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Letter to the editor

Use of botulinum toxin in dermatology

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

Dear Editor,

I am writing to indicate new therapeutic options for botulinum toxin (BoNT) in dermatological diseases. The anaerobic bacterium Clostridium botulinum produces BoNT and blocks the release of acetylcholine in the neuromuscular junction, which inhibits muscle contraction. It has been widely used in medicine for dystonia, spasticity, infantile cerebral palsy, hemifacial spasm, tics, tremors, and bladder and gastrointestinal tract motility disorders. It is now widely used in aesthetic medicine. Below, I will present some new therapeutic options for using BoNT.

Hidradenitis Suppurativa

Hidradenitis Suppurativa (HS), also referred to as acne inversa. It's a chronic inflammatory skin condition characterized by the formation of painful nodules, abscesses, and sinus tracts in the skin folds, typically in areas like the axilla, groin, and perianal region (1). BoNT-A injections have been explored as a treatment option for HS due to their ability to inhibit the release of certain neurotransmitters involved in pain signaling and inflammation. A possible therapeutic effect can be caused by reduced sweat excretion, which diminishes the production of proinflammatory cytokines by the skin microbiota. Grimstad et al. Evaluated the effectiveness of BoNT-B in a clinical trial on 20 patients with hidradenitis suppurativa. After 6 months of therapy, a significant improvement according to clinical condition and quality of life was observed in patients (2). However, more extensive research, including controlled clinical trials, is needed to establish the safety and efficacy of BoNT-A injections as a standard treatment for HS.

Rosacea

Rosacea is a chronic skin condition that primarily affects the face, although it can also involve the eyes in some cases. It is characterized by erythema, persistent facial redness, flushing, telangiectasia, papules, pustules, and, in some instances, ocular involvement. Several studies evaluated the use of botulinum toxin in rosacea treatment. In the study conducted by Park et al., intradermal injection of botulinum toxin significantly reduced erythema severity in 17 of the 20 patients. However, three other patients experienced undesired paralysis of facial muscles after receiving botulinum toxin injections (3). Another study also showed statistically significant improvement in erythema grade in patients with rosacea at 1, 2, and 3 months after treatment compared with baseline (4). However, the exact pathomechanism is not fully elucidated. Therefore, there is a need to give insight into the molecular mechanism involved in treating rosacea with botulinum toxin.

Androgenic alopecia

Androgenetic alopecia, commonly known as male-pattern baldness or female-pattern hair loss, is characterized by progressive hair follicular miniaturization. This condition primarily affects the scalp and is influenced by genetic and hormonal factors (5). The 2010 pilot study conducted by Freund et al. investigated the potential effects of intramuscular botulinum toxin type A injections on men with androgenetic alopecia (AGA). Participants experienced a significant increase in hair density within the 2 cm fixed area, with an average increase of 18%. The overall response rate, defined as participants achieving hair count changes greater than 0%, was 75%. This suggests that most participants responded positively to the treatment (6). Singh et al. conducted a study involving 150 units of botulinum toxin type A injections into the frontalis, temporalis, periauricular, and occipitalis muscles, evenly distributed across 30 injection sites, in men with AGA. The study comprised a single injection session, with evaluation endpoints set at 24 weeks. Results showed that, based on photographic assessment, 80% of subjects exhibited an excellent response, while 10% showed fair and poor

responses, respectively. No adverse events were reported during the study period (7). The potential mechanisms through which botulinum toxin may improve AGA are not definitively established, but there are speculations regarding two possible actions. First, it says that botulinum toxin injections may lead to decreased transforming growth factor beta 1 (TGF-β1) activity in dermal papilla cells. TGF-β1 is known to play a role in hair follicle miniaturization and inhibition of hair growth. By reducing TGF-β1 activity, botulinum toxin injections may promote hair follicle growth and mitigate the effects of AGA (8). The second one indicated that BoNT may induce relaxation of the scalp perimeter muscles. This relaxation could alleviate tension and stress on the scalp, which may contribute to improved blood circulation and nutrient delivery to the hair follicles (9).

Plaque psoriasis

Psoriasis is a chronic inflammatory skin condition characterized by increased keratinocyte proliferation, leading to the formation of plaques on the skin. It is believed to result from the activation of the immune system, particularly T-cells. Some reports have noted improvements in psoriatic lesions following injuries that affected certain peripheral nervous system branches. Therefore, the use of BoNT in psoriasis could be beneficial by blocking neuromodulators, resulting in decreased neurogenic inflammation. Cutaneous nerve fibers play a crucial role in the progression of psoriasis by establishing communication between epidermal keratinocytes and immunocytes. These nerve fibers facilitate bidirectional signaling between the nervous and immune systems within the skin microenvironment (10). The comparative study conducted in thirty-five patients with chronic plaque psoriasis aimed to assess the efficacy of split-body therapy using two different treatment modalities: intradermal BoNT and intralesional 5-fluorouracil (5-FU). The response rate to treatment was high for both modalities, with 85% of patients showing improvement on the BoNT treatment side and 90% on the 5-FU treatment side (11). One case report showed a 75-year-old woman with chronic plaque psoriasis received intradermal injections of abobotulinumtoxinA on a lesion on her left buttock. The treatment resulted in significant improvement (12). Concurrently, she experienced a cutaneous herpes simplex virus outbreak on her right buttock. This case suggests the potential efficacy of intradermal botulinum toxin injections for localized plaque psoriasis but highlights the need for long-term monitoring. It could be a potential option for localized psoriatic plaques, but further research is needed to confirm the clinical efficacy and safety of this drug.

Primary hyperhidrosis

Hyperhidrosis is a dermatological condition characterized by excessive sweating that extends beyond the body's thermoregulatory needs, significantly impacting patients' quality of life. It distinguishes between primary hyperhidrosis, typically focal and idiopathic, and secondary hyperhidrosis, which is often generalized and triggered by underlying medical conditions or medication use. Treatment options for primary hyperhidrosis include surgical and nonsurgical approaches. Notably, BoNT injections are considered highly effective in small doses and are commonly used as a second-line treatment option for primary hyperhidrosis when topical treatments have proven ineffective (13). BnNT inhibits oil secretion, narrows pores, and impedes sweat production (14). The clinical development program for onabotulinumtoxinA for hyperhidrosis encompassed two double-blind, placebo-controlled pivotal trials, immunogenicity studies, long-term safety and efficacy investigations, and quality-of-life assessments. Primary efficacy measures included gravimetric measurement of axillary sweat production and improved Hyperhidrosis Disease Severity Scale (HDSS) scores, respectively. Compared to the placebo, treatment with onabotulinumtoxinA led to significant reductions in

axillary sweat production and severity of axillary hyperhidrosis. The effects became apparent within one week post-injection and persisted for at least six months (15).

Recent studies suggest that BoNT injections may offer alternative therapeutic options for various conditions, including hyperhidrosis, hidradenitis suppurative, rosacea, androgenic alopecia, and plaque psoriasis. While numerous studies highlight the effectiveness of BoNT in these diseases, it's important to note that much of the evidence is derived from publications of low scientific quality, indicating a need for more rigorous clinical trials. Although, the use of botulinum toxin is not without its drawbacks and complications. Dermatologists must be aware of both on-label and off-label applications of BoNT to provide relevant therapy and mitigate associated risks effectively.

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