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Original Research

Botulinum toxins types A and B for brow furrows: preliminary experiences with type B toxin dosing

Nicholas J Lowe, Paul S Yamauchi, Gary P Lask, Rickie Patnaik & Donna Moore

Authors:
Nicholas J Lowe[1,2],
Paul S Yamauchi[1,2], *Gary P Lask*[1,2],
Rickie Patnaik[2] *& Donna Moore*[2]
[1]*UCLA School of Medicine, Los Angeles, CA, USA and* [2]*Clinical Research Specialists Santa Monica, CA, USA*

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BACKGROUND: Facial lines resulting from hyperactivity can be misleading manifestations of negative emotions, fatigue and stress. They may also contribute to a perception of facial aging. A well established treatment is botulinum toxin type A (BTX-A). Recently, botulinum toxin type B (BTX-B) has become available for the treatment of cervical dystonia. There has been little comparison on the efficacy of the two different types of botulinum toxins, nor is there information on appropriate dosing of BTX-B for facial muscles.

OBJECTIVES: The purpose of this pilot study was to observe the effects of BTX-B in comparison to BTX-A, on patients with brow furrows assessing initial efficacy and duration of effect.

METHODS: Patients were injected with BTX-B in two different dose conversions against BTX-A to the corrugator-procerus complex. Some patients received a conversion of 50 units of BTX-B (total of 1000 units) to one unit of BTX-A while others received a conversion of 100 units of BTX-B (total of 2000 units) to one unit of BTX-A. The patients treated with BTX-A received a total of 20 units. These patients were clinically assessed prior to treatment and 3 days, 1 week, 4 weeks, 12 weeks and 16 weeks after treatment.

RESULTS: Both types of botulinum toxin were effective at improving glabellar frown lines. The onset of actions occurred slightly sooner (2–3 days) with BTX-B than with BTX-A (3–7 days). Duration of effect with BTX-A was at least 16 weeks. With 1000 units of BTX-B, dose duration was 6–8 weeks and with 2000 units of BTX-B, duration was 10–12 weeks.

SUMMARY: Both types of botulinum toxin are effective at correcting deep glabellar furrows. At least with the doses used, BTX-B has a quicker onset of action and BTX-A has longer benefit for glabellar wrinkles. These data strongly suggest that further dose ranging studies of BTX-B are necessary and indicated in controlled double blind studies in a larger patient population. *J Cosmetic and Laser Ther* 2002; 4: 15–18

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Correspondence: Nicholas J Lowe, 2001 Santa Monica Blvd, Suite 490W, Santa Monica, CA 90404, USA.

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Introduction

Facial lines due to hyperactivity can be interpreted as manifestations of negative emotions, fatigue, stress and can lead to a perception of aging. There are a variety of different treatment options available for this problem including endoscopic brow surgery, skin resurfacing, the use of filler agents, and the relaxation of the hyperfunctional mid forehead and glabellar muscles.

There are seven antigenically distinct types of botulinum toxin (A–G) produced by anaerobic *Clostridium botulinum* bacterium. Botulinum toxins bind to unique receptors at the neural-muscular junction and prevent the release of acetylcholine from the presynaptic vesicles without affecting neuronal conduction.[1] BTX-A is the best characterized and most investigated of these types and has been used safely for over 25 years in a variety of indications.[2]

Several studies of BTX-A have been reported on facial lines, including initial anecdotal uncontrolled studies.[3–6] Previous double blind studies confirmed the efficacy of BTX-A against placebo.[7] A mean duration of efficacy of 17.6 weeks was observed when a dose of 20 units of BTX-A was used to treat the corrugator and procerus muscles.

Recently, botulinum toxin B (BTX-B) has been approved for cervical dystonia.[8–10] This preliminary report describes the authors' experiences on initial efficacy and duration plus observations of side effects comparing BTX-A and BTX-B in a small group of patients using dose conversions of one unit of BTX-A to 50 or 100 units of BTX-B. We conclude that further larger controlled studies are needed to elucidate these observations further.

