Review Article

Microdroplet Botulinum Toxin: A Review

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Abstract

Microbotox is the administration of multiple microdroplets of botulinum toxin in intradermal plane. It is increasingly becoming popular owing to its more favorable outcome and better safety profile than the conventional technique. The intention is to treat fine lines and wrinkles without imparting an undesired "frozen face like" appearance. Besides facial rejuvenation, it has found its way into the management of other indications such as rosacea, hyperhidrosis, keloid, and seborrhea. Being a relatively newer method, knowledge about the various dilution methods, desired volume, and correct depth of injection involved in this technique remain scarce. In this article, the authors have highlighted various indications, procedures, adverse effects, and contraindications of microbotox.

Keywords: Botulinum toxin, facelift, facial wrinkles, mesobotox, microbotox, microdroplet technique

Introduction

"Microbotox," "mesobotox," or the "microdroplet technique" has become a common *off-label* use of botulinum toxin type A (BoNT) over the past 2 decades. The original technique involved administration of uniformly placed, intradermal, microdroplets of onabotulinumtoxin type A (ONA) (Botox; Allergan Inc., Westport, Ireland) in lower concentrations compared with the traditional technique.[1,2] Although the initial use of the technique involved ONA, other types of BoNT have since been used.[3]

The aim is to provide relaxation of fine lines and wrinkles, without the undesired "frozen" or "plastic" appearance. Besides facial rejuvenation, the technique has been used for hyperhidrosis, seborrhoea, and keloids.[4-9]

Mechanism of Action

Although microdroplet BoNT acts by the same mechanism as conventional BoNT,[2,10] the depth of injection and the resultant intensity of muscle weakness varies. Figure 1 compares traditional BoNT and the microdroplet technique. The varying mechanisms are below.

Action on superficial muscle fibers

Microdroplet BoNT acts on the superficial fibers of facial muscles, attached to the lower dermis. The higher dilution and low-concentration inhibit the "pulling" effects of the superficial fibers, and preserves the function of the deep muscle fibers, imparting a rested appearance to the face.[11,12]

Decrease in sweat and sebum production

Microdroplet BoNT has the potential to induce reversible atrophy of the sweat and sebaceous glands, thereby, improving skin texture, and luster.[4,10,11,13]

Neurochemical blockade of acetylcholine from the cholinergic neurons innervating the sweat glands and smooth muscle is responsible for decreased sweat production. The action on sebaceous glands is unclear since they are regulated via androgen-mediated neurons. It is postulated that inhibition of parasympathetic response of sebaceous glands and erector pili muscles, results in a heightened sympathetic response responsible for the reduction of facial pores.[14,15]

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Fluid retention

Microdroplet BoNT causes relaxation of muscles guarding lymphatic channels and an increased osmolarity in the dermis, leading to fluid retention in the compact dermis.[16] This effect makes the face appear luminous, and usually lasts for 3 months.[1] The multiple needle pricks, relaxed depressor muscles, volume effect, and fibroblast contraction demonstrates a mini "facelift" feel.[16]

Procedure

Dilution

Microdroplet BoNT using ONA is prepared by using 1:5 dilutions, which is 100 U in 5 mL of solution. Dilutions of 1:10 have also been used resulting in 10 U of neurotoxin per mL or four markings of a standard 40 U insulin syringe corresponding to 1 unit of ONA. One may use 1–5 such syringes depending on the indication being addressed.

Alternatively, a standard dilution of ONA (2.5 mL saline to 100 U) may be further diluted, according to the area being addressed, for example, 24 U (0.6 mL in a 40 U insulin syringe, topped up with saline) providing 24 U in 1 mL solution while treating the forehead, similarly 8–12 U for the under-eye area and 24 U for the neck and jawline.[1]

Recent data have shown the safety and efficacy of microdroplet abobotulinumtoxin (ABO, Dysport) in facial lift.[17,18] Sapra *et al*., reported a comparable improvement in skin texture, wrinkles, and midface lift, with microdroplet ABO (300 U in 6 mL saline) and ONA (100 U in 5 mL saline).[3] *In vitro* comparison between varying BoNT A preparations reveal that product selection and dilution are crucial for facial lifting [Table 1].[19]

Injection technique and dosing

The technique is carried out post-topical anesthesia using a 30–32 G needle, advanced gradually, with bevel pointed downward and almost parallel to the skin. Gentle pressure is applied to the plunger, sufficient enough to raise a small bleb.[20] Resistance on the plunger suggests an intradermal delivery, while an easy flow denotes an incorrect, deep placement of solution.

