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Techniques of using botulinum toxin for forehead wrinkles: A narrative review

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Abstract

The use of botulinum toxin extracted from bacteria Clostridium Botulinum for obliteration of forehead wrinkles has proven to be exceptionally efficient. Injection techniques are based on muscle groups targeted with minimal adverse effects when executed by a professional. Outcome is determined by a grading scale and differs based on the type of wrinkles. It is judged on day 1-4 post injection and peak effects are noticed around 1-4 weeks. It was seen that wrinkle reduction was dependent on dilution criteria and dose of the toxin. Bruising and hematoma formation are common local complications. Adverse effects are seen with concomitant use of other medications like Aminoglycosides, muscle relaxants and Anticholinergic drugs.

Keyword: Botulinum toxin; Dynamic wrinkles; Static wrinkles; Outcome; Complications.

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Abbreviations used: SNARE: Soluble N-ethylmale-imide sensitive factor Attachment protein Receptor; SNAP: Soluble NSF Attachment Protein; BoNT: Botulinum Neurotoxin.

Introduction

Aging is an unavoidable process resulting in physical and psychological changes in our body and mind respectively, with skin playing the role of top representator in the form of wrinkles. Face is the earliest part to be affected by wrinkles. Although wrinkles also appear while we give facial expressions; they are temporary wrinkles. With aging there is loss of collagen and elastin that manifests in the form of static wrinkles.[1] Different therapeutic approaches have been used for treatment of wrinkles and one of those is Botulinum Toxin A. Botulinum toxin is being used for both cosmetic and non-cosmetic issues for past several years.[2] In 2002, the use of Botox was approved by United States Food and Drug Administration for temporary improvement of wrinkles. It gained popularity as it provides a non-surgical alternative, has neurobiological precision[3] and has a credible safety profile. This article summarizes mechanism of action of Botox, various injection techniques based on the type of forehead wrinkles and associated injection site reactions,[4] indications and contra-indications and outcome of application. This article is aimed to fill the existing literature gap regarding summarized view of different techniques of using Botulinum Toxin A for forehead wrinkles. Aging is an unavoidable process resulting in physical and psychological changes in our body and mind respectively, with skin playing the role of top representator in the form of wrinkles. Face is the earliest part to be affected by wrinkles. Although wrinkles also appear while we give facial expressions; they are temporary wrinkles. With aging there is loss of collagen and elastin that manifests in the form of static wrinkles.[1] Different therapeutic approaches have been

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Anatomy of facial muscles and types of forehead wrinkles

The unique feature of muscles of facial expression lies in their attachment to skin in contrast to most muscles that attach to the bones.[5] The repetitive contraction of these muscles causes characteristic rhytids (wrinkles) to form perpendicular to the direction of vector of contraction **(Figure 2[6])**.

Facial wrinkles are classified as dynamic wrinkles and static wrinkles. Dynamic wrinkles are caused by movements of muscles e.g. when we smile, laugh or squint. Static wrinkles are caused by loss of skin elasticity and collagen or due to damage by sun exposure and smoking.[1]

Facial wrinkles include horizontal wrinkles also called as frontal lines and vertical wrinkles also called as glabellar or frown lines.[7] Frontal lines are made by frontal muscle that originates from the aponeurosis just below the coronal suture and inserts into skin of eyebrow where it intermingles with fibers of procerus, corrugator and orbicularis oculi.[8] There are multiple patterns of frontal lines according to Braz and Sakuna's (2010) classification and BoNT injection points **(Figure 3[8])**. Similarly glabellar lines are formed by glabellar complex muscles that include corrugators and orbicularis oculi of the eyelid, procerus and inferior

1. Frontalis.
2. Temporalis
3. Corrugator Supercilli
4. Procerus
5. Depressor supercilli
6. Orbicularis
7. Nasalis
8. Levator labialis superioris alaque nasi
9. Zygomacticus minor
10. Zygomacticus major
11. Orbicularis oris
12. Modeulus
13. Fusorius
14. Platysma
15. Depressor anguli oris
16. Mentalis m.
17. Depressor labialis inferioris
18. Masseter
19. Buccinator m.
20. Levator angularis oris
21. Levator labi superioris

Figure 1[5] Facial muscles are organized into superficial and deep layers.

fibers of frontalis muscle. There are multiple pattern of glabellar lines proposed by classification of Almeida et al. (2011) and injection points of BoNT **(Figure 4[8])**.