Materials and methods

Thirteen patients with moderate to severe glabellar frown lines were selected for treatment. The patients had not received prior treatment with botulinum toxin. The BTX-A was from Allergan, Inc. (Irvine, CA, USA) under the trade name Botox® and the BTX-B was from Elan Pharmaceuticals (Dublin, Ireland) under the trade name Myobloc™.

Grading of severity

Physician grading of severity was based on an established score and made at maximum frown and at rest.[6,11] Grading was rated as zero, mild, moderate, and severe. The duration of botulinum toxin treatment based on glabellar line severity was assessed at each visit.

Photographs were taken with standard facial photography using the Canfield system (Canfield Clinical Systems, Fairfield, NJ, USA). All patients enrolled in the study were female and their ages ranged from 33 to 72 years old (mean age 50 years). No patients had any condition that would interfere with the safety or efficacy of botulinum toxin. There was neither evidence of ptosis nor history of neuromuscular disorders. None was on any medication that would likely interact with botulinum toxin nor were any pregnant or planning pregnancy.

Dosing and injection technique

Vials containing 100 units of BTX-A were diluted with 2.5 cc of sterile 0.9% saline without preservative to give 4 units per 0.1 cc. Vials containing 5000 units of BTX-B were diluted with sterile 0.9% saline without preservative to give concentrations of either 200 units per 0.1 cc or 400 units per 0.1 cc.

Injections at five sites were performed to treat the glabellar lines. Each site received 0.1 cc of either BTX-A or BTX-B. One injection was performed at the procerus muscle and two injections each at the inferior-medial and superior-lateral aspects of the corrugator muscles.

Results

Figure 1 shows that BTX-B has a faster onset of action in reducing glabellar furrows than BTX-A by 1–2 days. In general, BTX-A exhibited efficacy starting at days 3 to 7 after injection while BTX-B diminished frown lines beginning at days 2 to 3. The effects of BTX-A and the two different concentrations of BTX-B peaked similarly at up to weeks 3–4. After week 4, there was a steady decline in the improvement of the brow lines with both types of toxin. BTX-A showed a slower rate of decline than BTX-B. The rate in decreased efficacy for BTX-B was dose dependent

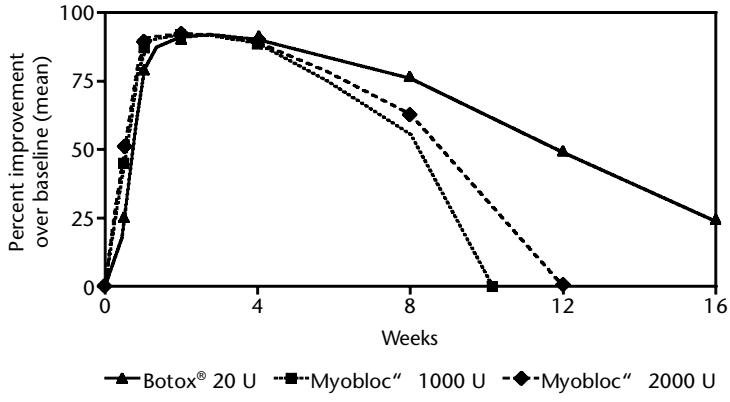

Figure 1
Kinetics of BTX-A versus BTX-B in the treatment of glabellar rhytides. BTX-A (20 units), BTX-B (1000 units), or BTX-B (2000 units) were injected at five sites in the glabellar area and the efficacy of diminishing brow furrows was evaluated at different time intervals following injection.

