs (Canon 700D, Tokyo, Japan) of the scar were taken under the same light source and illumination conditions using a standard light source box [8]. Written informed consent and permissions were obtained prior to taking all photographs.

### Wound Assessment

Immediately after taking the photographs, both the length and width of the forehead wound were measured directly on the patients using a caliper by a single plastic surgeon blinded to the study condition. The Vancouver scar scale (VSS) was assessed by two plastic surgeons in an independent, blinded fashion to quantify scar appearance at the 1-month and 6-month visits. VSS score agreement between the two raters was assessed by determining the intraclass correlation coefficient and corresponding 95% confidence interval. The mean VSS scores of each group were calculated for both visits, and the Mann–Whitney test was used for between-group comparisons. The mean width of the forehead wound of each group was likewise determined for both the 1-month and 6-month visits, and between-group comparisons were performed using the Mann–Whitney test.

Because the VSS score provides relatively subjective ratings, quantified color differences between the scar and surrounding normal skin were measured and compared using the Commission International d'Eclairage (CIE) $L^*a^*b^*$ color coordinates for each patient. $L^*a^*b^*$ values of the region of interest were obtained using Adobe Photoshop 7.0 (Adobe Systems Incorporated, San Jose, CA.), and the total $L^*a^*b^*$ color difference between normal skin and scar was calculated using the following equation:

$$\Delta T = \left[(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2\right]^{1/2}$$

The mean total $L^*a^*b^*$ color difference for each group was determined for the 1-month and 6-month visits and compared in the same manner as for the VSS scores and laceration widths. All statistical analyses were performed using R version 3.3.1 (The R Foundation for Statistical

Computing, Vienna, Austria), and a $p$ value less than 0.05 was considered statistically significant.

## Results

Of the 18 patients in the BTA treatment group, 3 were excluded for the following reasons: 2 were lost during follow-up and 1 developed an abscess requiring revision. Of the same number of patients in the control group, 3 were lost during follow-up. No other complications or adverse effects were noted during the follow-up period. The mean age of the treatment group was 34.33 years (range 18–69), and the mean age of the control group was 30.27 years (range 18–53). The characteristics of the forehead wounds and amount of injected BTA are shown in Table 1.

The mean VSS score of the treatment group at the 1-month visit was 7.8, compared with 8.1 in the control group. Based on the Mann–Whitney test, these VSS scores were not significantly different between groups ($p = 0.436$). However, statistical significance was achieved when comparing the 6-month VSS scores ($p = 0.003$) and the VSS score improvement grade between 1 and 6 months ($p = 0.001$), denoting improved VSS scores among patients who received BTA injections (Table 2). The concordance of VSS scores between raters was acceptable, with an intraclass correlation coefficient of 0.90 (95% confidence interval, 0.85 and 0.95).

