CLINICAL EVALUATION OF THE EFFICACY OF BOTULINUM TOXIN A FOR IMPROVING FACIAL SCARS (RANDOMIZED CLINICAL TRIAL)

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ABSTRACT
INTRODUCTION: Scars widen when the underlying musculature (frontalis muscles, procerus, and corrugator supercili muscles) pulls apart suture lines, and scars oriented against relaxed skin tension lines (RSTL) 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.

OBJECTIVE: To evaluate the efficacy and safety of Botulinum Toxin type A injection on improving vertical or oblique facial scars when injected in early postoperative days.

MATERIALS AND METHODS: Twelve individuals with vertical or oblique recent forehead lacerations were randomly selected. The sample was chosen based on a set of inclusion and exclusion criteria and was then randomized to one of two groups: The BTA injection was given to one group (n = 6) within five days of primary closure, while the other group (n = 6) received no further treatment. Assessment included measurement of wound width and Vancouver scar scale, along with clinical photographs.

RESULTS: In comparison to the control group, patients treated with BTA injections had a significant improvement in VSS and a less gain in wound width. At the 3- and 6-month examinations, all significant changes were found, but not at the 1-month appointment. All cases showed uneventful healing.

CONCLUSION: This study showed that when BTA injections are administrated during the early postoperative days it shows great improvement in the scar quality.

KEYWORDS: Botulinum Toxin A, Facial scarring, 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 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, 3). 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 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).

Different approaches have been suggested to overcome the problem of wide scars such as corticosteroids injections (5), irradiation, ultrasound silicone application (6, 7) and surgical maneuvers (8) as well as many others, but none of them prevent the underlying pathologic process, which is the distracting force of muscle pull. However, such techniques cannot eliminate the muscle tension that acts on the healing wound. Because Botulinum Toxin A (BTA) irreversibly blocks acetylcholine release at the neuromuscular junction causing muscle paralysis (9), Then BTA can be used to eliminate all tensile forces resulting from the underlying musculature of a facial wound. One of the most widely used drugs for wrinkle reduction and facial contouring is Botulinum Toxin
type A (10, 11). It has also been proven to be safe and reliable, with reversible side effects. Several trials have suggested that Botulinum Toxin type A can be injected into adjacent musculature around traumatic or incisional wounds (2, 12-17). The purpose of this clinical trial was to evaluate the effectiveness of BTA using qualitative assessment and quantitative measurements to verify its positive effect on facial scarring. The null hypothesis of this study is that there will be no difference in scar widening of forehead lacerations between the group that was injected with Botulinum Toxin type A and the group that received no further treatment.

MATERIALS AND METHODS

Informed consent
- Before initiating the study, the research ethics committee of the Faculty of Dentistry at Alexandria University gave its approval.
- Prior to being included in the trial, all patients were informed about the procedure that was performed and each participant signed a written consent. Each patient was also informed that he or she had the ability to withdraw from the study at any point with no repercussions.

Sample size calculation (3, 18, 19)
Sample size was estimated based on assuming 95% confidence level and 80% study power. The median of forehead scar width for group with Botulinum Toxin (BTA) injection measured with Vancouver Scar Scale (VSS) was 7, max= 8 and min= 6, while for the no treatment group, the median 6.25, max = 5 and min = 7 (3). The means and standard deviations (SD) were estimated based on Hozo et al. Method (20). The mean (SD) scar width of the two groups respectively was 7 (0.5) and 6.025 (0.5). The minimal sample size was calculated to be 5 patients per group and this will be increased to 6 to make up for loss to follow up with total sample of 12 for the two groups.

Software
Sample size was based on Rosner’s method (18). Calculated by Brant’s sample size calculator at the University of British Columbia (19).

1. Study Design
This prospective study was a randomized controlled clinical trial with a 1:1 allocation ratio conducted on twelve patients suffering recent traumatic vertical or oblique forehead lacerations selected from the Emergency Clinic in the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University.

Participants were randomly assigned using a computer-generated list of random numbers to either the study or the control group.

Group 1: Consisting of 6 patients that acted as the control group.

Group 2: Consisting of 6 patients received 12.5 speywood unit/cm (SU/cm) Dysport intramuscular & intradermal injections, within the first 5 postoperative days of the trauma.