Mechanism of action

Botulinum toxin A is produced by a bacteria known as Clostridium Botulinum. Although seven different types of botulinum toxin are known, mostly type A and type B are used clinically.[9] Botulinum A is a zinc dependent proteolytic enzyme with two components heavy chain and light chain.[1] The heavy chain fuses with presynaptic receptors at neuro-muscular junction followed by the internalization of toxin via endocytosis.[1] In the cytoplasm the light chain binds with high affinity with SNARE protein complex and cleaves the SNAP-25, a protein that is required for fusion of vesicles to the presynaptic membrane and release of neurotransmitter, thereby inhibiting the

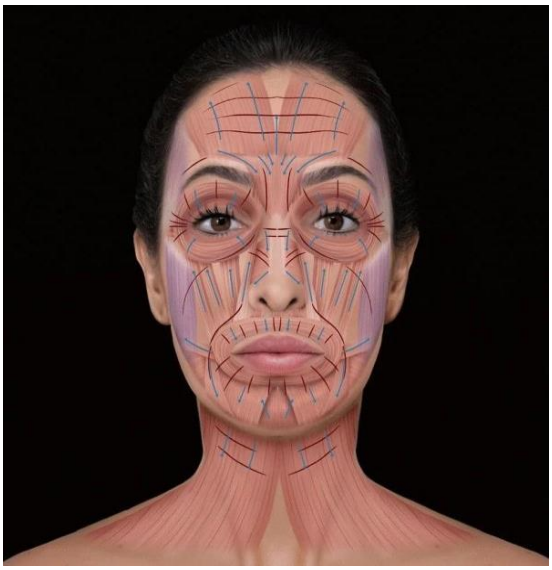

Figure 2 [6] Muscle strength vectors of facial muscles. (The arrows correspond to the direction of muscle force. The expression lines created by muscle contraction are perpendicular to the vectors shown)

Legend : a) Total pattern, b) Medial pattern; c) Lateral pattern; d) Lateral pattern with a predominance of the rhytids on the upper part and the extremities of the frontalis muscle on the right; e) Medial pattern with a predominance of rhytids on the extremities of the frontalis muscle on the left. f) Lateral pattern, with a predominance of the rhytids on the right.

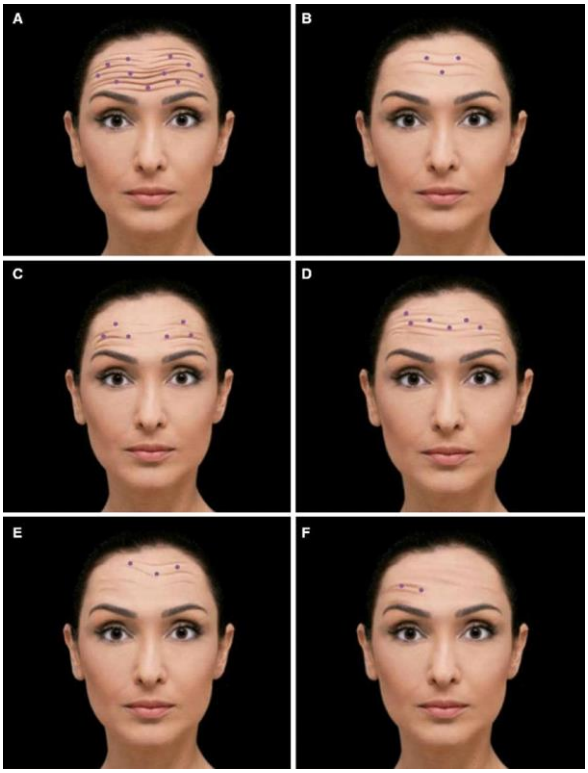

Figure 3[8] Pattern of frontal lines according to Braz and Sakuna's classification (2010).

