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REVIEW ARTICLE

A Brief Overview about Mesobotox and its Applications in Dermatology

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ABSTRACT

Background: Mesobotox, also referred to as intradermal microinjection of diluted botulinum toxin, has emerged as an innovative approach in aesthetic dermatology and facial rejuvenation. Unlike conventional techniques of deep injections, mesobotox involves multiple microdroplet injections into the dermis and superficial subcutaneous layers. This review summarizes the mechanism of action, clinical techniques, therapeutic applications, and safety considerations of mesobotox, while also highlighting future directions for research to widen clinical applications and to optimize treatment outcomes.

conclusions: Mesobotox primarily influences dermal structures, sebaceous glands, and superficial muscle fibers, resulting in improvement of facial wrinkles and fine lines, pore size reduction, and enhanced skin quality. Furthermore, it offers a versatile application profile, including the management of seborrhea and rosacea, in addition to excessive sweating, keloid scars, and post-acne scarring. The procedure's minimally invasive nature and favorable safety profile have contributed to its growing popularity, though variability in injection protocols, dosing, and patient selection criteria remain a challenge. Mesobotox use is generally safe, with minimal to no complications, provided safety precautions, such as the injection site and amount, are followed. Future studies are recommended to determine the efficacy and safety limits in the current indications as well as to investigate its therapeutic effect on other skin lesions such as striae.

Keywords: Clostridium botulinum Toxin, Neurotoxins, Skin Diseases, Rejuvenation.

INTRODUCTION

Botulinum neurotoxin (BoNT) is a potent neurotoxin produced by the bacterium Clostridium botulinum. This Gram-positive, anaerobic bacterium is commonly found in soil, water, and the intestinal tracts of animals. Clostridium botulinum produces eight distinct neurotoxin serotypes (A, B, C1, C2, D, E, F, and G), with types A, B, and E being associated with human botulism [1].

The clinical application of botulinum neurotoxins (BoNTs) originated in the late 1970s through a collaborative effort between ophthalmologist Dr. Allen Scott and microbiologist Dr. Edward Schantz. Their research, which initially focused on the non-surgical treatment of eye muscle hyperactivity in monkeys, demonstrated the safety and efficacy of BoNT. Subsequently, the Schantz and Johnson product, Oculinum®, was registered for clinical use. While treating involuntary blinking in patients, ophthalmologists accidentally noticed the cosmetic benefits of BoNT, leading to its subsequent application in aesthetic medicine [2].

Microbotox, a technique in which several microdroplets of BoNTs are injected into the skin, has become increasingly popular due to its more positive results and safety compared to traditional procedures. Mesobotox can be used for various skin conditions such as fine lines, rosacea, hyperhidrosis, keloids and seborrhea [3]. This technique has gained increasing attention as a new rejuvenating technique in aesthetic medicine with minimal side effects for use in cosmetic treatments, including improving facial wrinkles, which impose a significant psychological burden on patients [4]. Since its FDA approval for the

treatment of frown lines, BoNT has rapidly become one of the most important cosmetic procedures. Over the past decade, its use has increased with advances in technology and the emergence of new indications, not only in cosmetic fields but also for medical purposes, including the treatment of asymmetry, muscle hypertrophy, and certain conditions, such as depression and Raynaud's phenomenon [5]. Understanding more about the specific structures, mechanism of action, and applications of BoNT microdroplets in dermatology known as mesobotex, which is the aim of this review, is crucial to improving treatment protocols and outcomes.

METHODS

Previous scientific databases, including Google Scholar, PubMed, Embase, Scopus, and others, were searched using key search terms (research titles and keywords). The obtained data were analyzed and summarized in a simplified report. In this review, we focused on investigating recent publications and research.

RESULTS and DISCUSSION

Structure of BoNT

BoNT is produced by Clostridium botulinum as a single-chain polypeptide with a molecular weight of 150 kDa. For this polypeptide to become active, it undergoes proteolytic cleavage, resulting in a 100 kDa heavy chain (HC) and a 50 kDa light chain (LC), linked by a disulfide bond (Figure 1). LC acts as a zinc metalloprotease, specifically targeting proteins involved in the synaptic vesicle fusion complex. By cleaving these proteins, LC prevents the release of neurotransmitters, such as acetylcholine (ACh), from nerve terminals. This can cause loss of cholinergic signals and leads to temporary denervation and modification of muscle activity [6]. On the other hand, HC plays a crucial role in delivering the LC to its target within cells. The C-terminal half of HC, known as the receptor-binding domain, binds to specific receptors on the neuronal cell surface. Subsequently, the N-terminal half of HC, the translocation domain, facilitates the translocation of the LC into the cytosol, where it exerts its neurotoxic effect [7].