2. Criteria for patient selection
Patients with traumatic forehead vertical or oblique recent lacerations with more than 0.25 inch (6.5 mm) depth where fat, muscle or bones are exposed.

Inclusion criteria (3, 21)
- Patients aged from 18 to 40 years.
- Patients free from any systemic disease.
- Patients who understand verbal and written instructions.

Exclusion criteria (3, 21)
- Patients with horizontal forehead lacerations.
- Patients suffering from complicated forehead lacerations that require grafting.
- Patients with forehead burns.
- Patients with neuromuscular disorders.
- Patients with previous surgical or non-surgical intervention.
- Patients allergic to drugs used in this study.

3. Materials
- Abo Botulinum Toxin type A (Dysport) (IPSEN, Cambridge, United Kingdom).
- Insulin syringe (Sterile single-use insulin syringe, Concord Pharma, Korea).
- Digital Vernier Caliper (150 mm 6 inch Electronic Digital vernier caliper Stainless Steel Micrometer).
- A 0.9% Saline (El Fath for drugs and cosmetics industry (FIPCO), Borg El Arab City, Alexandria, Egypt).
- Jacy topical cream (SABSHiRe Pharmaceuticals, Egypt).
- Scaro topical cream (Macro group pharmaceuticals, Egypt).
- Lidocaine 2.5% and prilocaine 2.5% topical cream (EMLA cream; Astra Zeneca, Sodertalje, Sweden).

4. Methods
I. Pre-operative assessment and examination (21)

History and clinical examination
- History was taken to all the patients including name, age, sex, occupation, residence, chief complaint, systemic diseases, drugs and previous operations.
- Thorough clinical examination extra orally was carried out to determine the following:
  1. Swellings assessed by Edema scale from 1-4.
  2. Erythema assessed by visual grading five-point scale.
  3. Presence of burn by examining color change, presence of blisters and pain.

Preoperative patient preparation
All primary repairs were performed under local anaesthesia (1% lidocaine containing vasoconstrictors) by a plastic surgeon who was...
blinded of the experimental settings. All suture procedures were done with ethilone 4-0 (Ethicon* Co., Delhi, India) and 6-0 prolene (Ethicon Co., Delhi, India) (2, 3).

**Operative procedures (Fig. 1)**

Figure (1): (a-e) Operative procedures.

1. All procedures were performed under local anesthesia (1% lidocaine).
2. Using nonalcoholic solution after makeup removal, a single surgeon performed the procedures under complete aseptic technique (21).
3. All patients wore a disposable cap to contain hair.
4. Pain at the injected sites was minimized before each injection by applying topical anesthetics and cold iced devices.
5. Micro fine 1.0 ml insulin syringes with a 29-G or 30-G needle were used.
6. The dosages of the preparations were related to biological activity and are given in biological units (U). The units were termed according to the manufacturer as Speywood U (SU) for Dysport.
7. The drugs used were AboBotulinumToxin A Dysport (500 SU) was reconstituted with 2.0 mL of sodium chloride 9 mg/mL (0.9%) injection solution. This resulted in a clear solution containing the 500 SU of the active ingredient in a concentration of 250 units per 1.0 mL of the reconstituted solution. The reconstitution was performed in accordance with the rules of good clinical practice, particularly with respect to asepsis and within 15 day of reconstitution (21-23).
8. The injections were done in the first 5 days after primary closure.
9. The total dose was approximately 105 SU.
10. The total dose was divided into 75 SU injected by a (1-ml, 30-gauge needle) insulin syringe along the scar length at the rate of approximately 12.5 SU (0.15 ml) per cm of wound length, in a linear pattern on either side of the wound, with the needle prick positioned approximately 5 mm from the edge of the wound. The injection was repeated every cm throughout the entire wound length and 30 SU are injected into frontalis muscle (2, 3, 11).
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12. To prevent eyebrow ptosis, the drugs were not injected around the supraorbital rim (3).
13. Injections were determined by a skin marker and done under the supervision of a qualified licensed supervisor.
14. The Dysport vial was stored up to 15 days after reconstitution, in the refrigerator at temperature 2°C–8°C, without loss of efficacy and with no sign of microbiological contamination (23).