A 0.05 mL of solution is injected at 1 cm intervals, intradermally, in a uniform, grid-like fashion.[2,10] One must remove air bubbles from the syringe before injecting to achieve accuracy and prevent wastage.

Alternatively, automatic injectors can be less time-consuming and may provide better accuracy and reduced wastage.[17]

Indications

Microdroplet BoNT is used for varying indications [Table 2].[2,4-10]

Upper face treatment

Global recommendations demonstrate an evolving trend suggesting the use of microdroplet BoNT for the upper face.[18] The technique is useful in women desiring an eyebrow lift and prevents an akinetic forehead [Figure 2].

The dosing protocol for the upper face has been depicted in Table 3.

Midface treatment

The mid-face and under-eye region should be addressed by experienced injectors, as inaccurate placement of the solution

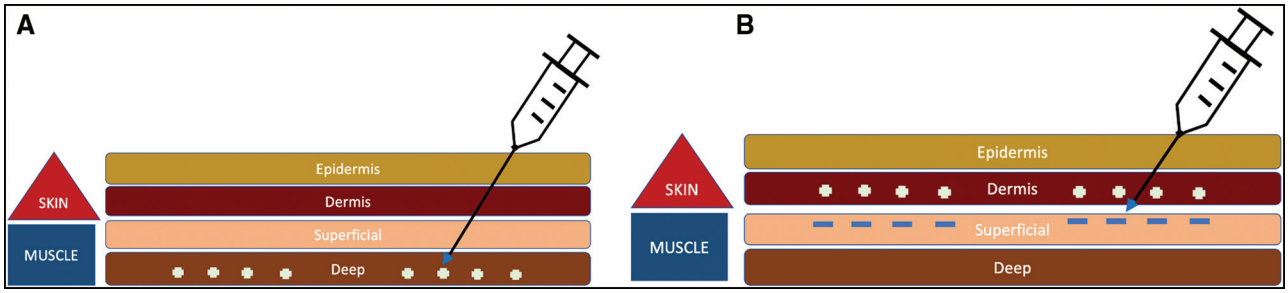

Figure 1: (a) Traditional technique of administration of botulinum toxin into the deeper fibers of the muscle. (b) Microdroplet technique showing administration of neurotoxin in intradermal plane, into the superficial muscle fibers thus sparing the deeper muscle fibers.

Table 1: Various dilution techniques for microbotox

Neurotoxin	Dilution
ONA	100 U in 10 mL normal saline, 1 unit = 0.25 mL 100 U in 5 mL normal saline, 1 unit = 0.5 mL 100 U in 2.5 mL normal saline, 1 unit = 0.1 mL (dose used as per area injected)
ABO	500 U in 2.5 mL saline 70 units/mL (0.35 mL) further diluted in 0.65 mL
INCO/Medytox/Prabotulinum toxin	No exclusive data May be used in similar dilution as ONA

INCO = incobotulinum toxin A

and large droplet size may lead to diffusion to deeper muscle fibers and undesirable effects [Figure 3a and b].[20] For the undereye region, a minimal dose of 8–12 U of ONA in 1 mL solution has been suggested to prevent an inanimate lower lid; however, for the cheeks and nose 20 U in 1 mL saline may be used [Figure 4].

Differing techniques have demonstrated a mid-face lift, using up to 50 U/side of ONA, 100–180 U/side of ABO, or 30 U/side of incobotulinum toxin A (INCO) [Table 3].[3,18,20-22]

Lower face and neck treatment

The relaxation of the lower face depressors and superficial fibers of platysma creates a defined cervicomental angle and sharper jawline, imparting a "mini neck lift."[1] The boundaries for the injection in the lower face and neck have been illustrated in Figure 5.

In the authors' experience, microdroplet technique is more beneficial when combined with conventional BoNT for the lower face and neck. Although conventional BoNT debulks the masseter and relaxes the platysmal bands, the microdroplet technique provides tightness to the skin on the neck, especially in patients with fine horizontal necklines and "crepe-like skin" as shown in Figure 6.

Furthermore, energy-based devices may be combined for optimizing outcomes. 28 U of BoNT in 1-mL solution is used (1–3 syringes) up to the platysmal fibers attached to the masseter. The dilution may vary in patients with thin necks (20 U/mL) and visibly thicker necks (28 U/mL).[2,10,23] ABO has been used in dilution of 1:7. Depending on the neck size, 2–3 syringes each containing 70 U may be used [Table 3].

