Talking Toxins: Initial Thoughts on Two Preparations of Botulinum Toxin Type A

With FDA approval possible in the next few years, a new formulation of botulinum toxin type A may become a treatment option for US dermatologists.

Botulinum Toxin Serotypes

Two serotypes of botulinum toxin are currently marketed for therapeutic indications. In addition to type A (Botox, BoNTA1), type B is also FDA approved and marketed as Myobloc (BoNTB, Solstice Neurosciences). Myobloc is approved in the US for management of cervical dystonia. BoNTB has been investigated for treatment of facial rhytides. Studies show the agent is effective for diminishing wrinkles but that duration of effect may not be as prolonged as with BoNTA. Investigators have proposed that BoNTB may be a worthwhile second-line option for patients who demonstrate diminished clinical response to BoNTA.

BoNTA2 (Dysport/Reloxin) is not yet FDA approved for use in the US. Based on the same serotype, BoNTA1 and BoNTA2 preparations incorporate different nontoxic proteins. In addition to pharmacologic differences between the two formulations, there are electrophysiological differences that contribute to differences in clinical effect.

Perhaps the most obvious difference between BoNTA1 and BoNTA2 is dosage. A unit of BoNTA1 is roughly equivalent to three-to-four units of BoNTA2, potentially resulting in volume differences that could affect clinical response. No standard conversion ratio exists, though some researchers are attempting to establish equivalencies.

Estimates from the neurology literature suggest no obvious difference in the rate of antibody development to each BoNTA preparation. The rate of antibody-induced treatment failure is reportedly less than one percent for BoNTA1.

Clinical Differences

Data from head-to-head comparisons of the two BoNTA preparations for cosmetic indications are limited, though more reports are emerging. In a pilot study presented at the AAD Annual Meeting in San Francisco this March, investigators reported more apparent diffusion with BoNTA2 than with BoNTA1. The study enrolled a total of 20 patients with forehead hyperhidrosis who received two injections of BoNTA1 on one side of the forehead and two injections of BoNTA2 on the other side. Patients received both BoNTA2 injections at a randomly assigned dose that was either 2.5 times, three-times, or four-times the dose of BoNTA1. Injection volumes were kept identical for all injections. As early as 24 hours after treatment, patients in both groups demonstrated anhidrosis. From week one through six months, BoNTA2-
treated patients had larger areas of anhidrosis—a marker for diffusion—compared to BoNTA1-treated patients. The “halo area” increased at the higher BoNTA2 to BoNTA1 ratios.

Using evaluator-blinded assessment of patient photographs, investigators also assessed forehead wrinkles among 12 of the enrolled patients at baseline and following injections. Analysis revealed no correlation between anhidrotic area size and inhibition of contraction of the frontalis muscle. From a clinical viewpoint, incidence of diffusion may be more important for certain indications and treatment locations.

A second study with a double-blind, randomized design compared 20 units of BoNTA1 to 50 units of BoNTA2 for treatment of glabellar lines through photographic assessment of photos at baseline, weeks two, eight, 12, and 16. A total of 62 patients were investigated (31 per group).

While the incidence of patients with at least a 1-grade improvement reportedly peaked at week eight in both groups, duration of improvement was more prolonged in the BoNTA1 group. At 12 weeks, 77 percent of BoNTA1-treated patients had 1-grade improvement versus 59 percent of BoNTA2-treated patients. At week 16, the incidence of 1-grade improvement was 53 percent for BoNTA1 and 28 percent for BoNTA2. Estimated incidence of relapse at week 16 was 23 percent for BoNTA1 and 40 percent for BoNTA2.

Patient satisfaction ratings and self-assessment of appearance at week 12 were higher for BoNTA1 (statistically significant).

A Tale of Two Toxins

Though these are early comparative studies involving relatively small patient groups, they suggest clinically-relevant differences between BoNTA1 and BoNTA2 that may prove important in patient care. Though not yet approved in the US, BoNTA2 has been used worldwide, providing a resource of information about the efficacy and utility of the agent.

Because no single dose conversion ratio exists, making direct comparisons between BoNTA1 and BoNTA2 can be challenging. Nevertheless, current data suggest that the two formulations may differ in diffusion rates and duration of effect. Further studies may indicate specific instances in which clinicians can capitalize on these differences to enhance therapeutic outcomes and improve patient experience.