**Wound assessment**

- The facial anatomy, mimic muscular contraction, facial expression, and any pre-existing asymmetry were examined before treatment (2).
- Immediately after taking the photographs, both the length and width of the forehead wound were measured directly on the patients using a digital vernier caliper by a single plastic surgeon blinded to the study.
- Due to muscles contraction the BTA was injected on skin folds at various levels (intramuscular, subcutaneous, or intradermal) in several points for each region. The injections were administrated directly into the point of intense muscular contraction. Where the contraction was weak, however, the injection was made at a deep or superficial intradermal level. Depth was also determined by the effect we seek to achieve: intramuscular has a strong effect, while subcutaneous or intradermal has a mild effect (24).

**Post-operative care**

The following post-operative medications were prescribed for all groups:

- Jacy topical cream (containing Jojoba oil, glycerol, beeswax, olive oil and ascorbic acid) 2-3 times daily for the first 14 days, till closure of wound, to provide the optimum environment required for skin regeneration.
- Scaro gel (containing silicone fluid, vitamin A, vitamin E, almond oil and polydimethylsiloxane) twice daily for 2-6 months on closed scar site, applied in one direction. To improve texture and color of skin.

All the patients were given the same postoperative instructions as the following:
• Staying in a vertical position for 6 hours.
• All patients were asked to wear sunblock daily for 6 months (3).
• Avoiding intensive exercise and excessive heat for the first 24 hours.
• After treatment, avoid manipulating the injected area for at least 6 hours.
• A cold compress or gentle massage was performed by the surgeon who performed the procedure, to the ruptured vessels in the case of ecchymosis. These precautions prevent the BTA from spreading to nearby muscles, allowing a more specific action (2).

**Postoperative clinical evaluation**

• After 48 hours, all patients were evaluated by asking them to raise their eyebrows and frown to assess the presence or absence of wrinkles in the forehead, to see how severe their muscle paralysis was and whether they needed an additional 25–50 SU botulinum toxin administered (21). To alleviate the pain, lidocaine prilocaine 5 % was administered to the wound during the initial examination. Participants were instructed to keep the muscles around the wound relaxed for 45 minutes. Any remaining muscular contractions were observed, and more botulinum toxin injections were given as needed (2).

• Subcuticular stitches were removed after five days, after that wounds were kept without a dressing and jacy gel was applied twice daily for 14 days (2, 3).

• All participants requested for follow-up appointments at one-month intervals for a minimum of six months; at these sessions, images and documentation of any counter effects were acquired (3).

• Using a standard light source box, digital images of the scar (Canon 700D, Tokyo, Japan) were taken under the same light source and illumination settings (25). Prior to taking any images, written informed consent and permissions were acquired.

**Outcome assessment**

**Wound width**
The mean width of the forehead wound of each group was likewise determined for both the 1-month, 3-month and 6-month visits.

**Vancouver scar scale**
The Vancouver scar scale was assessed by two plastic surgeons in an independent, blinded fashion to quantify scar appearance at the 1-month, 3-month and 6-month visits.

<table>
<thead>
<tr>
<th>Scar characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascularity</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td>Pink</td>
<td>1</td>
</tr>
<tr>
<td>Red</td>
<td>2</td>
</tr>
<tr>
<td>Purple</td>
<td>3</td>
</tr>
<tr>
<td>Pigmentation</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td>Hypopigmentation</td>
<td>1</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>2</td>
</tr>
<tr>
<td>Mixed pigmentation</td>
<td>3</td>
</tr>
<tr>
<td>Malleability</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td>Supple</td>
<td>1</td>
</tr>
<tr>
<td>Yielding</td>
<td>2</td>
</tr>
<tr>
<td>Firm</td>
<td>3</td>
</tr>
<tr>
<td>Ropies</td>
<td>4</td>
</tr>
<tr>
<td>Contraction</td>
<td>5</td>
</tr>
<tr>
<td>Height</td>
<td></td>
</tr>
<tr>
<td>Flat</td>
<td>0</td>
</tr>
<tr>
<td>&lt;2 mm</td>
<td>1</td>
</tr>
<tr>
<td>2-5 mm</td>
<td>2</td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>3</td>
</tr>
<tr>
<td>Total score</td>
<td>14</td>
</tr>
</tbody>
</table>

**Statistical analysis**

Normality was checked for quantitative variables using descriptive statistics, plots, and normality tests. Means and standard deviations (SD) were calculated for normally distributed variables (age and wound width in mm), in addition to median and interquartile range (IQR) for qualitative ordinal variable (Vancouver scar scale), while frequencies and percentages were calculated for qualitative variable (gender).