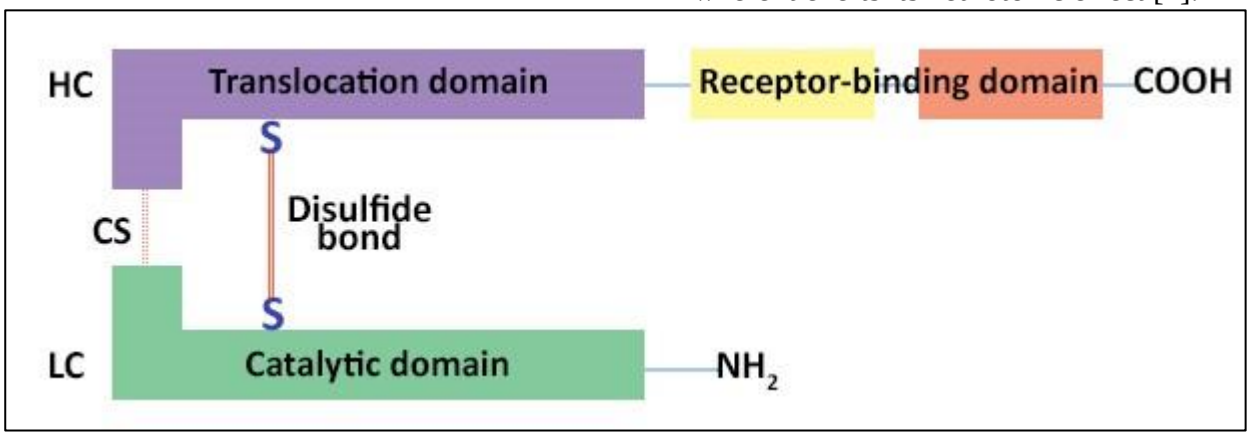

Figure 1: Botulinum toxin A structure: HC (heavy chain) containing translocation and receptor-binding domains, and LC (light chain) with a catalytic domain, and the disulfide bond between the two chains. CS: Cleavage site.

Mechanism of BoNT action

BoNT primarily functions by inhibiting the release of ACh from the presynaptic membrane. This inhibition occurs by targeting a complex of proteins known as SNAREs (Soluble-N Ethylmaleimide, Sensitive Factor Attachment Protein Receptor), which are essential for the fusion of synaptic vesicles with the plasma membrane. The SNARE complex consists of three key proteins: synaptobrevin/VAMP (Vesicle associated membrane protein), syntaxin, and SNAP-25 (Synaptosomal-Associated Protein, 25kDa) [8].

The HC of BoNT binds to specific receptors on the neuronal cell surface and facilitates the translocation of the LC into the cell. Once inside, LC, a zinc-dependent metalloprotease, cleaves the SNARE proteins, preventing the formation of the SNARE complex and subsequent neurotransmitter release. This

ultimately leads to muscle paralysis or chemical denervation [8, 9].

Kandhari et al., reported that microdroplet and conventional BoNT have similar function by inhibiting neurotransmitter release, yet they differ in terms of injection depth and the resulting intensity of muscle weakness (Figure 2) [3].