Table 2: Indications of microdroplet BoNT

Common indications
Lower facelift and necklines
Mid facelift
Upper forehead expression lines
Lateral canthal lines
Less common indications
Open pores and rosacea
Keloids
Hyperhidrosis
Acne

Dilated pores and rosacea

Microdroplet BoNT has the potential to decrease sweat and sebaceous gland activity.[14]

Treatment for dilated pores may be combined with fractional technology for optimal outcomes. A single session improves the dilated pores albeit for a short duration, requiring repetition in 3–4 months.

Microdroplet technique with hyaluronic acid

When microdroplet BoNT is delivered with microhyaluronic acid (microHA) known as hydrotoxin, the procedure is twice as effective than monotherapy.[16] Improvement in skin roughness and hydration is noticeable in 5–7 days and 1–2 weeks respectively. In most cases, the results of a single treatment session last for 6 months.[17]

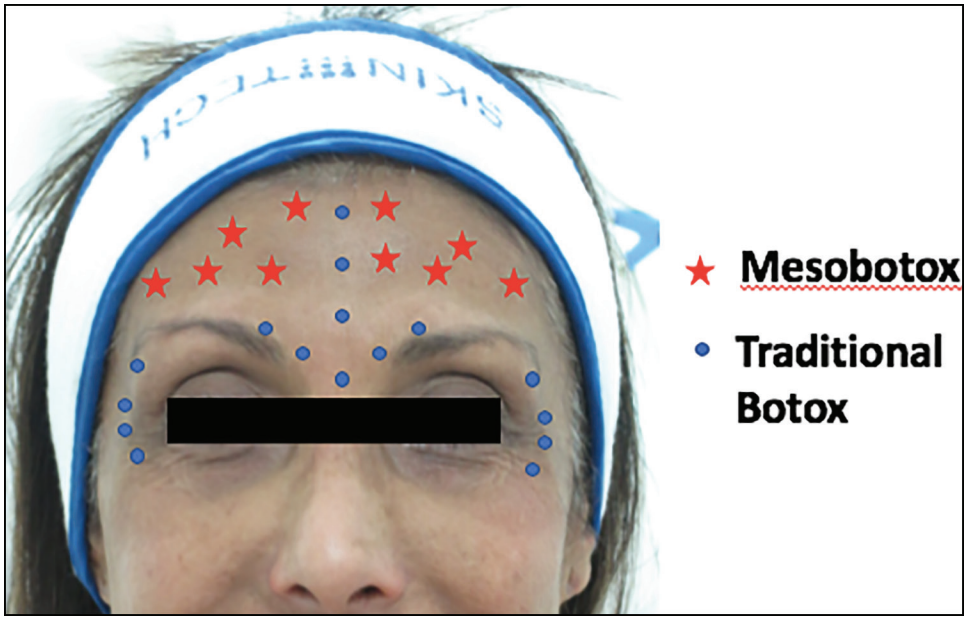

Figure 2: Combination of microdroplet BoNT with traditional botulinum toxin for brow lift.

The technique has been used with 2 mL of stabilized HA (Neuramis Light, Medytox, Korea) mixed with 1 mL of 40 U ONA delivered via an injector (Neurajet, Medytox, Korea).[16] Alternatively, 1 mL of monophasic HA (Belotero Balance, Merz Pharmaceuticals) with 40 U of INCO has been used with similar results.[14]

Table 3: Region wise onabotulinum toxin A administration

Region	Differing techniques	Comments
Forehead	24–28 U (0.6 -0.7 mL of standard dilution ONA in 1 mL saline) – single syringe[7] OR 8–20 microdroplets of 0.5–1.5 U each.[20]	If traditional dilution ONA is administered to the glabella, eyebrow, and central forehead regions to create a brow lift, then 16 U is sufficient just for the lateral forehead alone.
Periorbital	Under eye – 8 to 12 U (0.2–0.3 mL of standard dilution ONA in 1 mL saline)[7] Lateral canthal lines – 1–5 microdroplets of 1–4 U each.[20]	Small margin for error – Use tiny droplets. Too little BoNT will lead to negligible results and too much (large droplets) will lead to adverse effects.
Mid face	20 U (0.5 mL of standard dilution ONA in 1ml saline) – single syringe[7]	Small, uniform droplets to avoid inadvertent diffusion into deeper muscle fibers.
Lower face Jawline and neck	Jawline and neck – 24 U (0.6 mL of standard dilution ONA in 1 mL saline) – two syringes.	May require a third syringe depending upon severity of lines. Great technique for fine lines and creases on the neck.