Gender was compared using Fisher’s Exact test. Groups were compared regarding age and wound width in mm using independent t test while changes within each group across time were assessed using One Way Repeated Measures ANOVA and followed by post hoc comparisons with Bonferroni correction. Vancouver Scar Scale was compared using Mann Whitney U test and changes across time was evaluated using Friedman test and followed by post hoc comparison with Bonferroni correction.

Percent change for all variables was calculated according to the following formula:

\[
\frac{([\text{value after} - \text{value before}] / \text{value before}) \times 100}{\text{value after}}
\]

Data were analyzed using SPSS for Windows version 25.0. Significance level was set at p value 0.0.

**RESULTS**

Of the 12 patients in both groups, none were excluded or lost during follow-up. No complications or adverse effects were noted during the follow-up period. The mean age of the control group was 31.66 years with a range (19 to 38). (Fig. 2, Fig. 3) and the mean age of the study group was 28.00 years with a range (19 to 39). (Fig. 4, Fig. 5) Table 1 shows the characteristics of the forehead wounds and also the amount of BTA injection. (Table 1)
Table (1): Types of trauma and characteristics of forehead wounds

<table>
<thead>
<tr>
<th>No</th>
<th>Age/sex</th>
<th>Trauma Type</th>
<th>Wound Depth</th>
<th>Wound Length (cm)</th>
<th>Suture Type</th>
<th>Treatment/Injected Unit (SU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26/f</td>
<td>Slip down Muscles</td>
<td>4 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(50)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>19/m</td>
<td>In-car traffic accident</td>
<td>Subcutaneous</td>
<td>5 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(62.5)</td>
</tr>
<tr>
<td>3</td>
<td>33/m</td>
<td>Motorcycle traffic accident</td>
<td>Subcutaneous</td>
<td>3.5 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(44)</td>
</tr>
<tr>
<td>4</td>
<td>39/m</td>
<td>Slip down Muscles</td>
<td>9 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(125)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29/m</td>
<td>In-car traffic accident</td>
<td>Subcutaneous</td>
<td>6 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(75)</td>
</tr>
<tr>
<td>6</td>
<td>22/m</td>
<td>Punctual</td>
<td>4 cm</td>
<td>Layered, interrupted</td>
<td>Dysport(50)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>38/f</td>
<td>Punctual</td>
<td>4 cm</td>
<td>Layered, interrupted</td>
<td>control</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>19/m</td>
<td>Motorcycle traffic accident</td>
<td>Subcutaneous</td>
<td>3.5 cm</td>
<td>Layered, interrupted</td>
<td>control</td>
</tr>
<tr>
<td>9</td>
<td>28/m</td>
<td>Slap injury</td>
<td>3.5 cm</td>
<td>Layered, interrupted</td>
<td>control</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>37/m</td>
<td>Slip down Muscles</td>
<td>4 cm</td>
<td>Layered, interrupted</td>
<td>control</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>39/m</td>
<td>Punctual</td>
<td>3.5 cm</td>
<td>Layered, interrupted</td>
<td>control</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>29/m</td>
<td>Dermis</td>
<td>3 cm</td>
<td>Interrupted</td>
<td>control</td>
<td></td>
</tr>
</tbody>
</table>

Figure (2): (a-d) On postoperative day 5, a 26-year-old woman was given botulinum toxin A, a was taken on the day of injection, b was taken at the patient's one-month visit, c was taken at the patient's three-month visit, and d was taken at the patient's six-month visit. Patient report improved scar quality and erythema, as well as higher satisfaction.

Figure (3): (a-d) On postoperative day 5, A 26 year old male was given botulinum toxin A, a was taken on the day of injection, b was taken at the patient's one-month visit, c was taken at the patient's three-month visit, and d was taken the patient's six-month visit. Apart from a mild discoloration of the prior wound, the scar's quality has improved, and there is no obvious erythema.