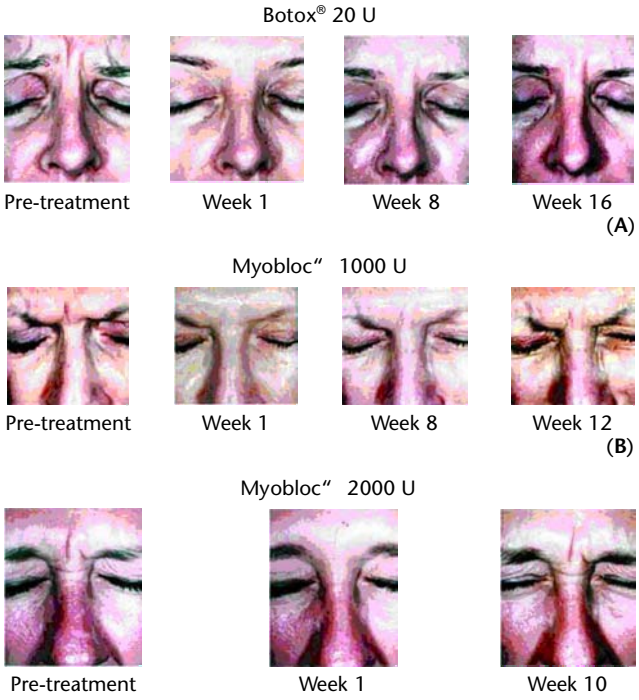

Figure 2
Reduction of glabellar wrinkles following botulinum toxin treatment. (A) 20 units BTX-A. (B) 1000 units BTX-B. (C) 2000 units BTX-B.

with the 2000 unit dose exhibiting a slower decrement than the 1000 unit dose. BTX-A at 20 units had a duration of efficacy for at least 16 weeks. The duration of BTX-B appeared to be dose dependent with lower doses at 1000 units lasting 8–10 weeks and the higher dose at 2000 units lasting 10–12 weeks. Figure 2 shows facial photographs of patients who received each type of botulinum toxin at pre-treatment and different weeks after injection.

Potential side effects such as ptosis, bruising, dry eyes or mouth were not present with either BTX-A or BTX-B in this limited number of patients (Table 1). One person reported a minor headache that lasted for a few days after injection with 1000 units of BTX-B. A few patients complained of increased pain associated with the injections from BTX-B that was transient. In general, the safety profile of both types of toxins was excellent.

Discussion

Botulinum toxin is used to treat an increasing variety of disorders.[4–6,12] Until recently, only BTX-A was available and approved for human use. BTX-B has recently been approved for cervical dystonia.[7–9]

We were therefore interested in this pilot study to observe the effects of BTX-A and BTX-B on glabellar furrows. A previous study compared the efficacy of BTX-A and BTX-B in paralyzing the extensor digitorum brevis in human volunteers where a dose of approximately 45 units of BTX-B was used for every unit of BTX-A. Based on the BTX-B dosing by Brashear et al[8] and Sloop et al,[13] we elected to use total doses of BTX-B that were either 50 times or 100 times the dose of BTX-A. Either 20 units of BTX-A or 1000 or 2000 units of BTX-B was injected at 5 sites – two injections into each corrugator on each side and one injection into the procerus.

In this small study, both BTX-A and BTX-B were effective in treating glabellar rhytides. BTX-B seems to have a faster onset of action by 1–2 days over BTX-A. However, BTX-A at 20 units has a longer duration of efficacy for at least 16 weeks. The duration of BTX-B appears to be dose dependent with lower doses at 1000 units lasting 8–10 weeks and the higher dose at 2000 units lasting 10–12 weeks. Both types of toxins exhibited excellent safety profiles.

Based on the data from the small number of patients in this study, we suggest that further dose ranging studies in a larger patient population size are necessary to find the optimal dose of BTX-B to prolong the duration of effect.

	BTX-A (20 U)	BTX-B (1000 U)	BTX-B (2000 U)
Ptosis	None	None	None
Headache	None	1	None
Pain on injection	Mild	Mild Moderate in 1	Mild Moderate in 2
Bruising	None	None	None
Dry eyes	None	None	None
Dry mouth	None	None	None

Table 1
Adverse effects from injections with BTX-A or BTX-B.

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