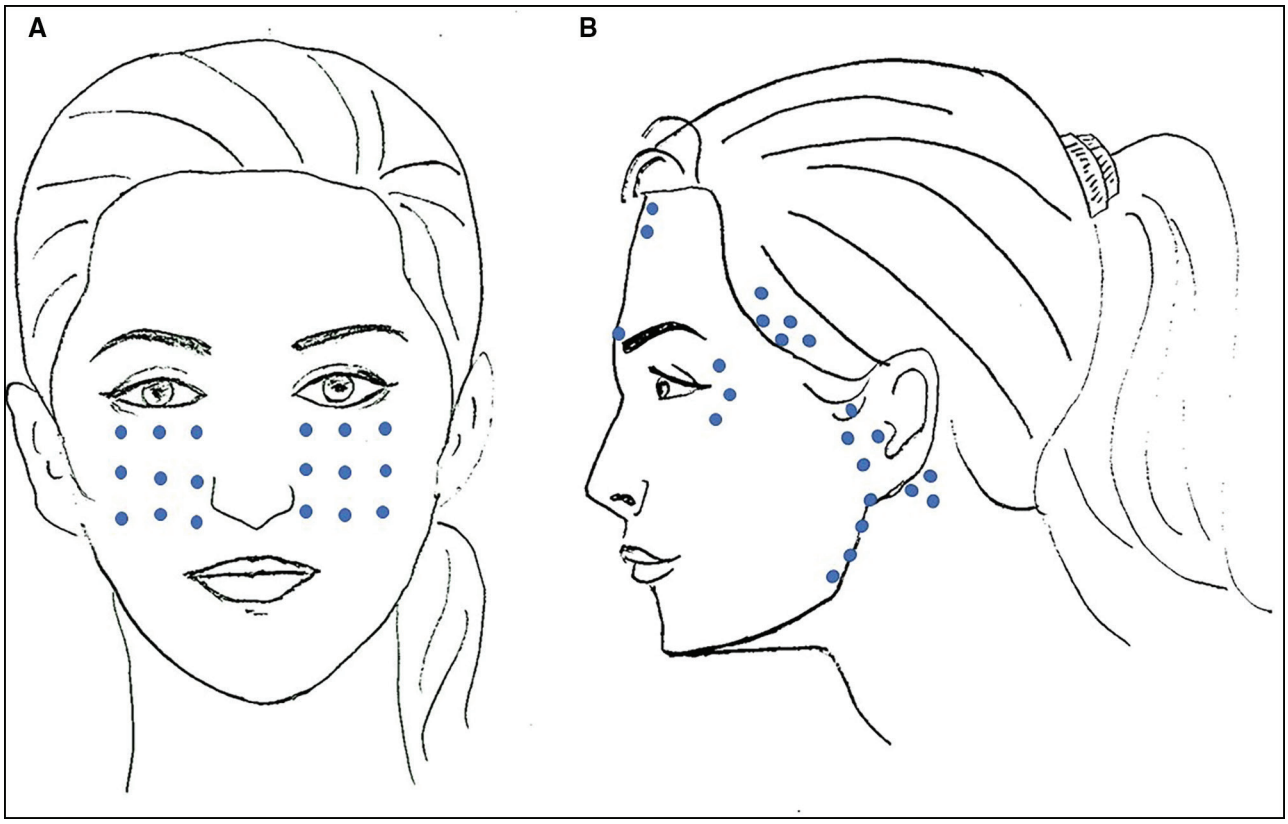

Figure 3: (a) Microdroplet technique for mid-facelift, administered in a grid pattern, with injection points 0.5–1 cm apart. (b) Alternative technique for mid-facelift with injection points in two rows over the frontalis, two rows at the temples along the hairline, lateral orbicularis oculi, pre auricular at the level of the tragus and along the mandibular line at 1 cm intervals.