Figure (4): (a-d) On postoperative day 5, A 36 year old female who received no botulinum toxin A, a was taken on the day of sutures removal, b was taken at the patient's one-month visit, c was taken at the patient's three-month visit, and d was taken at the patient's six-month visit. The issue of a widening and erythematous scar persists.

Figure (5): (a-d) On postoperative day 5, A 32 year old male who received no botulinum toxin A, a was taken on day of sutures removal, b was taken at the patient's one-month visit, c was taken at the patient's three-month visit, and d was taken at the patient's six-month visit. The scar with hyperpigmentation is still evident.
1- Wound Width
Regarding the wound width, it was measured preoperatively at the day of injection and at 1, 3 and 6 months visits. The wound width continued to increase gradually over the 6 months follow up in both the treatment and control groups. The mean scar width of the study group at 1-month was 0.25 cm and that of the control group was 0.25 cm (p = 1). At 3-months, the mean width increased to 0.31 cm in the study group and 0.46 cm at the control group. At 6-months, the mean width increased to 0.39 cm in the study group and 0.61 cm in the control group. The difference between groups was statistically significant at both at the 6-month visit (p< 0.0001) for the study group and (p = 0.001) for the control group. In the study group over the course of 6 months’ time less increase in wound width was apparent, which resulted in better esthetics in the study group. (Table 2)

2- Vancouver scar scale
The mean VSS of the study group at 1-month visit was 8.08, compared with 6.75 in the control group. At 3-month visit the VSS of the study group was 6.66, compared to 6.00 in the control group. And at 6-month visit, the VSS of the study group was 3.00, compared to 4.66 in the control group. Statistical significance was achieved when comparing the 6-month VSS scores (p = 0.002) in both study and control groups. VSS score agreement between the two raters was assessed by determining the interclass correlation coefficient and corresponding 95% confidence interval. The mean VSS scores of each group were calculated for all visits, and the Mann–Whitney test was used for between-group comparisons. (Fig. 6)

**Table (2):** Comparison of the wound width in mm between the Botox and control groups at different time intervals

<table>
<thead>
<tr>
<th></th>
<th>BTA group (n=6)</th>
<th>Control group (n=6)</th>
<th>T test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Month</td>
<td>Mean (SD)</td>
<td>0.25 (0.07)</td>
<td>0.25 (0.05)</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>0.25 (0.14)</td>
<td>0.24 (0.11)</td>
<td>0.099</td>
</tr>
<tr>
<td>3 Months</td>
<td>Mean (SD)</td>
<td>0.31 (0.08)</td>
<td>0.46 (0.19)</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>0.32 (0.17)</td>
<td>0.42 (0.26)</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>Mean (SD)</td>
<td>0.39 (0.10)</td>
<td>0.61 (0.25)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>0.41 (0.17)</td>
<td>0.56 (0.41)</td>
<td></td>
</tr>
</tbody>
</table>

Repeated measures ANOVA

| P value        | 0.0001*         | 0.001*             |

*Statistically significant at p value≤0.05

**Table (3):** Post hoc comparison of Vancouver scar scale within the Botox and control groups

<table>
<thead>
<tr>
<th>Time point</th>
<th>Compared to</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Month</td>
<td>3 Months</td>
<td>0.250</td>
</tr>
<tr>
<td>6 Months</td>
<td>0.002*</td>
<td>0.002*</td>
</tr>
<tr>
<td>3 Months</td>
<td>6 Months</td>
<td>0.250</td>
</tr>
</tbody>
</table>

*Statistically significant at p value≤0.05

P value adjusted using Bonferroni correction

**DISCUSSION**
Scars on the face can disrupt a person’s psychological well-being and, in some cases, give others a poor opinion, degrading a person’s social role. The present randomized controlled study demonstrated that the injection of botulinum toxin type A in the early first five days after primary closure could improve the appearance of facial scars and reduce their width. Our results prompted further questions about the use and efficacy of botulinum toxin type A for facial scars, which we address below (15).

The wound healing process consists of a brief coagulation phase, a days-long inflammatory phase, a weeks-long proliferative phase, and a year-long remodeling phase; these phases may occur simultaneously, with overlap of the respective processes (26). BTA can be most effective in the early stages of wound healing, and one approach to accomplish this is to reconstitute BTA in a solution of 1% lidocaine with 1:100,000 epinephrine, which results in immediate muscle paralysis rather than the 48- to 72-hour chemomobilization that occurs with BTA in 0.9 percent saline (27, 28).