Legend: a) V-pattern, b) U-pattern, c) Omega pattern, d) Pattern in converging arrows, e) Pattern in inverted omega.

Indications

Aesthetic indication of botox include facial wrinkles whether dynamic or static. Upper face wrinkles are mostly dynamic i.e. those of forehead area, glabellar or frown lines and periorbital wrinkles including crow's feet and bunny lines. Static wrinkles form over lower part of face includes marionette lines, nasolabial folds, perioral wrinkles.[12] Previously the use of Botox was confined to muscles of facial expressions but presently its applications are vast from creases and wrinkles all over face and chin, medial and lateral brow lifts, to maintain evened out contour of jaws and cheeks from all directions,[13] to smooth out neck and chest cleavage wrinkles,[18] for platysmal bands and wrinkling[14] thus causing flattening of skin and improvement in overall facial and skin appearance and results in restoring a youthful appearance to aging face.[14,15]

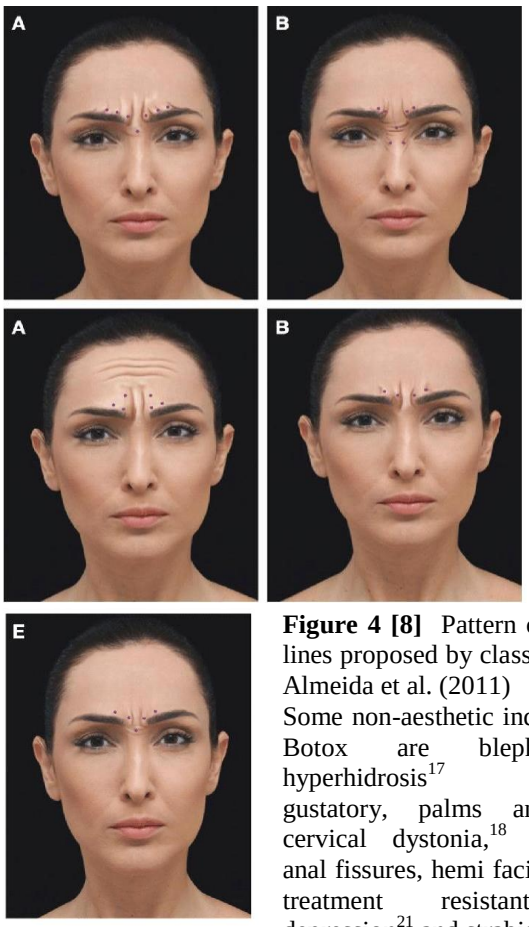

Figure 4 [8] Pattern of glabellar lines proposed by classification of Almeida et al. (2011)

Some non-aesthetic indications of Botox are blephrospasm,[16] hyperhidrosis[17] (Axillae, gustatory, palms and soles), cervical dystonia,[18] migraine,[19] anal fissures, hemi facial spasm,[20] treatment resistant major depression[21] and strabismus.[22]

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Contraindications

Exclusion criteria for the use of Botulinum toxin include:

- Peripheral motor neuropathic diseases (Amyotrophic lateral sclerosis, Toxic neuropathy, Diabetic neuropathy).
- Injection site inflammatory skin disorders.
- Neuromuscular functional disorders (Myasthenia Gravis and Lambert Eaton Syndrome).
- Patients taking Aminoglycosides.
- Co-administration with medications that interfere with neuromuscular transmission[23] Penicillamine and Quinine, Pancuronium, Tubocurarine and Succinylcholine.
- Medicines that affect the coagulation process like Anticoagulants, Acetylsalicylic acid and Vitamin.[24]
- Neonates and children.
- Allergy or hypersensitivity to Botox.
- Patients with previous lower eyelid surgery.
- Pregnancy (Although, Botox is non-teratogenic and injected pregnant women had uneventful childbirths, still it is classified as Class-C) and lactation.[25]

Injection techniques and treatment protocols

While injecting the botulinum toxin injections, the following general considerations should be taken into account

Marking of the injection points should be carried out, even for expert clinicians.