**Table 1** Types of trauma and characteristics of forehead wounds

| No. | Age/sex | Trauma type | Wound depth | Wound length (cm) | Suture type | Treatment (injected unit) |
|---|---|---|---|---|---|---|
| 1 | 24/M | Blunt | Muscle | 11 | Layered, interrupted | BTA (50) |
| 2 | 48/M | In-car traffic accident | Subcutaneous | 5.3 | Layered, interrupted | BTA (26) |
| 3 | 69/F | Slip down | Subcutaneous | 5 | Layered, interrupted | BTA (25) |
| 4 | 18/M | Blunt | Subcutaneous | 5.7 | Layered, interrupted | BTA (28) |
| 5 | 55/M | Blunt | Subcutaneous | 6.5 | Layered, interrupted | BTA (32) |
| 6 | 22/M | Stab injury | Subcutaneous | 3.5 | Layered, interrupted | BTA (18) |
| 7 | 24/M | Blunt | Muscle | 10.1 | Layered, interrupted | BTA (50) |
| 8 | 29/F | Blunt | Subcutaneous | 6.7 | Layered, interrupted | BTA (35) |
| 9 | 18/M | Blunt | Subcutaneous | 5.7 | Layered, interrupted | BTA (28) |
| 10 | 20/M | Motorcycle traffic accident | Dermis | 3.3 | Interrupted | BTA (17) |
| 11 | 54/M | In-car traffic accident | Subcutaneous | 9.5 | Layered, interrupted | BTA (50) |
| 12 | 23/F | Blunt | Muscle | 6.1 | Layered, interrupted | BTA (30) |
| 13 | 44/F | Blunt | Subcutaneous | 4.6 | Layered, interrupted | BTA (23) |
| 14 | 18/F | Slip down | Muscle | 9.8 | Layered, interrupted | BTA(50) |
| 15 | 49/F | Slip down | Subcutaneous | 5.5 | Layered, interrupted | BTA (27) |
| 16 | 20/F | Stab injury | Dermis | 2.8 | Interrupted | Control |
| 17 | 53/M | In-car traffic accident | Muscle | 13.2 | Layered, interrupted | Control |
| 18 | 29/M | Slip down | Subcutaneous | 6.8 | Layered, interrupted | Control |
| 19 | 19/M | Slip down | Subcutaneous | 2.3 | Layered, interrupted | Control |
| 20 | 35/F | Slip down | Subcutaneous | 7.8 | Layered, interrupted | Control |
| 21 | 30/M | Blunt | Muscle | 6.7 | Layered, interrupted | Control |
| 22 | 18/F | Blunt | Subcutaneous | 5.8 | Layered, interrupted | Control |
| 23 | 21/M | Motorcycle traffic accident | Subcutaneous | 3.5 | Layered, interrupted | Control |
| 24 | 38/F | Slip down | Subcutaneous | 2.9 | Layered, interrupted | Control |
| 25 | 33/F | Slip down | Subcutaneous | 5.6 | Layered, interrupted | Control |
| 26 | 25/F | In-car traffic accident | Subcutaneous | 3.5 | Layered, interrupted | Control |
| 27 | 26/F | Stab injury | Muscle | 4.9 | Layered, interrupted | Control |
| 28 | 28/F | Slip down | Subcutaneous | 5.2 | Layered, interrupted | Control |
| 29 | 26/M | Slip down | Muscle | 7.8 | Layered, interrupted | Control |
| 30 | 53/M | Blunt | Muscle | 10.3 | Layered, interrupted | Control |

*M* male; *F* female; *BTA* botulinum toxin A

**Table 2** Average Vancouver scar scale between treatment and control groups

| No. | VSS | | Improvement grade |
|---|---|---|---|
| | 1st month | 6th month | |
| 1 | 8 | 3.5 | 4.5 |
| 2 | 9 | 4 | 5 |
| 3 | 6.5 | 3 | 3.5 |
| 4 | 7.5 | 2.5 | 5 |
| 5 | 8 | 6 | 2 |
| 6 | 7.5 | 3 | 4.5 |
| 7 | 9 | 4.5 | 4.5 |
| 8 | 7.5 | 2 | 5.5 |
| 9 | 9.5 | 5.5 | 4 |
| 10 | 7 | 3 | 4 |
| 11 | 9 | 3 | 6 |
| 12 | 6 | 2.5 | 3.5 |
| 13 | 7 | 3 | 4 |
| 14 | 7 | 5.5 | 1.5 |
| 15 | 8.5 | 3 | 5.5 |
| Mean | 7.8 | 3.6 | 4.2 |
| 16 | 9 | 4.5 | 4.5 |
| 17 | 10.5 | 7 | 3.5 |
| 18 | 8 | 5.5 | 2.5 |
| 19 | 6 | 4 | 2 |
| 20 | 9 | 6.5 | 2.5 |
| 21 | 9 | 6 | 3 |
| 22 | 8 | 5 | 3 |
| 23 | 9.5 | 7.5 | 2 |
| 24 | 11 | 8.5 | 2.5 |
| 25 | 7 | 4.5 | 2.5 |
| 26 | 7 | 5.5 | 1.5 |
| 27 | 8 | 5 | 3 |
| 28 | 5.5 | 3 | 2.5 |
| 29 | 4 | 3 | 1 |
| 30 | 10 | 7 | 3 |
| Mean | 8.1 | 5.5 | 2.6 |
| *p* | 0.436 | 0.003 | 0.001 |

