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An Algorithm Using Botox Injections for Facial Scar Improvement in Fitzpatrick Type IV–VI Skin

Debraj Shome, MD, FRCS
(Glasgow), FACS, MBA*
Stuti Khare, MD†
Rinky Kapoor, MD‡

Background: Wounds of the face are known to heal poorly with conspicuous scarring. Hence, it is crucial to address the distracting effect of muscle pull on immature collagen, which often leads to worsening of scars.

Study Design: Prospective clinical study.

Methods: One hundred patients with a minimum of 6 months follow-up were recruited. All patients with depressed scars underwent surgery for scar revision. Two weeks before surgical intervention, intramuscular Botulinum toxin was injected around the scar, to prevent movement of the facial muscles. From the second week postsurgery, Cicatrix (Formulation containing activated Centella Asiatica & Pinus Sylvestris, Catalysis, Spain) was routinely used, 3 times a day, for 6 months post the scar revision surgery. Six weeks postsurgery, Fractional CO₂ laser treatment was started and performed every 4 weeks.

Results: Using the Objective Assessment Score and the Subjective Assessment Score, the mean of the scores were taken. All patients had satisfactory results, as measured by a patient satisfaction survey and objectively by the physician assessment.

Discussion: Botulinum toxin injected before scar revision surgery resulted in the wound being stabilized, better wound healing, and prevention of wound widening during healing.

Conclusion: In view of the results of this study, it is considered worthwhile to offer patients with facial scars, Botulinum toxin injections before scar revision surgery, followed by Fractional CO₂ laser, along with the routine use of Cicatrix Cream. (*Plast Reconstr Surg Glob Open* 2018;6:e1888; doi: 10.1097/GOX.0000000000001888; Published online 8 August 2018.)

BACKGROUND

Facial scars are notorious for their unsightly appearance, following surgical or traumatic incisions. Widened facial scars remain a stigma and both the patients and the surgeons frequently end up disappointed. Scars widen when opposing forces that tend to pull apart the suture line are applied to newly formed collagen before it reaches final maturity, a process that can take several

months before being completed.¹ Facial scars are more notorious for widening and poor healing, owing to the abundant facial musculature that constantly pulls the scar in different directions, not giving the collagen any rest while it matures.²

Tensile distracting forces can be caused by elements such as muscle pull, elastic forces of adjacent skin, and external pressure; that is, widening of scars is mainly the result of mechanical influences on resilient and, as yet, immature collagen.³ Excessive expression of connective tissue growth factor (CTGF) is the important factor in the formation of hypertrophic scar.³ Healing is further compromised with the increase of melanin in skin.

Different approaches have been advocated to tackle the problem of wide scars. Corticosteroid injections are still quite popular, but the final, even more disfiguring outcome, consists of thin, atrophic, telangiectatic, erythematous skin, and hence many plastic surgeons around the world are reluctant to use them. Other modalities include irradiation, ultrasound and silicone applications, and many others, but

*From the *Department of Facial Plastic Surgery & Director, The Esthetic Clinics, Mumbai, India; †Department of Clinical Dermatology, Cosmetic Dermatology & Dermato-Surgery, The Esthetic Clinics, Mumbai, India; and ‡Department of Dermatology, Cosmetic Dermatology & Dermato-Surgery & Director, The Esthetic Clinics, Mumbai, India.*

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they do nothing to prevent the underlying pathologic process, which is the distracting force of facial muscle pull.⁴

On occasions, a scar is present and requires revision or sometimes a lesion requires excision and there is a need to plan the best outcome. A scar may not naturally conform to the best direction of the relaxed skin tension lines of the face or body. Although excision techniques such as Z or W plasty are useful in reorientation of scar direction, they are not always completely effective alternatives and may create elongation of the scar.⁵ Such surgical techniques, when carefully executed, reduce rather than eliminate the muscle tension that acts on the healing wound. Repeated micro trauma caused by the continuous displacement of injured tissue induces a prolonged inflammatory response and an increased metabolic activity during healing. Therefore, extracellular deposition of collagen and glycosaminoglycans can intensify and lead to hypertrophic scars.