A well lightened procedure area as to visualize the visible veins and to prevent bruising from injections.

Thoroughly consider and document any asymmetries that may differ from patient to patient.

If the post injection results are to be visualized by digital photographs, pre- injection photography should be ensured.[26]

Glabellar complex is structured by procerus ,depressor supercilli and corrugator supercilli.[27] Glabella is a site commonly involved with blindness due to Botox injections, therefore it is necessary to avoid branches of Ophthalmic artery namely Supratrochlear artery, Paracentral and Central artery. When injecting glabella, extreme caution should be applied. It is imperative that the person administrating the injection be skillful with good knowledge of anatomy.

Following techniques are used for injection of Botulinum toxin:

Injection techniques based on the targeted muscle

Frontalis injections: The frontalis elevates the brows and is treated for forehead lines. To prevent brow ptosis, the lower 1-2 cm near the orbital rim is avoided.[33] Using a diluted, angled intradermal injection helps reach insertion fibers. Typically, 5-7 injections are placed 2-3 cm above the brows, not lower than midway between the hairline and eyebrows.[28] Lateral injections should stay within 2 cm of the brow's outer edge, and areas intended for lateral lift should not be treated.[29]

Figure 5[30] Injection into Frontalis muscle.

Glabellar Injections: Glabellar complex muscles are procerus, corrugator and depressor supercilli.

For injections into procerus which is located at glabella and upper part of nose, the pathway of intercanthal vein should be taken into account as the radix of nose is a potential danger zone of face and can propagate infection causing cavernous sinus thrombosis.[31] Two points are marked, one at the junction of lines from the medial brow to the contralateral medial canthus. 2nd point is marked 1cm above the previous point.

When injecting corrugators, the medial part is injected deeply and lateral superficially, further efficacy can be achieved by giving a third additional injection into the lateral eyebrow.[32] To minimize the risk of brow ptosis, botulinum toxin should be injected into the corrugator supercilii muscle approximately 1cm above the orbital rim along the mid-pupillary line.[33] It is important to evaluate the dermal insertion point of the corrugator muscle, as this defines how far laterally the injections should be administered. Injections placed directly above the brow in line with the pupil should be avoided, as they carry a significant risk of inducing eyelid ptosis.[34] The aesthetic effects of the treatment generally persist for a period ranging from three to six months. In male patients, higher doses are often necessary due to increased muscle bulk.[35]

Figure 6[35] Injection site for corrugator supercilli and procerus muscle.

Injecting Orbicularis Oculi for Crow's feet

Injections should be placed at least 1 cm lateral to the lateral orbital rim to avoid toxin diffusion into the orbit.[36,37] The top injection point lies just below the brow, with the lower one 1-2 cm beneath it. Procedures must be done with the patient relaxed and not smiling to prevent upper lip droop from zygomaticus involvement.[38] Injections should remain superficial to avoid the orbital septum and reduce the risk of diplopia.[39]

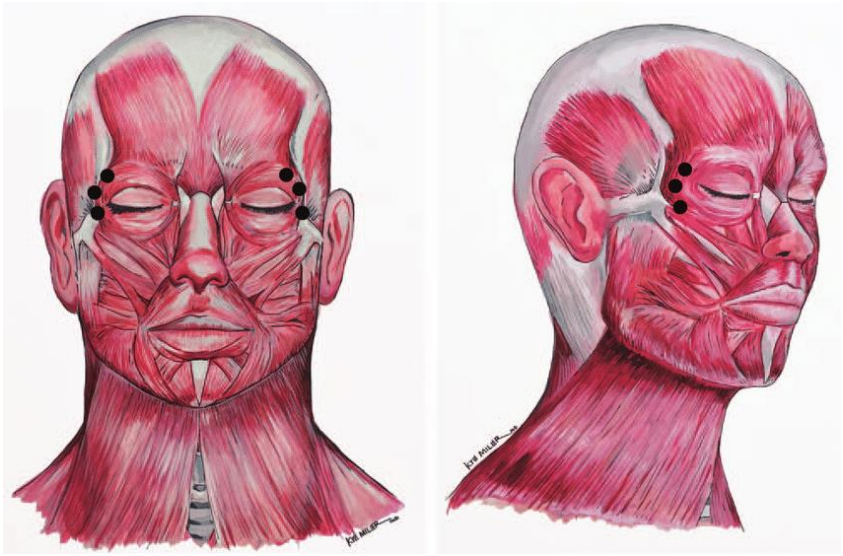

Figure 7[35] Injecting Orbucalris Oculi.