*VSS* Vancouver scar scale

**Table 3** Width of the forehead wound between treatment and control groups

| No. | Wound width (cm) | | Improvement grade |
|---|---|---|---|
| | 1st month | 6th month | |
| 1 | 0.28 | 0.3 | − 0.02 |
| 2 | 0.18 | 0.28 | − 0.1 |
| 3 | 0.15 | 0.15 | 0 |
| 4 | 0.28 | 0.42 | − 0.14 |
| 5 | 0.22 | 0.41 | − 0.19 |
| 6 | 0.12 | 0.15 | − 0.03 |
| 7 | 0.35 | 0.55 | − 0.2 |
| 8 | 0.18 | 0.28 | − 0.1 |
| 9 | 0.29 | 0.38 | − 0.09 |
| 10 | 0.21 | 0.25 | − 0.04 |
| 11 | 0.31 | 0.45 | − 0.14 |
| 12 | 0.24 | 0.27 | − 0.03 |
| 13 | 0.19 | 0.32 | − 0.13 |
| 14 | 0.31 | 0.41 | − 0.1 |
| 15 | 0.26 | 0.25 | 0.01 |
| Mean | 0.238 | 0.32 | − 0.087 |
| 16 | 0.18 | 0.32 | − 0.14 |
| 17 | 0.22 | 0.55 | − 0.33 |
| 18 | 0.21 | 0.52 | − 0.31 |
| 19 | 0.3 | 0.45 | − 0.15 |
| 20 | 0.29 | 0.45 | − 0.16 |
| 21 | 0.25 | 0.57 | − 0.32 |
| 22 | 0.28 | 0.38 | − 0.1 |
| 23 | 0.19 | 0.39 | − 0.2 |
| 24 | 0.35 | 0.58 | − 0.23 |
| 25 | 0.1 | 0.34 | − 0.24 |
| 26 | 0.22 | 0.48 | − 0.26 |
| 27 | 0.33 | 0.82 | − 0.49 |
| 28 | 0.2 | 0.22 | − 0.02 |
| 29 | 0.22 | 0.32 | − 0.1 |
| 30 | 0.31 | 0.95 | − 0.64 |
| Mean | 0.243 | 0.489 | − 0.246 |
| *p* | 0.744 | 0.007 | 0.001 |

The mean scar width of the treatment group at the 1-month visit was 0.238 cm and that of the control group was 0.243 cm ($p = 0.744$). The mean width increased to 0.320 cm in the treatment group and 0.489 cm in the control group at 6 months; the difference between groups was statistically significant ($p = 0.007$) (Table 3). Less increase in wound width was seen in the BTA-treated group. There was a propensity for improved VSS scores over time, whereas slightly increasing width of the forehead wound was seen in both groups.

Because color match between a scar and the surrounding normal skin is one of the most important factors in scar aesthetics [9], we added photographic analysis to produce an objective, quantitative measurement of scar color using the $L^*a^*b^*$ color coordinates [10]. Statistically significant differences were noted between the groups for the mean total $L^*a^*b^*$ color difference at the 6-month visit ($p < 0.0001$) and the $L^*a^*b^*$ color difference improvement grade between 1 to 6 months ($p = 0.021$) (Table 4).

Figures 1a and 2a show two patients with BTA injection at the 1-month visit, and Figs. 1b and 2b show the status of the same patients at the 6-month visit. Improved width and color of the wound can be noted, and the patients were