Microdroplet BoNT for keloids

The role of BoNT in keloids is inconclusive and needs larger studies. A triple therapy combining intense pulsed light (IPL), intralesional triamcinolone, and microbotox has shown success. Following IPL therapy, microbotox is injected into the keloid and the surrounding skin, followed

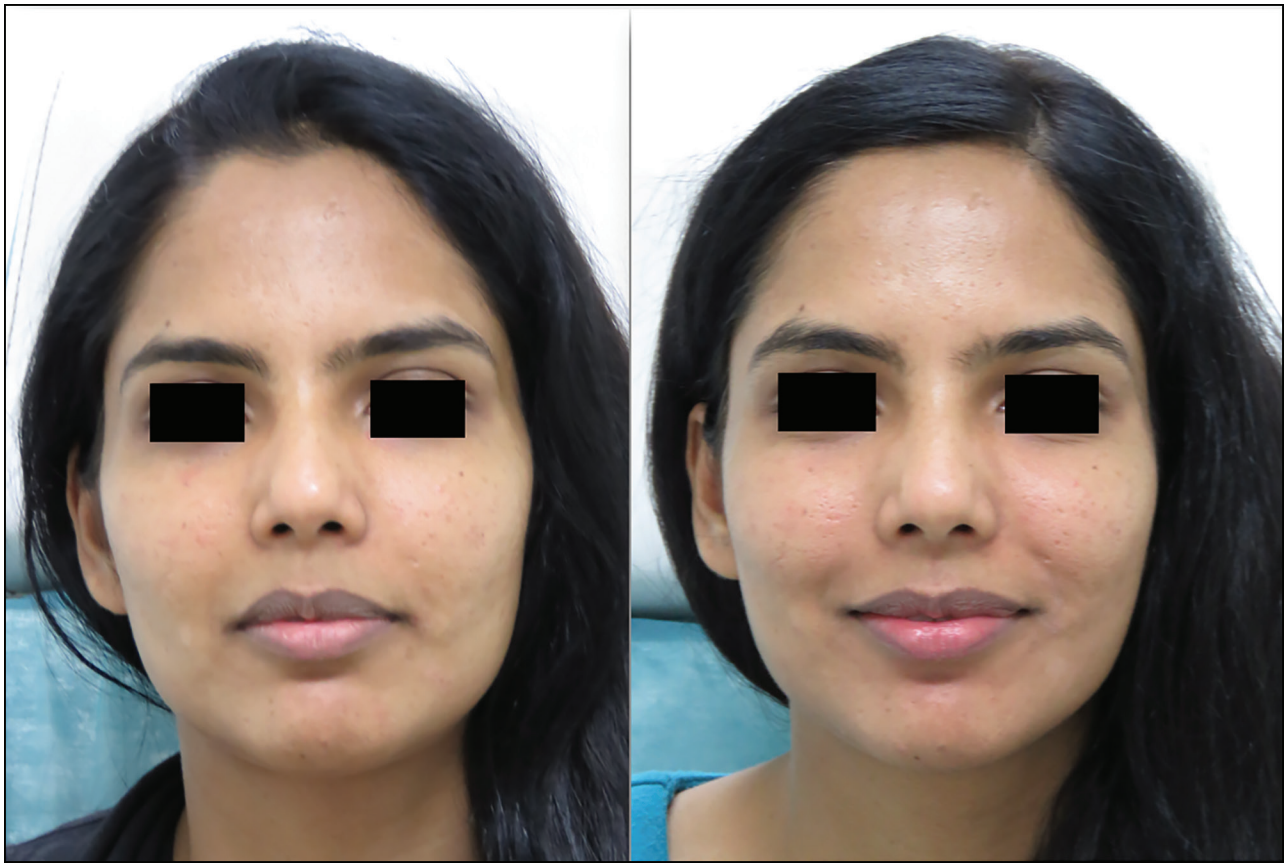

Figure 4: Mid facelift demonstrating a rested appearance with microbotox technique, 20 U ONA in 1 mL of solution (right).

