Investigating the Potential for Neuromodulators in the Treatment of Psoriasis

BY ERIN GILBERT, MD, PhD

Neuromodulators such as onabotulinumtoxinA (Botox, Allergan) have been used in our field for more than a decade in specific cosmetic applications relating to dynamic muscular movement in the face and neck. During that time, new agents such as abobotulinumtoxinA (Dysport, Medicis/Valeant) and incobotulinumtoxinA (Xeomin, Merz Aesthetics) have entered the market, and physicians have developed new ways of using them to achieve increasingly subtle aesthetic outcomes.

While neuromodulators have been used to treat a variety of neurological and other conditions for even longer, the notion of exploring alternative uses for them within the field of dermatology is fairly recent. Early indications, including case reports published by Zanchi M, et al., Chroni E, et al., and Saber M, et al., suggest that neuromodulators also may be beneficial in the treatment of certain cases of inflammatory dermatoses, specifically psoriasis.1-3

Over the past several years, I have collaborated with my neuroscience colleague Dr. Nicole Ward, to investigate the potential of using neuromodulators in the treatment of psoriasis. Beyond the successful replication of the clinical improvements following the injection of botulinum neurotoxin type A for psoriasis, we have also uncovered important elements of the mechanism by which the molecule improves the appearance of psoriasis plaques in mouse models. It is our hope that our research findings may shape new therapeutic modalities in the management of psoriasis and other inflammatory diseases.

PRELIMINARY FINDINGS

Although still in its early stages, the potential for treating psoriasis with neuromodulators is an exciting area of investigation. Until now, very little research has considered the effect of neurotoxins outside of their more well-known cosmetic applications. We started our investigation by testing botulinum toxins in a psoriatic mouse model. Specifically, we looked at how abobotulinumtoxinA affects the clinical phenotype in psoriasis.

In our initial study, we injected a relatively small amount of abobotulinumtoxinA (9 units/kg) into psoriatic plaques in mice.4 At just two weeks, we were able to see a reduction in inflammation and thickness in psoriatic plaques. Moreover, we found significant improvement in acanthosis, as well as a significant reduction in dermal DC and CD4+ T-cell infiltration.5 We also looked at these same plaques six weeks later and found a similar and robust effect, with both the clinical phenotype and inflammatory mediators being reduced. The overall effect was similar if not identical to surgical denervation.

Our goal was to assess the ways in which we could alter the neurocutaneous response in the skin by injecting neuromodulators. Our findings suggest that a future for this kind of treatment is certainly possible and warrants continued research and consideration.

CLINICAL CONSIDERATIONS AND FUTURE RESEARCH

While our initial findings are promising, particularly for patients with localized disease, neurotoxins may be cost-prohibitive for patients with widespread involvement and high PASI scores. However, these agents may be beneficial for patients who have been treated with TNF-alpha inhibitors with refractory plaques, or patients who have been using topical medications but either cannot apply in hard-to-reach areas or would prefer the simplicity of a single-dose treatment that lasts months. Toxins may also be particularly helpful in treating troublesome cases of scalp psoriasis, as patients often find topical interventions hard to apply and cosmetically unappealing.
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**NEXT STEPS**

A better understanding of the mechanism by which botulinum neurotoxin type-A functions as a drug beyond its role in reducing muscular contraction may allow us to use this drug in a wide variety of medical and potentially more sophisticated aesthetic applications. We’re now beginning to learn that the method of action and the effect of botulinum toxins may be far broader than we initially conceived. As we delve deeper into the possible treatment of a variety of conditions including hyperhidrosis, rosacea, acne, and other inflammatory disorders like psoriasis, we’re discovering that additional neuropathways are being affected by this agent.

While one can imagine the neuropathways as a structural element of the communication between the botulinum toxin type-A and the nerve, one must consider additional players in the game such as neuropeptides, their receptors, and the vascular and lymphatic structures in the treated area. Understanding the full anatomical and neurochemical picture will allow us to better extrapolate potential medical applications and beyond.

It remains to be seen whether this promising and potentially lucrative field of research will yield support from pharmaceutical manufacturers. If they can envision broader applications for this class of drug, we may begin to see more resources allocated to the design and execution of controlled studies to further explore that potential.

We have compared the efficacy of all three toxins in both mice and humans, and are eager to continue these studies on a larger scale. Our goal is to improve the lives of those suffering with psoriasis and other inflammatory diseases of the skin. Clinical trials performed with patients are the best hope to definitively determine the mechanism of action and efficacy of this treatment.

Article based on Dr. Gilbert’s Scientific Session at the 2014 AAD in Denver, Co. and on her presentation at the 2013 Cosmetic Surgery Forum. For registration information, visit www.cosmeticsurgeryforum.com.

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To determine the antidepressant effect of onabotulinumtoxinA (OBA) treatment of corrugator and procerus muscles in patients with major depressive disorder, a double blind, randomized, placebo-controlled trial was conducted among 85 subjects with DSM-IV major depression. (J Psychiatr Res. 2014 May; 52: 1-6.) Subjects were randomized to receive either OBA (29 units for females and 40 units for males) or saline injections into corrugator and procerus frown muscles (74 subjects were entered into the analysis). Subjects were rated at screening, and three and six weeks after OBA treatment. Response rates at six weeks from the date of injection were 52 percent and 15 percent in the OBA and placebo groups, respectively (Chi-Square (1) = 11.2, p < 0.001, Fisher p < 0.001), according to the study. The secondary outcome measure of remission rate (MADRS score of 10 or less) was 27 percent with OBA and 7 percent with placebo (Chi-square (1) = 5.1, p < 0.02, Fisher p < 0.03). Six weeks after a single treatment, MADRS scores of subjects were reduced on average by 47 percent in those given OBA compared to 21 percent in those given placebo (Mann–Whitney U, p < 0.0005).

—PD Staff