**Table 4** *L*a*b** color difference (ΔT) between treatment and control groups

| No. | *L*a*b* score (ΔT) | | Improvement grade |
|---|---|---|---|
| | 1st month | 6th month | |
| 1 | 44.07 | 22.25 | 21.82 |
| 2 | 63.83 | 16.88 | 46.95 |
| 3 | 78.56 | 33.38 | 45.18 |
| 4 | 64.33 | 25.81 | 38.52 |
| 5 | 68.54 | 34.99 | 33.55 |
| 6 | 41.06 | 12.69 | 28.37 |
| 7 | 67.04 | 26.72 | 40.32 |
| 8 | 64.42 | 34.58 | 29.84 |
| 9 | 47.35 | 30.51 | 16.84 |
| 10 | 53.04 | 21.63 | 31.41 |
| 11 | 37.01 | 11.58 | 25.43 |
| 12 | 41.86 | 12.69 | 29.17 |
| 13 | 50.58 | 25.63 | 24.95 |
| 14 | 37.96 | 17.23 | 20.73 |
| 15 | 37.97 | 23.09 | 14.88 |
| Mean | 53.175 | 23.311 | 29.864 |
| 16 | 82.67 | 53.15 | 29.52 |
| 17 | 67.65 | 54.27 | 13.38 |
| 18 | 74.53 | 53.9 | 20.63 |
| 19 | 80.91 | 69.49 | 11.42 |
| 20 | 45.92 | 28.13 | 17.79 |
| 21 | 57.71 | 26.82 | 30.89 |
| 22 | 69.89 | 40.14 | 29.75 |
| 23 | 58.17 | 36.54 | 21.63 |
| 24 | 68.25 | 40.68 | 27.57 |
| 25 | 54.34 | 37.73 | 16.61 |
| 26 | 51.49 | 23.79 | 27.7 |
| 27 | 73.77 | 48.22 | 25.55 |
| 28 | 31.11 | 16.55 | 14.56 |
| 29 | 45.66 | 27.14 | 18.52 |
| 30 | 64.32 | 42.34 | 21.98 |
| Mean | 61.76 | 39.926 | 21.833 |
| *p* | 0.081 | 0 | 0.021 |

satisfied with the result. In contrast, Figs. 3b and 4b show the status of wound of two other patients in the control group at the 6-month visit. Clearly, there seems to be no improvement in either the width or color of the wound, compared with the photograph taken at the 1-month visit (Figs. 3a and 4a).

## Discussion

Visible scars on the face disturb a person's psychological well-being and sometimes give a negative impression to others, thereby reducing a person's social role. In minimizing the formation of a conspicuous scar, measures routinely employed to facilitate favorable healing include minimizing reactive suture material, performing a good-quality closure, applying occlusive or semi-occlusive dressings, avoiding sun exposure [11], and applying various types of scar care products. Minimizing tension acting on the wound edges is more important than the modalities listed above, which is why BTA injections have gained attention for the prevention of disfiguring scars.

The forehead was chosen for this study for a few reasons: a substantial number of patients with lacerations in this area visit our emergency department; the frontalis, procerus, and corrugator supercilii muscles constantly exert tension on the forehead skin; paralysis of these muscles would lead to no functional deficit [7]. BTA induces chemodenervation through its action on the presynaptic neuron, preventing release of acetylcholine, which leads to functional denervation of striated muscle for 2–6 months after injection [12]. All of our patients experienced varying degrees of forehead muscle paralysis at their 1-month visit. Although there were no statistically significant differences between groups at this visit, parameters of wound assessment were significantly superior at the 6-month visit in patients who received BTA. Because scar maturation takes months to complete, and our assessment measures (VSS score, width, and *L*a*b** score) all relied on the final outcomes of the histopathologic healing process regardless of functional effects of the drug, it is quite predictable that it may take more than 1 month to visualize the effects of BTA on scar maturation. Our consistent data demonstrate that injection of BTA has a positive effect on scars, when assessed by both subjective and objective methods.

Scars consist of several components, such as texture, size, and color. Because validated scar assessment scales, evaluating healing outcomes of complex wounds, are not discriminant enough to compare two groups of patients with simple facial wounds [13], we analyzed the width and *L*a*b** coordinates as objective scar assessment methods. Interestingly, the use of BTA improved scar discoloration, as demonstrated by a significant decrease in the total *L*a*b** color difference (ΔT). Cutaneous injuries invoke an inflammatory response, and many important cellular mediators in this response influence melanocytes and melanogenesis in a variety of ways: Nitric oxide, histamine, p53, and transforming growth factor β1 (TGF-β1), which are all released by the inflammatory response, induce melanogenesis [14]. The mechanism behind postinflammatory hyperpigmentation is not fully understood but may involve activation of melanocytes by inflammatory mediators or reactive oxidative species released from the damaged skin [15]. Once injury to the skin occurs, repeated microtrauma, caused by continuous displacement of injured tissue, induces a prolonged