Crest injection technique for glabella

Under aseptic measures, skin is numbed and the patient is asked to frown. The physician than pinches the wrinkles to bleach the skin. This stretching of the skin allows superficial injection by averting the line to the top of the skin crest and occluding the paracentral artery. Injection needle is advanced between skin and subcutaneous tissue to sub-reticular dermal plane. Even a small amount as 0.1 ml can effectively reduce a deep wrinkle, small rhytides require smaller doses of injections. Evaluation of wrinkle is done after each injection. This injection technique remarkably lessens the incidence of skin necrosis and ocular complications resulting in safer administration of botulinum toxin **(Figure 8)**.[40]

Outcome

To determine outcome in dynamic wrinkles, patients were assessed using grading scale for Dynamic forehead wrinkles, which classifies the patients as:[41]

0 = no wrinkles

1 = minimal wrinkles

2 = mild wrinkles

3 = moderate wrinkles

4 = severe wrinkles

Patient satisfaction is judged from 2 weeks to 3 months after injection based on a four-point-scoring system as follows:[42]

0 = not satisfied

1 = moderately satisfied

2 = satisfied

3 = very satisfied

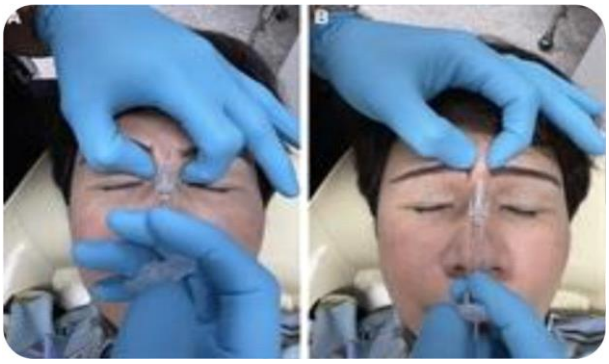

Figure 8 [40] Crest injection technique.

The clinical outcome of Botox injection was evident on day 1-4 post injection, peak effect was seen in 1-4 weeks and resolution takes place in 3-4 months.[42]

Another method is to determine the efficacy of treatment based on injection site pattern. A 3 and 5 injection site pattern are used for central forehead and glabellar rhytides and wrinkles. Severity is assessed between 0 and 4 weeks using digital photographs and clinical scale. This standardize scale ranges from 0 = no wrinkles to 4 = severe wrinkles. A reduction of minimum 1 point is taken as successful treatment.[43]

One method is to assess the outcome by considering the injection site itself and the dilution criteria of Abobotulinum toxin A. It showed that the most preferred sub-site is the glabellar region. The greater the dilution of toxin, more is the respondent surface area. Concentrated solution produces a lesser amount of rhytid reduction.[40]

Toxin dose also serves as a tool to determine success rates in patients. Assigning of dose to patients in done at random. 20 U or 30 U dose is assigned and Botox is injected into Procerus muscle, both Corrugator Supercilli muscles and above the mid-pupillary line, effects are evaluated on 30, 60, 90 and 120 days. Wrinkle severity is graded based on the same above mentioned FWS (Facial Wrinkle Scale). The effect lasted a bit longer in 30 U dose although it wasn't statistically significant. By day 120 the effects of both doses were the same, concluding that both doses can be given successfully without the danger of long term adverse effects.[44]