On intramuscular injection of Botulinum toxin at therapeutic doses, partial chemical denervation of the muscle occurs. This results in a localized reduction in muscle activity,⁶ which eliminates the tension caused by local muscle, thereby minimizing the effect of muscle pull on these wounds. This stops the distraction of the wounds, which are still in the process of healing. Thus, the temporary paralysis of the facial muscles gives the crucial advantage of providing rest to the healing wound, until the collagen matures, avoiding the subsequent microtrauma and eventually the scar hypertrophy.⁷

This hypothesis could be especially helpful in Asian Indian patients, with Fitzpatrick's type IV–VI skin, in whom wound healing and scar formation is even worse. The cause of poor healing in this population has not been very well understood. Melanocytes and melanin, present in abundance in type IV–VI skin, is hypothesized to be responsible for the signaling mechanisms for the phenomenon of skin scarring. Multiple constellation of factors, such as a combination of cytokines (TGF- β 1, Interleukin-6, Interleukin-8), act dimensionally in inducing the differentiation of dermal fibroblasts to myofibroblasts.⁵ This further might lead to excessive synthesis of fibrotic extracellular matrix, perturbed matrix homeostasis, contraction, and diminished matrix metalloproteases synthesis, which is significantly involved in signaling pathways in in vitro scar formation, leading to hypertrophic and pigmented scars sometimes.

We hypothesized the use of a new protocol for scar healing and scar improvement, including Botulinum toxin injections given 2 weeks before surgery in adequate doses and the use of meticulously performed scar revision surgery, followed by daily topical applications of Cicatrix (Centella asiatica based skin cream) and FCO₂ laser done at 4 weekly intervals. Given that our understanding of anatomy and the physiology of scar healing is constantly evolving and also given that peer-reviewed literature has hardly any articles on methods to improve wound healing in skin types IV–VI, we decided to test this protocol in a prospective clinical study involving 100 patients.

Study Design

A prospective clinical study was conducted, until 100 patients with a minimum of 6 months follow-up, were recruited.

Inclusion Criteria

Adults of both genders of Asian Indian origin, who consented to participate in the trial and signed a detailed informed consent form.

Facial scars of greater than 6 months origin.

Exclusion Criteria

Patients taking active treatment for the scars, within 3 months of the date of induction, into this trial.

Scars anywhere else on the body, other than the face.

Keloidal and large hypertrophic scars.

Study Dates: January 2016 to November 2017.

MATERIALS AND METHODS

A prospective clinical study in which patients were enrolled, until we reached a total of 100 patients with a minimum of 6-month follow-up. All sequential patients, presenting to us for scar improvement, who agreed to participate in the trial, were included. The classification by Kwok and Tao⁸ for facial scars was used, and scars were classified into depressed and elevated scars.

We thus looked at elevated, flat, and depressed scars and suggested different scar treatment techniques for each of the above subtypes. The elevated and the flat scars (n = 2) were treated with laser resurfacing, scar creams and other nonsurgical techniques, whereas the depressed scars (n = 98) all underwent surgery for scar revision, followed by using our scar protocol to treat the scars, described below.

Presurgery

Two weeks before surgical intervention, we used intramuscular Botulinum toxin injections around the scar, to prevent movement of the facial muscles, around the scar. Botox injections were “enough” in unitage, and distributed in multiple locations around the scar, to prevent any muscular movements around the scar, for at least 2 months postsurgery.

We hypothesized that this “wound stabilization” would lead to better scar healing, by preventing facial movement from interfering with wound healing and scar maturation. Then, scar revision surgery was performed.

Surgical Management

The surgery involved making sure the wound was closed in multiple layers, with eversion of the wound edges. As far as possible, the surgery oriented the scar lines along the relaxed skin tension lines. Asymmetric or broken line incisions were used in all the cases to diminish the visibility. Significant undermining of the skin and subcutaneous tissue was performed, so that the edges of the wound could be opposed without any tension. Closure was performed in 4 layers.

Deep Tissue to Deep Tissue: This was performed with Polyglactin 4-0 or 5-0 sutures (depending upon the area of the face). The objective was to get the wound edges as close as possible.

Subcutaneous to Subcutaneous Tissue: This was also performed with Polyglactin 4-0 or 5-0 sutures. The objective of this layer was to get the edges of wound as close as possible.

The entire tension of the wound apposition was borne by these 2 sets of sutures. Then, after this, we took,

Subcuticular tissue sutures: 5-0 or 6-0 Polyglactin, continuous sutures, were used to oppose the wound edges completely.

Following this,

Skin closure: Along the length of the wound, a few vertical matrix sutures were taken first, to evert the wound edges. After this, a continuous 5-0 or 6-0 Polypropylene suture was used to appose the wound edges. We have had previous experience of wounds gaping in patients with Asian Indian skin, if the sutures were removed up to 7 days. Hence, these skin sutures were removed at 10 days, postsurgery. Because the skin sutures were non bioreactive, we believe that scar irritation, postsurgery pigmentation and subsequent scar hypertrophy was significantly minimized.