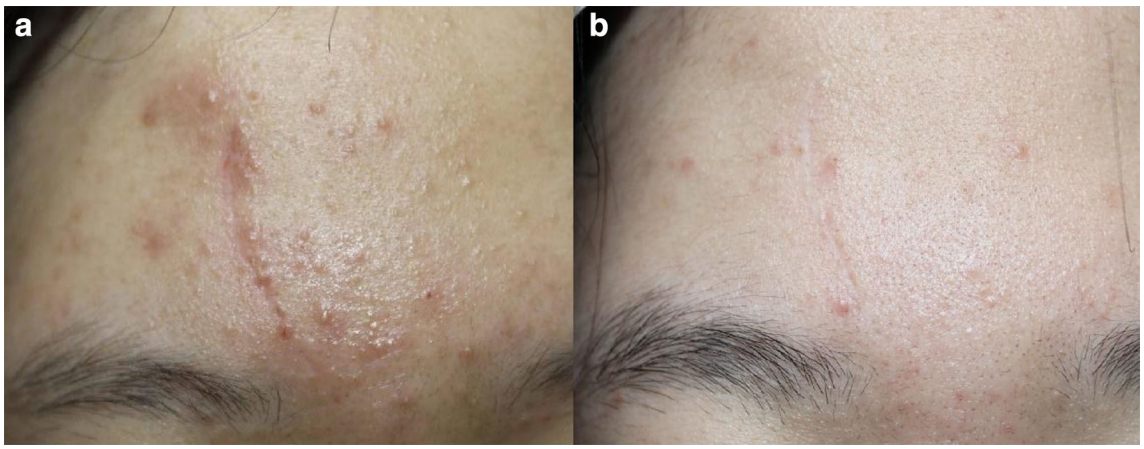


**Fig. 1** An 18-year-old male who received the botulinum toxin A injection on postoperative day 5. **a** was taken at patient's 1-month visit, and **b** was taken at 6-month visit. Improved scar quality and erythema are noted with subsequent patient satisfaction

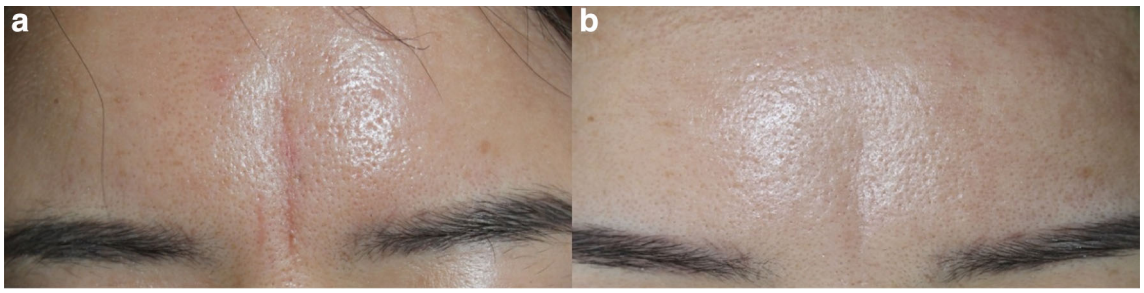


**Fig. 2** A 49-year-old female who received the botulinum toxin A injection on postoperative day 5. **a** was taken at patient's 1-month visit, and **b** was taken at 6-month visit. Other than slight depression of the previous wound, the quality of scar is improved with no visible erythema