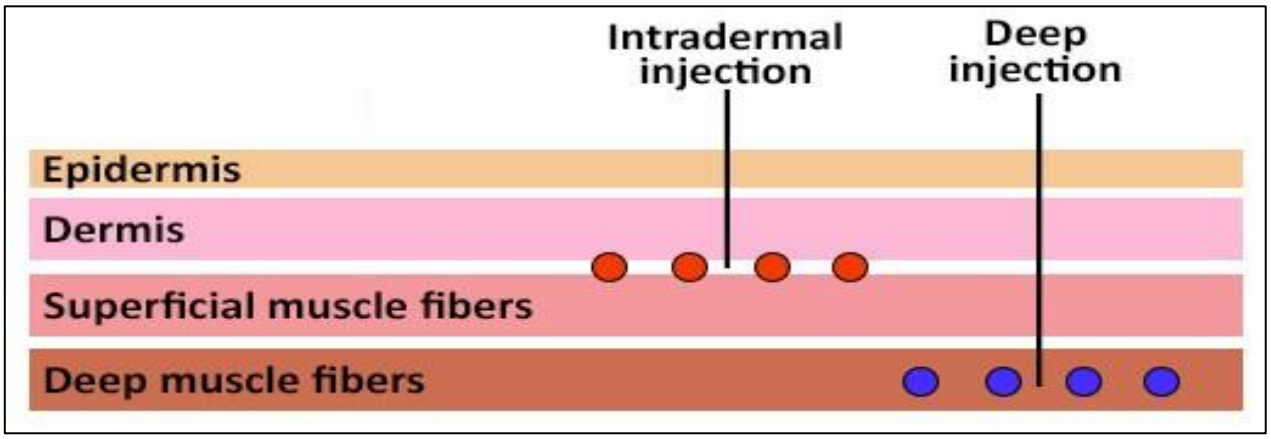

Figure 2: Levels of BoNT injections: BoNT microdroplet superficial injection affecting the dermis and superficial muscle fibers (red circles), and conventional technique of BoNT injection into the deep muscle fibers (blue circles).

Preparation of mesobotox, injection technique and storage

Microdroplet BoNT is typically prepared using a 1:5 dilution, resulting in a concentration of 100 Units of BoNT per 5 mL of solution. Alternatively, a 1:10 dilution can be used, yielding a concentration of 10 Units per mL [3].

Fabi et al., [10] reported that 20 U/mL of BoNT can be used for wide facial pores, seborrhea, facial hyperhidrosis, rosacea and acne. While a concentration of 24 U/mL is preferred for glabellar, forehead, and crow's feet lines in females as well as axillary hyperhidrosis. As for neck contouring, glabellar, forehead, and crow's feet lines in males, hypertrophic scars, and keloids; a concentration of 28 U/mL can be used.

After applying a topical anesthetic cream for 20 minutes and rinsing it off, microdroplet injections can be administered using a 1-mL syringe and a fine-gauge (32 or 34 gauge) 1-inch needle. For facial treatments, microdroplets ranging from 0.01 to 0.05 mL can be injected in a grid pattern with a 1-cm spacing. On the neck, microdroplets of approximately 0.01 mL can be injected in a similar grid pattern. It's crucial to insert the needle as superficially as possible to ensure precise placement of the toxin intradermally [10].

BoNT-A is typically distributed as a sterile, vacuum-dried powder in vials. After reconstitution, the product should be stored at 2-8°C in the refrigerator [11]. An expert consensus stated that reconstituted BoNT can be safely refrigerated or refrozen for up to four weeks without compromising its efficacy or increasing the risk of contamination, provided it is handled appropriately [12].

The three most common and commercially available BoNT type A (BoNT-A) formulations are abobotulinumtoxinA (Dysport®), incobotulinumtoxinA (Xeomin®), and onabotulinumtoxinA (Botox®) [13].

A key difference lies in their protein composition: incobotulinumtoxinA exclusively contains the 150 kDa active BoNT-A component, purified from clostridial proteins. In contrast, abobotulinumtoxinA and onabotulinumtoxinA contain variable amounts of hemagglutinin (HA) and non-toxic non-hemagglutinin (NTNHA) proteins that are complexed with the 150 kDa BoNT. Despite these structural differences, blinded comparative studies to date have not revealed clear differences in clinical efficacy among these three formulations [13, 14].

Dermatological applications of mesobotox

Facial rejuvenation

Microbotox is effective for facial rejuvenation, particularly in younger

individuals. It can be used to reduce fine wrinkles in the forehead, periocular, and cheek areas. By using smaller doses and injecting into superficial muscle layers, microbotox can achieve a more natural appearance and minimize the risk of complications like brow ptosis. For patients with fine wrinkles in the entire forehead, microbotox can be applied to the entire area. However, for those with moderate to severe wrinkles, a combination approach may be more effective [15].

In the eyebrow and periocular areas, microbotox can help elevate the eyebrows and rejuvenate the periocular region. To avoid brow ptosis, injections should be limited to the lower level of the eyebrow cilia. For the glabella area, the traditional injection technique is generally more effective than microbotox [15].

Seborrhea and enlarged facial pores

In addition to reduced sebum secretion, patients treated with BoNT often report a perceived reduction in pore size. A number of studies have supported these findings, demonstrating that intradermal BoNT injections can lead to a decrease in sebum production and a reduction in the number and size of visible facial pores [16].

