Botulinum Toxin Type B for Dynamic Glabellar Rhytides Refractory to Botulinum Toxin Type A

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BACKGROUND. **Botulinum toxin type B (BTX-B; Myobloc) has recently been introduced for the treatment of dynamic rhytides. This serotype is structurally similar to botulinum toxin type A (BTX-A; Botox) and appears to produce equivalent muscular paralysis. Because of the fact that some patients may become resistant to the effects of BTX-A with its continued use or may require large doses of type A to exert adequate muscular paralysis, the use of BTX-B may prove beneficial in these cases.**

OBJECTIVE. **To determine the effect of BTX-B on glabellar rhytides refractory or showing decreased clinical effect to treatment with BTX-A.**

METHODS. **Twenty females (mean age, 43 years) with vertical glabellar rhytides showing decreased or negligible clinical effect to BTX-A were treated with intramuscular injections of BTX-B. Five standardized intramuscular sites (procerus, inferomedial corrugator muscles, superior middle corrugator muscles) received a total dose of 2,500 U. Patients were evaluated at pretreatment and 48 to 72 hours, 1 week, and 2 and 4 months after injection.**

RESULTS. **All glabellar rhytides improved after treatment with BTX-B injections. Peak clinical effect was noted 1 month after treatment, with 50% of peak effect evident at the 2-month follow-up. Near complete dissolution of effect was seen at 4 months after treatment. Side effects were transient and were limited to moderate injectional pain and rare bruising and frontal brow tightness.**

CONCLUSIONS. **BTX-B is an effective treatment modality for glabellar rhytides refractory or exhibiting decreased clinical effect to BTX-A. The duration of effect using the 2,500 U dosing schedule described herein was shorter than that typically achieved after equivalent BTX-A injection.**

T. S. ALSTER, MD, AND J. R. LUPTON, MD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

BOTULINUM EXOTOXIN type B (BTX-B) is produced from the anaerobic spore-forming bacterium *Clostridium botulinum*. The type B form is an antigenically distinct serotype that is available in a liquid formulation that was approved by the U.S. Food and Drug Administration in December 2000 for treatment of cervical dystonia. More recently, it has been touted for the treatment of hyperdynamic facial lines.[1–3] Although equivalent dosing of the different exotoxins has not been determined, clinical dosing of BTX-B has been estimated at 100 times that of BTX-A.[4,5] All serotypes of botulinum toxin induce temporary muscle paralysis by the same mechanism——inhibiting the release of acetylcholine at peripheral neuromuscular junctions and synapses.[1,5] Multiple studies evaluating the use of exotoxin type A have confirmed effective clinical paralysis averaging 4 to 6 months.[6–8] The type B form has been proven helpful in the treatment of cervical dystonia, even in those patients who have become resistant to the type A form.[1] The major advantage of the type B formulation is its relative longevity and stability——with cellular viability seen up to 9 months at room temperature and over 30 months when refrigerated.

With the surging popularity of cosmetic botulinum injections, it is expected that an increased number of patients will eventually demonstrate resistance to exotoxin type A. This study was designed to evaluate the clinical efficacy of the newer BTX-B formulation for hyperfunctional facial lines demonstrating decreased clinical responsiveness to treatment with BTX- A.

Methods

Twenty females with demonstrable vertical glabellar rhytides (28 to 63 years; mean, 43 years) were included for study. Each patient had received two to four previous BTX-A treatments (average dose, 30 U per treatment) with less than 50% clinical reduction in contraction of the corrugator muscles. No BTX-A or any soft tissue fillers had been received by any patient for at least 6 months before study initiation. Other exclusion criteria included cosmetic procedures invol-

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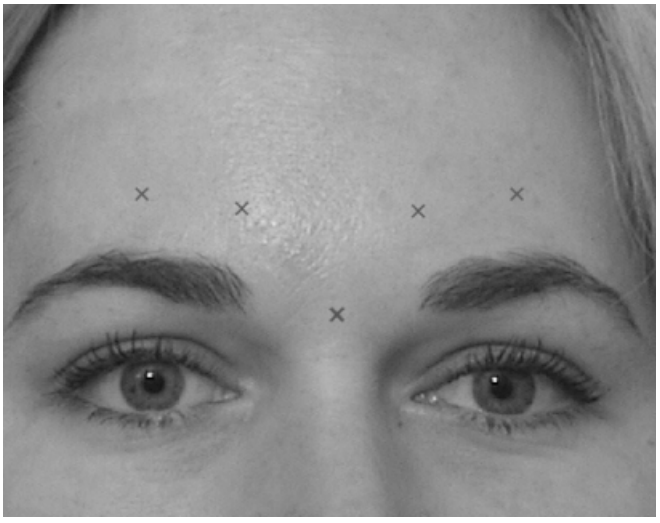

Figure 1. Sites of injection (procerus, inferomedial corrugator, and superior middle corrugator muscles).

ving the brow or glabella in the preceding 6 months, the presence of neuromuscular disease, and/or concurrent pregnancy or breastfeeding.

Treatment was standardized to include five intramuscular injection sites using 2,500 units of BTX-B (Myobloc; Elan Pharmaceuticals, San Diego, CA) divided equally into the procerus muscle, the inferomedial corrugator muscles bilaterally, and the superior middle corrugator muscles bilaterally (Figure 1).