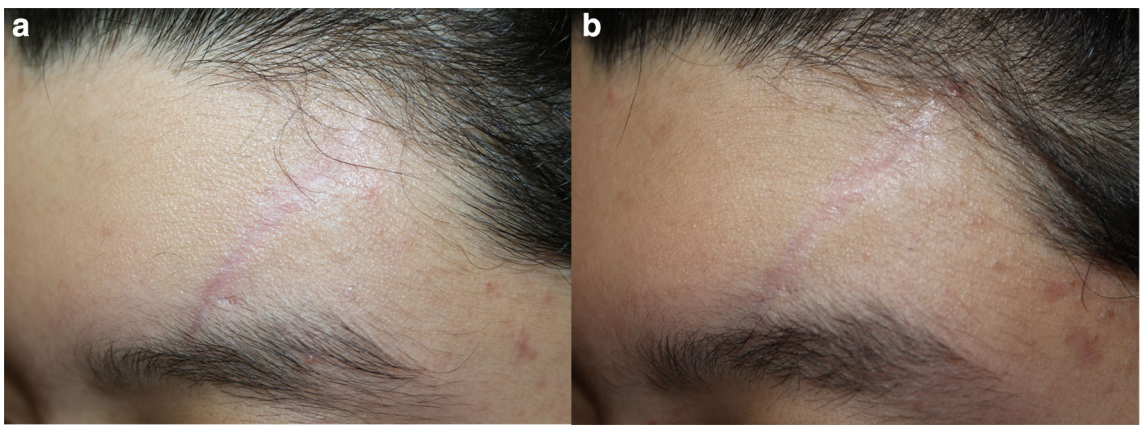


**Fig. 3** A 30-year-old male with no botulinum toxin A injection. **a** was taken at patient's 1-month visit, and **b** was taken at 6-month visit. Widened and erythematous scar continues to be problematic

inflammatory response and distortion of healing tissue before strength and maturity are achieved [16]. Accordingly, using BTA to induce temporary paralysis of muscles underlying a wound should minimize tension on the healing wound and, therefore, lead to a decreased inflammatory response. In a rat surgical wound model, Lee et al. observed less infiltration of inflammatory cells, less fibrosis, and lower expression of TGF-β1 with BTA compared with control [17]. Moreover, in a study conducted by Ward et al. decreased dermal dendritic cell and CD4+ T cell infiltrations were seen in a KC-Tie2 mouse model after BTA injection, indicating significantly improved psoriasiform skin inflammation [18]. The mechanism behind reduced inflammation involves inhibition of nerve-derived

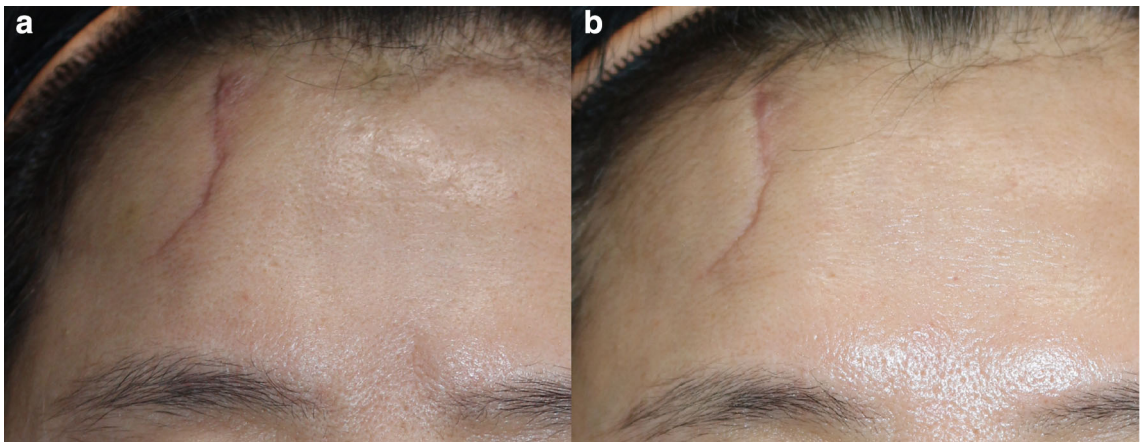


**Fig. 4** A 33-year-old female with no botulinum toxin A injection. **a** was taken at patient's 1-month visit, and **b** was taken at 6-month visit. Still visible scar with hyperpigmentation remains

release of calcitonin gene-related peptide and substance P, in addition to cleavage of SNAP25 protein, by BTA injection [19]. Together, these observations indicate that the tension-relieving properties of BTA, with its inhibitory effects on inflammation, support the use of BTA in scar prevention.