In previous studies, botulinum toxin type A was injected at times that ranged from immediately before or after skin closure to 9 days after surgery. Although Kim et al. (29), presented excellent results for thyroidectomy scars on injection of botulinum
toxin type A 6.6 days post-surgery, botulinum toxin type A may be more beneficial in the very early stages of wound healing. Therefore, we chose to inject botulinum toxin type A in the first 5 days after primary closure.

Remarkably, using BTA reduced scar discoloration, as shown by the VSS scores and in the images of follow up visits. Even though many essential cellular mediators in this response have a variety of effects on melanocytes and melanogenesis. As subcutaneous injuries trigger an inflammatory reaction in a number of ways: Nitric oxide, histamine, p53, and transforming growth factor b1 (TGF-b1) are all produced during an inflammatory reaction, and they all promote melanogenesis and cause skin discoloration (30, 31).

Our results were consistent with a number of studies as Lee et al. Who discovered fewer invasions of inflammatory cells, less fibrosis, and lower expression of TGF-b1 in a rat surgical wound model with BTA compared to control (32). Furthermore, Ward et al. Reported that BTA injection reduced dermal dendritic cell and CD4 T cell infiltration in a KC-Tie2 mouse model, demonstrating significantly improved skin inflammation (33). BTA injection reduces inflammation by inhibiting nerve-derived release of calcitonin gene-related peptide and substance P, as well as cleavage of the SNAP25 protein (34).

We looked at the wound width coordinates as objective scar assessment method because validated scar assessment scales for assessing healing outcomes of complex wounds aren't discriminant enough to compare two groups of patients with simple facial wounds (35). In this study there was a significant difference in the less increase of wound width in the study group in comparison with the control group.

Ziade et al. (35), also reported similar results for botulinum toxin type A treatment of facial wounds. With regard to surgical scars, Wilson found that the outcome for facial scars after botulinum toxin type A injection during revision surgery was highly satisfactory (2). Chang et al. demonstrated that botulinum toxin type A injections produced more aesthetic and narrower cheiloplasty scars at the 6-month follow-up assessment. The results of all studies emphasize the benefit of using botulinum toxin A for facial scars (36).

Botulinum Toxin A causes chemodenervation by inhibiting acetylcholine release in the presynaptic neuron, resulting in functional denervation of striated muscle for 2–6 months after injection (37). After a skin injury, repetitive micro-trauma from constant displacement of damaged tissue causes a prolonged inflammatory response as well as distortion of healing tissue until strength and maturity are accomplished (38). According to these findings, using BTA to temporarily paralyze muscles underneath a wound should reduce tension on the healing wound and, as a result, reduce inflammatory response, as a result, reduce inflammatory response.

At their one-month appointment, all of our patients had varying degrees of paralysis of the forehead muscles, although there was no statistical significant difference noted between groups at this visit. Since scar maturation takes months, and our assessment measures (VSS score, and wound width) all based on the final outcomes of the histopathologic healing process regardless of functional effects of the drug, it's understandable that visualizing the effects of BTA on scar maturation could take longer than a month. When measured by both subjective and quantitative methods, the wound assessment parameters in patients who received BTA were significantly superior at the six-month visit.

This research may have some limitations. For starters, there was no restriction on the exact position of the wound inside the forehead. Depending on the precise position on the forehead, there may be varying degrees of distracting forces acting on the skin. Less distract, for example. Selecting patients with a clear wound position would have been optimal. Second, in this research, we were unable to conduct histopathologic evaluations. Animal models were used in the studies that showed a reduced inflammatory response, and human trials are required to confirm the underlying mechanism of action of BTA. Ultimately, due to the delayed onset of action of BTA, it would have been better to administer BTA injections earlier in the healing process, ideally upon wound closure.

CONCLUSIONS

The results of this study concluded that, individuals who received BTA injections within the first 5 days of primary closure of a wound had a minimum increase in scar width and better scar discoloration. The BTA group demonstrated better in both qualitative and quantitative measures that were dependent on the observer.

CONFLICT OF INTERSET

There are no conflicts of interest declared by the authors.

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