Patients assessed the treatment pain experienced immediately after the series of injections on a visual analog scale (0 = no pain to 10 = most pain imaginable). Standardized digital photographs using identical camera settings, lighting, and patient positioning were obtained of the treatment areas in repose and full contraction before treatment (baseline) and 48 to 72 hours, 1 week, and 1, 2, and 4 months after injection. Side effects of treatment were assessed at time of injection and at each posttreatment visit. Two medical evaluators independently graded the degree of rhytide severity seen in the photographs displayed in random order using an established clinical wrinkle scale (0 = no wrinkles, 1 = mild wrinkles, 2 = moderate wrinkles, and 3 = severe wrinkles).

Results

All 20 patients showed improvement of their wrinkles after a single treatment session (Figure 2a,b). Average wrinkle scores were reduced by 42% within 48 to 72 hours after treatment, peaking in clinical effect (drop in wrinkle scores by 78%) at 1 month (Figure 3).

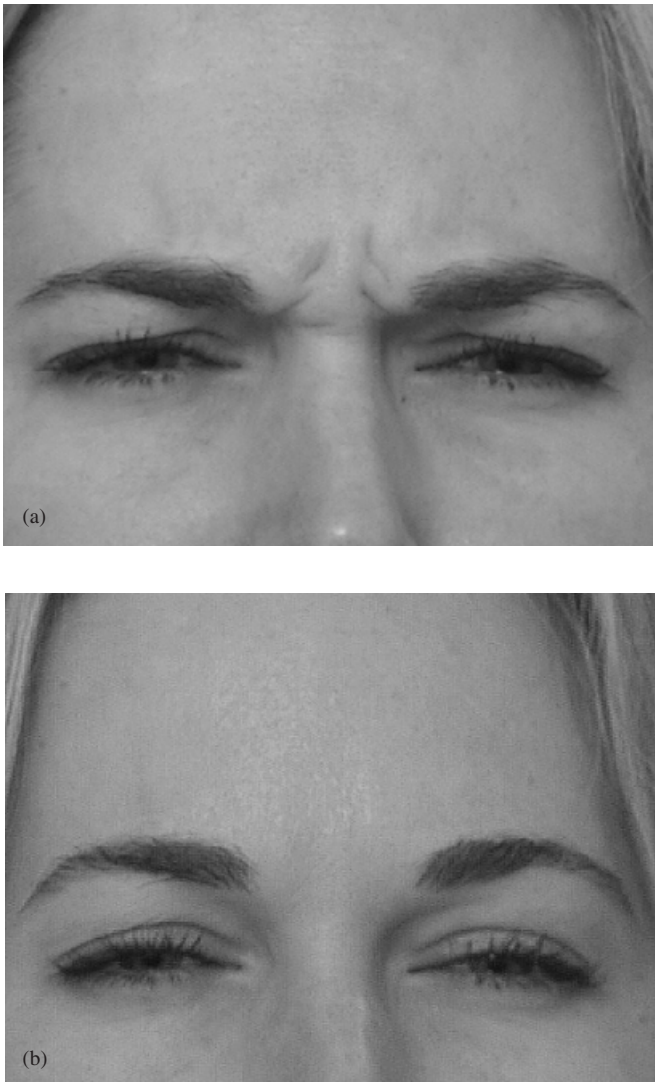

Figure 2. (a) Full contraction before treatment (baseline). (b) Full contraction 1 month after injection of 2,500 U of BTX-B.

Effect of treatment waned by 2 months with no patients maintaining improvement 4 months after treatment. Average pain ratings of 6.6 (moderate pain) were associated with the injections. One patient reported a feeling of fullness in the brow area lasting several hours. Another patient who was receiving high-dose aspirin therapy experienced temporary bruising at the injection sites. No other side effects of treatment were encountered.

Discussion

This study demonstrates that BTX-B is safe and effective for patients with hyperdynamic rhytides recalcitrant or showing decreased clinical effect to

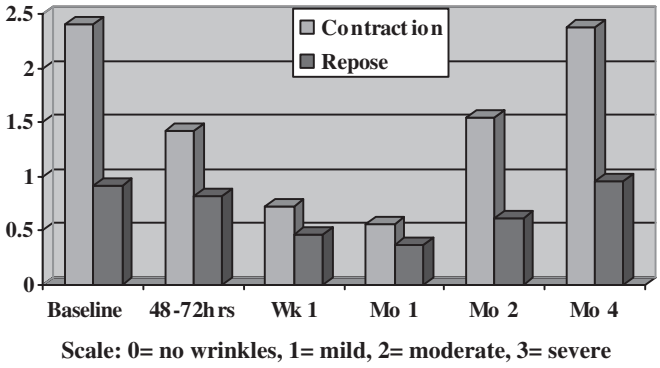

Figure 3. Clinical wrinkles scores.

treatment with BTX-A. Our five standardized injection site technique using equally divided doses of 2,500 U effectively immobilized the muscles of the glabellar region and temporarily erased the deepest vertical frown lines in all patients studied. Similar to the pilot study reported by Sadick[3] wherein 1,800 U of BTX-B was delivered, our 2,500-U BTX-B treatment group also showed a more rapid onset of action and smoother aesthetic appearance. Our study patients, however, experienced more severe injection discomfort, with their ultimate satisfaction rates being lower than those reported by Sadick. A longer duration of effect was not observed with the more rapid onset of action. In fact, the longevity of clinical results was markedly shorter than that typically seen after delivery of equivalent BTX-A doses (25 U). It is expected that the use of even higher doses would effect a longer duration of action.

In summary, intramuscular injections of BTX-B may be used safely for dynamic glabellar rhytides in the manner described herein with little risk of untoward effects. The type B form of the exotoxin offers a viable solution for patients who show decreased clinical response or fail to respond to treatment with BTX-A (Botox). Additional studies are needed to determine whether increased dosages effect longer periods of muscle paralysis.

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