Reckenbeil et al. [20] reported that insulin-like growth factor (IGF) promoted proliferation and wound healing of periodontal inflammation by exerting mitogenic and metabolic effects to promote growth, survival, and differentiation of different cell types. Because paralyzed or denervated muscle fibers induce terminal sprouting by secreted cytokines and neurotrophic factors, such as IGF [21], we hypothesized that a regional increase in IGF concentration from muscle paralysis induced by BTA may also promote wound healing. Future in vivo experiments are necessary to explore this issue. In addition, Shaarawy et al. reported that intralesional BTA was equally effective and better tolerated than intralesional steroid for treating keloids [22], and Carruthers demonstrated improved telangiectasia and erythema with intense pulsed light (IPL) plus BTA injection compared with IPL alone [23]; the mechanisms behind these improvements are not fully understood. Although it is possible that BTA has a direct biochemical effect on inflammatory cells or inhibits the inflammatory mediators by a direct mechanism, no studies have reported on these mechanisms of action. Further studies are necessary to establish the effective dose of BTA injection, with full understanding of the mechanisms behind its actions.

There are potential limitations to this study. First, we did not set any limitation of actual location of the wound within the forehead. On the forehead, there should be varying degrees of distracting forces acting on the skin depending on the exact location. For example, less distracting force is expected on the most lateral part of the forehead. It would have been ideal to select patients with a consistent wound location. Second, we were unable to perform histopathologic assessments in this study. The aforementioned studies, showing a decreased inflammatory response, were obtained from animal models, and human trials are necessary to confirm the underlying mechanism of the action of BTA. Lastly, it would have been preferable to perform BTA injections in the earlier healing phase, optimally upon wound closure, because of the delayed onset of action of BTA. The wound healing process consists of a brief coagulation phase, an inflammatory phase lasting for days, a proliferative phase lasting for weeks, and a remodeling phase taking up to a year to complete; these phases may occur simultaneously, with overlap of the respective processes [5]. Therefore, BTA may be most beneficial in the early stage of wound healing, and one way to achieve this is to reconstitute BTA in a solution of 1% lidocaine with 1:100,000 epinephrine, which leads to instant muscle paralysis, instead of the 48- to 72-hour delay of chemoimmobilization that occurs with BTA in 0.9% saline [24, 25].

## Conclusion

This study demonstrated less increase in scar width and improved discoloration of the scar in patients who received BTA injection. Both observer-dependent qualitative assessments and quantitative measurements were favorable in the BTA group.

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**Compliance with Ethical Standards**

**Conflict of interest** The authors have indicated no interest with commercial supporters.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## References