Park et al., [17] conducted a study demonstrating the potential of incobotulinumtoxinA in treating facial skin laxity, sebum secretion, and pore size.

Rosacea

Yuraitis and Jacob [18] first reported the efficacy of intradermal BoNT A in treating severe, recalcitrant facial flushing. A patient who had previously failed treatment with pulsed-dye laser (PDL) and clonidine was administered 10 Units of diluted BTX-A (2 Units/0.1 mL) intradermally into each cheek, spaced 1 cm apart. Two weeks post-treatment, the patient experienced a significant reduction in both resting and flushing-induced erythema.

Acne vulgaris

BoNT-A offers a novel approach to managing oily skin and acne vulgaris by targeting various aspects of the disease's pathophysiology, including sebum production and inflammation [19].

Ibrahim et al. [20] found that BoNT-A was equally effective as long-pulsed Nd:YAG laser in treating acne vulgaris. However, the study revealed a higher recurrence rate with BoNT-A compared to laser therapy.

Post-acne scars

BoNT can be a valuable tool in managing traumatic or post-acne scarring, particularly in areas where movement exacerbates the appearance of the scar. Scars located in the upper face (forehead, periorbital region, glabella) and lower face (chin and surrounding areas) are well-suited for BoNT treatment. By relaxing the underlying muscles, BoNT can help to soften the appearance of the scar and minimize its impact on facial expression. It is often used in conjunction with other cosmetic procedures, such as fillers, resurfacing, and surgery, to achieve optimal results [21].

Hyperhidrosis

BoNT intradermal injections were found to be effective and safe for the treatment of hyperhidrosis [22]. The European Medicines Agency (EMA) approved the use of onabotulinumtoxinA for the treatment of persistent, severe primary axillary hyperhidrosis in 2003. Subsequently, in 2004, the US Food and Drug Administration (FDA) approved the use of onabotulinumtoxinA for the same indication [23].

Post-operative scars

To minimize scarring in post-operative patients, intradermal injections of BoNT-A can be administered within and around the scar. Microdroplet techniques, which involve injecting small amounts of BoNT-A, can be used alone or in conjunction with steroids to reduce the need for higher steroid doses and their associated side effects. Treatment typically begins one week postoperative, and can be repeated

every two months until the scar resolves [10].

Striae rubrae

BoNT A improves erythema by inhibiting ACh release from autonomic peripheral nerves of the skin vasodilatory system as well as reducing the release of inflammatory mediators as substance P [24]. It also increases the organization of the dermal collagen as well as the production of procollagen, collagen and elastin [25]. Thus, it's hypothesized to be effective in treating striae rubrae.

Complications

Careful and superficial delivery of BoNT microdroplets is essential to avoid complications. Diffusion into deeper muscle layers, caused by subdermal injection or larger injection volumes, can lead to total or partial paralysis. However, due to the lower neurotoxin concentrations used in microbotox technique, these complications are typically temporary and resolve within two to three weeks [3].

Small [26] classified the complications of BoNT injection into:

1. Injection-related complications including pain, vasovagal attack, bruising, erythema and infection
2. BoNT-related complications as hypersensitivity reactions and diffusion of the toxin from the injected sites.

Although BoNT is generally safe for cosmetic use, there are concerns about immunogenicity and secondary treatment failure [27]. Therefore, its long-term safety and effectiveness remain the focus of ongoing research.

Contraindications of BoNT injection

BoNT is contraindicated in individuals with certain neuromuscular disorders that could amplify the effects of the toxin including myasthenia gravis, Eaton-Lambert syndrome, myopathies and amyotrophic lateral sclerosis. Additionally, BoNT should not be administered to individuals with active infections at the injection site or those with known hypersensitivity to any component of the product [28].

CONCLUSIONS

Mesobotox has been successfully used to treat a variety of dermatological and cosmetic conditions, such as fine lines and wrinkles on the face, excessive sweating, keloid scars, rosacea, seborrheic dermatitis, acne, and post-acne scarring. Its use is generally safe, with minimal to no complications, provided safety precautions, such as the injection site and amount, are followed. Future studies are recommended to determine the efficacy and safety limits in the current indications as well as to investigate its therapeutic effect on other skin lesions such as striae.

Authors' contributions

SAH, SMI, and HS contributed to the literature search, research design and implementation, drafting, and reviewing and approving the final version of the manuscript. SAH drew the figures.

Conflict of interests

The authors declare no conflict of Interest.

Financial disclosures

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The diagrams were drawn by the first author.

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