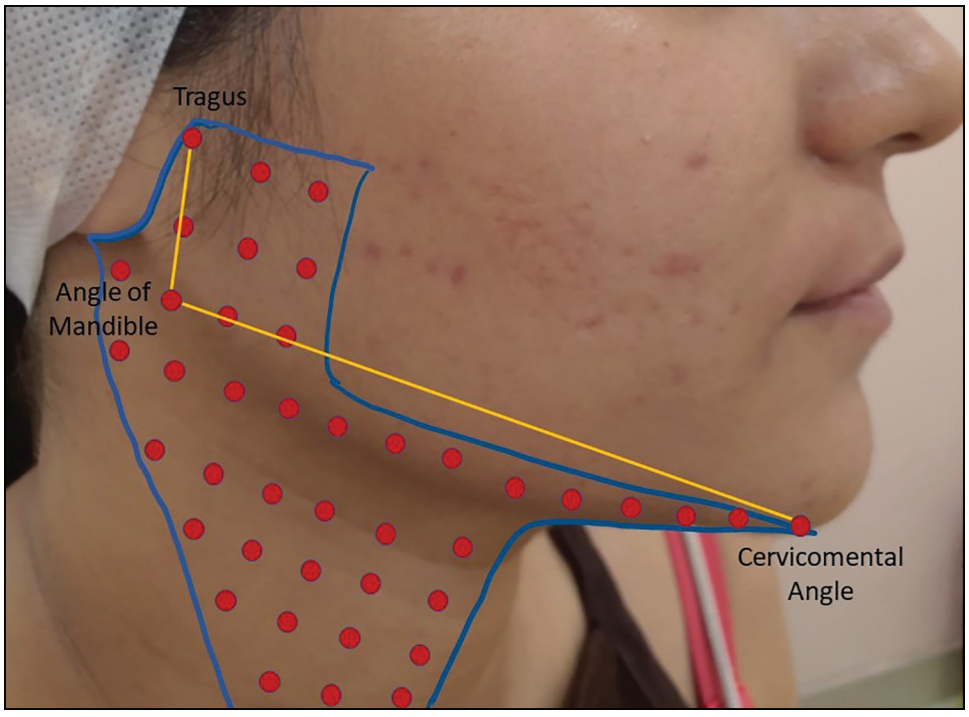

Figure 5: Target zone for lower face and neck lift with microdroplet technique.

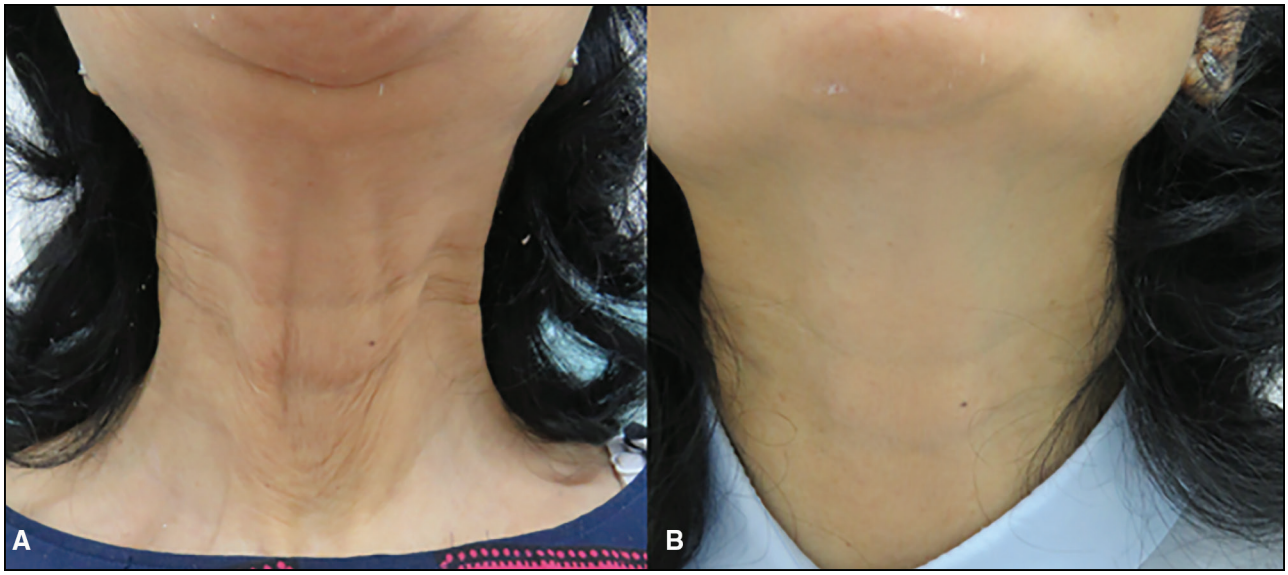

Figure 6: (a) "Crepe-like" skin on the neck, (b) neck lift with microdroplet technique demonstrating improvement post-administration of 42 U of ONA.