Postsurgical Management

In the immediate period until suture removal (10 days), the scar care regimen involved the use of wound cleaning with antiseptic lotion twice a day (Betadine) and application of antibiotic creams (Fusidic Acid based) on the wound. Post suture removal, steroid creams (Mometasone furoate) were used for 7 days, mainly to prevent any postsurgery hyperpigmentation. Patients were instructed to restrict exposure of the scar to the sun as much as possible, for the first 3 months. Regular use of sunscreen when in the sun was prescribed.

From the second week, use of Cicatrix (Formulation containing activated Centella Asiatica & Pinus Sylvestris, Catalysis, Spain) was routinely used, 3 times a day, for 6 months post the scar revision surgery. The main component of the cream is Centella Asiatica, which contains triterpenic saponins, Asiatic acid, and Madecassic acid. The mechanism of action involves a molecular activation process, stimulating the fibroblasts, producing collagen (collagen types I and III), regulating the epidermal homeostasis and modulating the chronic inflammation in the scar tissue.⁹

In addition, skin lightening creams containing kojic acid and hydroquinone 2% were used for a month, if the wounds began to become hyperpigmented, under supervision of our dermatologist.

After 6 weeks of surgery, FCO₂ ablative laser skin resurfacing was used in these patients. FCO₂ laser skin resurfacing is known to cause skin hyperpigmentation and hence the parameters must be closely monitored in Fitzpatrick types IV–VI skin. FCO₂ laser skin resurfacing parameter used were 30 Watts Power, Pulse Width was 1 msec, Point distance was 0.7–0.8 mm, and superimposition was maintained at 2–3. The laser sessions were repeated every 4 weeks, until the appearance of the scar appeared to have blended with the surrounding skin.

CLINICAL ASSESSMENTS

The scars were evaluated before and after treatment, at 1 month, 3 months, and at 6 months, by 3 neutral plastic surgeons. These evaluations were summated into a single number called the Objective Assessment Score, and the

Table 1. Showing Subjective Assessment and OASs at 1 Month, 3 Months, and 6 Months

Time	SSS	OASS 1	OASS 2	OASS 3
At 1 mo	1.2	1.3	1.4	1.6
At 3 mo	2.1	2.2	2.4	2.3
At 6 mo	3.9	3.7	3.8	3.6

OASS, Objective Assessment Scores.

Table 2. Showing Mean OASS and SSS at 1 Month, 3 Months, and 6 Months

Time	SSS	Mean OASS
At 1 mo	1.2	1.5
At 3 mo	2.1	2.3
At 6 mo	3.9	3.7

OASS, Objective Assessment Scores.

mean of the scores was taken (Tables 1, 2). Patients filled a questionnaire, evaluating the improvement of the scars, at 1 month, 3 months, and 6 months. These evaluations were summated into a single number called the Subjective Assessment Score (SSS), and the mean of the scores was taken (Tables 1, 2). Both these scores corresponded to improvement of 0–20% to 1, 21–40% to 2, 41–60% to 3, 61–80% to 4, and 81–90% to 5.



Fig. 1. Showing before image of patient 1, with the facial scar caused due to burns.

RESULTS

One hundred patients, treated with this regimen, had excellent results, for scars of different etiologies (Figs. 1–12). There were 46 men and 54 women, with mean age being 28 years (range, 19–47 years). With respect to the Fitzpatrick skin types, 68 were Fitzpatrick IV skin types, 23 were Fitzpatrick V skin types, and 9 were Fitzpatrick VI skin types.

The size of the scars varied from 1 inch to 7 inches in size. The scars had different configurations and shapes like linear, annular, crescent, and irregular. Ninety-eight patients had depressed scars, and 2 patients had elevated scars. Only 10 scars were along the lines of least surface tension.

Scar revision surgery was performed in 98 of the 100 patients. Before scar revision surgery, the scar was stabilized, with usage of Botulinum toxin (Botox, Allergan, Irvine, Calif.) injections. Mean Botulinum toxin injections used were 25 units (range, 10–40 units), on both sides of the scar. Two patients with elevated scars did not undergo surgery and chose to undergo use of the Cicatrix scar reduction creams and FCO₂ laser skin resurfacing. Asymmetric scar excision techniques like the

W plasty was used in 90 patients. Eight patients needed more complex procedures like tissue expansion surgery, serial scar excision, and so on. FCO₂ laser skin resurfacing was used in all patients; an average of 6 sessions of scar revision laser were required (range, 4–12 sessions). All patients had satisfactory results, as measured by a patient satisfaction survey and objectively by the physician assessment. Mean SSS was 3.8 (range, 3.6–4.4), demonstrating that patients felt that improvement in the scar posttreatments was a mean of 76% over the baseline presentation. Mean Objective Assessment Score was 3.7 (range, 3.6–3.8), demonstrating that physicians felt the improvement in the scar posttreatments was a mean of 75% over the baseline.