1. Wilson AM (2006) Use of botulinum toxin type A to prevent widening of facial scars. Plast Reconstr Surg 117(6):1758–1766
2. Sherris DA, Gassner HG (2002) Botulinum toxin to minimize facial scarring. Facial Plast Surg 18(1):35–39
3. Gassner HG, Brissett AE, Otley CC, Boahene DK, Boggust AJ, Weaver AL, Sherris DA (2006) Botulinum toxin to improve facial wound healing: a prospective, blinded, placebo-controlled study. Mayo Clin Proc 81(8):1023–1028
4. Sherris DA, Larrabee WF Jr, Murakami CS (1995) Management of scar contractures, hypertrophic scars, and keloids. Otolaryngol Clin North Am 28:1057–1068
5. Jablonka EM, Sherris DA, Gassner HG (2012) Botulinum toxin to minimize facial scarring. Facial Plast Surg 28(5):525–535
6. Huang W, Foster JA, Rogachefsky AS (2000) Pharmacology of botulinum toxin. J Am Acad Dermatol 43:249–259
7. Gassner HG, Sherris DA, Otley CC (2000) Treatment of facial wounds with botulinum toxin A improves cosmetic outcome in primates. Plast Reconstr Surg 105(6):1948–1953
8. Ikeda I, Urushihara K, Ono T (2003) A pitfall in clinical photography: the appearance of skin lesions depends upon the illumination device. Arch Dermatol Res 294:438–443
9. Nedelec B, Shankowsky HA, Tredget EE (2000) Rating the resolving hypertrophic scar: comparison of the Vancouver Scar Scale and scar volume. J Burn Care Rehabil 21:205–212
10. Cheon YW, Lee WJ, Rah DK (2010) Objective and quantitative evaluation of scar color using the $L^*a^*b^*$ color coordinates. J Craniofac Surg 21:679–684
11. Due E, Rossen K, Sorensen LT, Kliem A, Karlsmark T, Haedersdal M (2007) Effect of UV irradiation on cutaneous cicatrices: a randomized, controlled, trial with clinical, skin reflectance, histological, immunohistochemical and biochemical evaluations. Acta Derm Venereol 87(1):27–32
12. Fagien S (1999) Botox for the treatment of dynamic and hyperkinetic facial lines and furrows: adjunctive use in facial aesthetic surgery. Plast Reconstr Surg 103(2):701–713
13. Ziade M, Domergue S, Batifol D, Jreige R, Sebbane M, Goudot P, Yachouh J (2013) Use of botulinum toxin type A to improve treatment of facial wounds: a prospective randomized study. J Plast Reconstr Aesthet Surg 66(2):209–214
14. Chadwick S, Heath R, Shah M (2012) Abnormal pigmentation within cutaneous scars: a complication of wound healing. Indian J Plast Surg 45(2):403–411
15. Ortonne JP, Bissett DL (2008) Latest insights into skin hyperpigmentation. J Investig Dermatol Symp Proc 13:10–14
16. Courtiss EH, Longacre JJ, Destefano GA, Brizic L, Holmstrand K (1963) The placement of elective skin incisions. Plast Reconstr Surg 31:31–44
17. Lee BJ, Jeong JH, Wang SG, Lee JC, Goh EK, Kim HW (2009) Effect of botulinum toxin type A on a rat surgical wound model. Clin Exp Otorhinolaryngol 2(1):20–27
18. Ward NL, Kavlick KD, Diaconu D, Dawes SM, Michaels KA, Gilbert E (2012) Botulinum neurotoxin A decreases infiltrating cutaneous lymphocytes and improves acanthosis in the KC-Tie2 mouse model. J Incest Dermatol 132(7):1927–1930
19. Carmichael NM, Dostrovsky JO, Charlton MP (2010) Peptide-mediated transdermal delivery of botulinum neurotoxin type A reduces neurogenic inflammation in the skin. Pain 149:316–324
20. Reckenbeil J, Kraus D, Stark H, Rath-Deschner B, Jäger A, Wenghoefer M, Winter J, Götz W (2017) Insulin-like growth factor 1 (IGF1) affects proliferation and differentiation and wound healing processes in an inflammatory environment with p38 controlling early osteoblast differentiation in periodontal ligament cells. Arch Oral Biol 73:142–150
21. Wright MC, Cho WJ, Son YJ (2007) Distinct patterns of motor nerve terminal sprouting induced by ciliary neurotrophic factor vs. botulinum toxin. J Comp Neurol 504(1):1–16
22. Shaarawy E, Hegazy RA, Abdel Hay RM (2015) Intralesional botulinum toxin type A equally effective and better tolerated than intralesional steroid in the treatment of keloids: a randomized controlled trial. J Cosmet Dermatol 14:161–166
23. Carruthers J, Carruthers A (2004) The effect of full-face broadband light treatments alone and in combination with bilateral crow's feet botulinum toxin type A chemodenervation. Dermatol Surg 30(3):355–366
24. Gassner HG, Sherris DA (2000) Addition of an anesthetic agent to enhance the predictability of the effects of botulinum toxin A injection: randomized controlled study. Mayo Clin Proc 75(7):701–704
25. Gassner HG, Sherris DA (2003) Chemoimmobilization: improving predictability in the treatment of facial scars. Plast Reconstr Surg 112(5):1464–1466