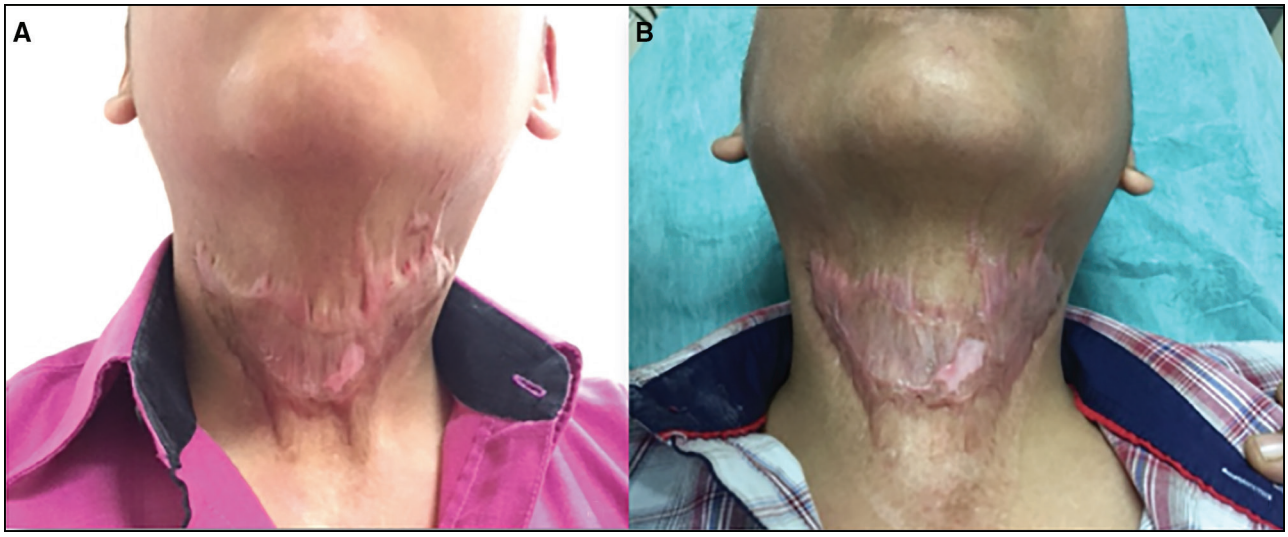

Figure 7: (a) Post-burn keloid on the neck (left), (b) Significant softening and improvement in range of motion with single session of 24 U in 1 mL solution of medytox combined with intralesional triamcinolone acetonide (40 mg/mL).

by intralesional triamcinolone.[7] Besides, a synergistic effect with triamcinolone and reducing the dose and adverse effects of triamcinolone, microbotox also reduces the overall risk and intensity of recurrence[7] [Figure 7]. It appears that BoNT decreases the muscular tension in a healing wound, inhibits the growth of fibroblasts, and alters the production of the transforming growth factor (TGF)-β1.[24]

Contraindications

Despite lower dose and volume, the microdroplet technique may have the following contraindications [Table 3].

Adverse Effects

Delivering microdroplets consistently and superficially avoids complications.[14] Inadvertent diffusion to the deeper muscle fibers, due to subdermal injection or delivery of larger volume results in total or partial paralysis.[21] Due to a lower neurotoxin concentration, these complications are temporary and usually subside within 2–3 weeks.[10]

(a) *Stiff immovable brow* – due to inadvertent diffusion into the deep fibers of the frontalis.
(b) *Weakness in neck movement* – due to diffusion into the sternocleidomastoid muscle.
(c) *Asymmetric smile and lower face atrophy* – due to diffusion into the depressor anguli oris, risorius, or depressor labii inferioris in the lower face or intermingling fibers of the platysma.[14]
(d) *Festooning or "inanimate lower eyelid"* – due to diffusion into the orbicularis oculi particularly in

patients with pre-existing skin laxity. Be judicious in patients with a sluggish "snap test."

The technique demonstrates a short duration of action warranting frequent sessions. Few patients may find the treatment uncomfortable due to multiple injection points.

Conclusion

Microdroplet technique can be considered a simple, relatively safe, and effective treatment used for facial and neck rejuvenation. Its ability to preserve muscle movement and provide "natural looking" results makes it a desirable option. Currently, large-scale studies and data on defined protocols are scarce. Authors suggest that while the technique should be used judiciously until proper guidelines are available, it is important to be aware of this evolving technology and its benefits.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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