DISCUSSION

Facial scars may heal badly, because of the continuous movement of the facial muscles, which impacts the wound healing and scar maturation process, leading to wider and more depressed scars. Scar revision techniques for the face are constantly evolving. Facial scar revision corrects skin changes caused by wounds, previous surgeries, or caused by injuries such as burns or acid attacks or facial trauma. Scar revision procedures also assist restore the function, by reducing skin and soft-tissue contractures.^{5,10}

In a series of articles, researchers at the Mayo Clinic initially showed favorable results in a randomized, double-blinded, placebo-controlled study for scars, in which the halves of foreheads that were injected with Botuli-



Fig. 2. Showing after image of patient 1, on whom scar revision surgery was performed for the facial scar caused due to burns. Results after 8 sessions of FCO₂ laser. Photographs pre and post, taken 12 months apart.



Fig. 3. Showing before image of patient 2.



Fig. 4. Showing after image of patient 2, on whom scar revision surgery was performed. Results after 6 sessions of FCO₂ laser. Photographs pre and post, taken 9 months apart.



Fig. 5. Showing before image of patient 3.

num toxin had a significantly better appearance than their placebo counterparts.⁹ Botulinum toxin has been studied in the prevention of scarring in animal models too, following traumatic wounding and has shown to prevent increase in collagen content during urethral wound healing.^{10,11}

Immobilization is a basic therapeutic principle in wound healing, common to the treatment of lesions of all kinds. Casts, plates, and sutures minimize the negative effects of muscle tension on healing wounds, including skin lesions. Repeated micro trauma caused by continuous displacement of injured tissue induces a prolonged inflammatory response and distortion of healing tissues, before they achieve strength and maturity.¹⁰

Botulinum toxin eliminates dynamic muscle tension on the healing wound. It produces its therapeutic effects, by acting selectively on peripheral cholinergic motor nerve endings, to inhibit the release of the neurotransmitter acetylcholine at the neuromuscular junction. This inhibition occurs as the neurotoxin cleaves synaptosomal-associated protein 25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings.¹⁰

Lee et al.¹¹ designed a prospective randomized experimental study to investigate the impact of Botox on the stages of wound healing in a rat surgical model, both at the macroscopic and the microscopic levels. They hypoth-

esized that Botox-induced paralysis of the musculature adjacent to the surgical wound with a skin defect, would minimize the repetitive tensile forces on the wound edges, and this would result in a decreased fibroblastic response and fibrosis of the wound.

In 2000, Gassner et al.¹² at the Mayo Clinic set out to pioneer an alternative use of Botulinum toxin in the treatment of facial wounds, to improve cosmetic outcomes in macaque monkeys. Multiple clinical trials were conducted by them. Results of which showed that wounds that had been immobilized with Botulinum toxin had a significantly better appearance than control wounds. This was further proved by histologic examination.¹³ Numerous academic centers in the United States, Europe, and Africa have now reported on their favorable experiences with BTX-A for chemo-immobilization for the treatment of cutaneous scars.¹⁴

The high efficacy of BTX-A in the treatment of scars is also attributed to the degrading effects of BTX-A on the activated dermal fibroblasts, which release CTGF. BTX-A is involved in regulating the fibroblast cell cycle, and in decreasing the Transforming Growth Factor- β 1 (TGF- β 1) and the CTGF expression in fibroblasts, involved in causing hypertrophic scars. Such researches provided the experimental background for using intradermal BTX-A injection for hypertrophic scars.



Fig. 6. Showing after image of patient 3, on whom scar revision surgery was performed. Results after 7 sessions of FCO_2 laser. Photographs pre and post, taken 12 months apart.



Fig. 7. Showing before image of patient 4.



Fig. 8. Showing after image of patient 4, on whom scar revision surgery was performed. Results after 8 sessions of FCO_2 laser. Photographs pre and post, taken 15 months apart.



Fig. 9. Showing before image of patient 5.