Treatment outcome also differ based on the type of wrinkles. Blinded retrospective data analysis shows that static glabellar wrinkles were reduced by -17% and -24 % while dynamic facial wrinkles showed reduction of -26 % and -21 % on day 30 and 90 post-injection. Thus, polls confirmed that dynamic facial wrinkles are reduced more and effects being more prominent show a better patient satisfaction.[45]

Adverse effects

Adverse effects of using botulinum toxin injections are less common and some of them are inversely proportional to the knowledge of anatomy and skill of

injection and some of them are not entirely technique dependent.[46] Complications are categorized into local complications, related to eyes and undesirable adverse effects.[47]

Local complications

Local complications include erythema, tenderness, edema, bruising and hematoma. They resolve within a day except bruising and hematoma that can be minimized by application of ice before and after injection.[48] Some patients suffer from headache after botulinum toxin injection, it can be spontaneous that settle within a day[49] or idiosyncratic severe headache that settle within 2-4 weeks after use of opioids and non-steroidal anti-inflammatory medications.[50] Some very rare side effects include injection site paresthesia, anxiety and vasovagal episodes. Vasovagal episodes can be minimized by reducing the anxiety of patients and counseling the patient.[51] However, the emergency protocols should be followed and emergency medicines should be in hand while using botulinum toxin injections.[51]

Complications related to eyes

These complications mostly occur due to penetration of drug outside the area to be treated.[52,53] Blepharoptosis occurs in 1 to 5% patients after botulinum toxin injection and involves lowering of upper eyelid by 2mm to 3mm. It is most marked at the end of the day **(Figure 9)**.[54,55]

Two solutions that are used over the counter are naphazoline 0.025% pheniramine 0.3% and apraclonidine. These medications cause Muller's muscle contraction that lead to elevation of eyelid. However, apraclonidine should be given after glaucoma is ruled out.[53] Other complications include diplopia, decrease in visual activity or loss of vision,[54] eyebrow asymmetry, lagophthalmos, palpebral ectropion, prominence of palpebral bags,[55] xerophthalmia[1] and epiphora.[56,57] Epiphora occurs due to weakening of medial part of palpebral muscle that causes pump failure and its incidence can be reduced by injecting lateral to lateral canthus.[56,57]

Figure 9 [54,55] Ptosis of both upper eyelids after injection of botulinum toxin A, above (before injection) and below (after injection).

Undesirable adverse effects

These are very rare adverse effects. Formation of antibody after injection of botulinum toxin A happens in less than 1% cases and renders the treatment ineffective.[58] Sometimes an increase in toxicity of botulinum toxin A is seen when used with other medications that cause neuromuscular blockage e.g. aminoglycosides, quinidine, muscle relaxants and anticholinergic drugs.[58] Delayed hypersensitivity reactions and foreign body granuloma are late complications that have no relationship to the injection technique.[59]

For treatment of immediate hypersensitivity reactions, diphenhydramine should be avoided because it has anticholinergic effects. Methylprednisolone and epinephrine should be used for treatment.[5,60]

Future direction and research

Future research on botulinum toxin A (BoNT-A) for forehead wrinkles is focusing on developing longer-lasting formulations like daxibotulinumtoxin A[61] and exploring non-invasive delivery systems such as microneedles and transdermal applications.[62] Efforts are underway to enhance injection accuracy using ultrasound and robotics.[63] Mechanistic studies aim to refine dosing by understanding BoNT-A's action at

varying depths and its long-term effects on muscle behavior.[64] Personalized treatment protocols are being designed based on individual anatomy and gender differences.[63] Combination therapies with fillers, lasers, and regenerative agents like PRP are being explored.[61] Researchers are also addressing resistance through studies on antibody formation and long-term safety. AI-driven facial analysis and 3D modeling are being integrated to tailor treatments. Lastly, microdosing for skin texture and preventive use in younger patients is gaining attention.[61]

Conclusion

For scaling down of forehead wrinkles, the use of botulinum toxin proves to be a safe, easy and efficacious method. It is an economical and painless substitute of surgical procedures accompanied with least possibilities of complications.

Declaration of patient consent The author certify that he has obtained all appropriate patient consent.

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Conflict of interest Author declared no conflict of interest.

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