BTX-A for scar treatment was further validated by the outcome of healing wounds, relative to the lines of Langer.¹⁵ These lines lie perpendicular to the tension vector of underlying muscular contraction: scars aligned with the lines of Langer are subject to reduced tension and heal well, whereas scars oriented against them are subject to repetitive tension, resulting in scar widening.

Cicatrix cream that was routinely used in all the patients contains *Centella asiatica* and *Pinus Sylvestris*. The traditional claim of wound healing of *Centella asiatica* extract as a cream, gel, or solution has been well documented. It



Fig. 10. Showing after image of patient 5, on whom scar revision surgery was performed. Results after 8 session of FCO₂ laser. Photographs pre and post, taken 18 months apart.

is helpful in (1) promoting the healing process by stimulating the reticulohistiocytic system and the vascularization in tissue. (2) Adjusting the connective tissue in keloids, hypertrophic scars, and burns. (3) Promoting the synthesis of collagen in the walls of the blood vessels and in preserving skin color. Pinus sylvestris is another component of the cream, which is crucial for healing, by strengthening blood vessels, and by its anti-inflammatory effects.

Centella asiatica belongs to the family Apiaceae (Umbeliferae). This herb is indigenous to the Indian subcontinent, Southeast Asia, and wetland regions of the Southeastern United States. The biologically active ingredients of this cream are triterpenes, namely, asiatic acid, madecassic acid, asiaticoside, and madecassoside.¹⁶ Asiatic acid is known to be 1 of the most effective constituent. It exhibits apoptotic effects in several tumor cell lines.¹⁷

Due to its ability to stimulate collagen synthesis, *Centella* has been used in skincare products for restoring skin firmness, elasticity, and improving skin appearance and is considered suitable for the treatment of fresh wounds such as heat burns or other minor injuries like blade cuts, scratches, and so on. World Health Organization recommends using *Centella Asiatica* to promote the healing process, especially for postoperative or posttraumatic scars.¹⁸

Laser resurfacing is supposed to work by stimulating collagen production in the dermis and by dermal remodeling of collagen fibers. Carbon dioxide (CO₂) laser is an ablative laser device that produces energy in the far-infrared region at a wavelength of 10,600 nm. With fractional photothermolysis, only a fraction of the whole skin is treated in a pixelated pattern while the intervening skin remains intact.¹⁹ In our trial, post the surgery, multiple sittings of fractional CO₂ lasers were given to the healing skin, which showed excellent response. The mechanism involved is that of denaturation of collagen by laser-generated heat. The shrinkage of colla-



Fig. 11. Showing before image of the patient 6, who suffered facial trauma due to road traffic accident.

gen is the primary mechanism of skin tightening, although vaporization of intracellular water and ablation contributes as well. Next, a wound-healing phase is initiated characterized by extremely high levels of collagenases (matrix metalloproteases), which degrades the fragmented collagenous matrix.¹⁹ Rapid reconstitution of the epidermis from adjacent epidermal cells, contrasts with healing after traditional resurfacing, in which new epidermis is derived from cells that migrate from adnexal structures. A prolonged period of dermal neocollagenesis of up to at least 6 months follows. This leads to far better outcomes in scars. However, FCO₂ laser resurfacing can lead to significant pigmentation in Fitzpatrick types IV–VI skin, especially postsurgical trauma, so careful and repeated evaluation by a dermatologist with experience in pigmented skin, is mandatory.

In conclusion, we have used a new scar treatment algorithm to treat scars in pigmented patients, where wound healing is typically compromised and scar formation is typically exaggerated. For flat scars and elevated scars, laser was performed. Depressed scars underwent scar revision surgery, which when followed by a painstakingly followed



Fig. 12. Showing after image of patient 6, after 8 sessions of FCO₂ laser. Photograph taken 18 months later.

regimen, gave excellent results. Botulinum toxin injected before scar revision surgery, resulted in the wound being stabilized, better wound healing and prevention of wound widening during healing. The algorithm of evaluating the scars, performing meticulous scar revision surgery in all flat, wide and depressed scars, using Botulinum toxin injections before the scar revision surgery to prevent scar widening during healing, using Cicatrix containing C. Asiatica for better scar healing for at least 6 months post-surgery and using multiple sittings of CO₂ laser skin resurfacing for better skin and scar texture postsurgery can provide excellent results in unsightly ugly scars.

Debraj Shome, MD, FRCS, FACS, MBA
The Esthetic Clinics
Mumbai, India.

E-mail: debraj.shome@theestheticclinic.com

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