Botulinum Toxin Type A Induced Brow Ptosis Reversal Using Bacteriostatic Saline

The authors present a 6-year retrospective case series of 22 patients who complained of brow ptosis within 1 to 3 weeks after receiving cosmetic botulinum toxin type A (BTXA) injections to the glabella and forehead. After that they administered 1 to 2 sets of weekly bacteriostatic saline (BS) injections right above the ptosis and right into their immobile areas of the lower frontalis and medial corrugator muscles. Twenty-one patients were able to raise their eyebrow again within 1 to 2 weeks and 1 after 3 weeks, either showing minimal or no brow ptosis. These patients (and the authors) had a high level of satisfaction with this quick reversal. Historically, brow or lid ptosis has a 5.4% incidence rate and tends to last over 6 weeks. With experienced injectors, the incidence of ptosis decreases significantly to around 1%.[1] During the time frame of this retrospective study, the incidence of brow ptosis at this treatment facility was 0.1%. The usual dose of BTXA used was 15 U for the glabellar frown and 10 U to the forehead. Onabotulinum toxin A (Botox, Allergan) was used in 18 cases, abobotulinum toxin A (Dysport, Galderma) was used in 3 cases, and daxibotulinum toxin A (Daxxify, Revance) was used in 1 case.

Technique

The authors' technique is to inject into multiple sites along the lower forehead (frontalis) and medial corrugator, where no muscle activity was noted when the patient was asked to raise their eyebrows. The total dosage amount of BS at each visit ranged from 0.5 to 2 mL (most commonly 1 mL), based off the physician's clinical judgment. Enough BS is injected to create a nodule (see **Supplemental Digital Content 1**, Figure 1A, http://links.lww.com/DSS/B410), using around 0.2 to 0.3 mL per site, which was then massaged upward away from the eye. Notice brow/lid correction 1 week later (see **Supplemental Digital Content 1**, Figure 1B, http://links.lww.com/DSS/B410).

Assessment

Seventeen patients returned approximately once per week for consecutive injections of BS into the affected area until the ptosis resolved. All patients were treated at no charge and asked to return in 1 week if still not satisfied. Five patients did not return after their only BS injection and were later telephoned for the purpose of this case series to confirm they were satisfied with the results.

Results

In total, 19 patients improved (minimal drooping or back to normal) after 1 injection of BS (86.4%). Two patients (9.1%) responded within 2 sets of BS injections. One patient (4.5%) required a total of 3 BS injections. Of note is that photographic review of this last patient's brows revealed preexisting lid ptosis at the age of 69 years.

Controls

In total, 4 controls were used to help determine the mechanism of this neurotoxin adverse event correction. Three female patients and 1 male patient were injected with 12 units of BTXA to treat their forehead frowns, staying above their lowest forehead crease (see **Supplemental Digital Content 1**, Figures 1A and 2, http://links.lww.com/DSS/B410). Two weeks later, when the controls' forehead muscles were immobile, the authors injected control #1 with 1cc of BS only on the right side of the forehead (Figure 1B, C). The second control was injected with sterile water (SW). The third control received normal saline (NS). Similarly, the fourth control, a male patient, who developed brow ptosis, received BS where muscle weakness was noted. The authors' protocol also included massaging, rubbing the BS up and away from the eyebrow, as in the retrospective study. The left side of the forehead of 4 controls was left uncorrected to serve as the internal control. The control patients were all examined 1 and 2 weeks later.

Results of the Controls

Both patients who received BS recovered their ability to raise their eyebrows within 1 to 2 weeks of the BS injection (Figure 1D). The 2 other controls, who received either sterile water or normal saline, remained unable to raise their eyebrows after 1 and 2 weeks of weekly injections. Massaging had no effect on the 2 patients who received SW or NS.

Discussion

Brow ptosis typically sets 2 to 10 days after the treatment with BTXA and is a result of diffusion or too low of an injection site, weakening the lower frontalis and impairing the patient's ability to raise the brow (and secondarily, the eyelids). The great majority of our patients (86.4%) whom the authors examined directly or called reliably recovered their lower frontalis movement within 1 to 2 weeks of injecting BS (after 1 injection of BS), which argues against

Dermatol Surg 2024;00:1–2
http://dx.doi.org/10.1097/DSS.0000000000004170

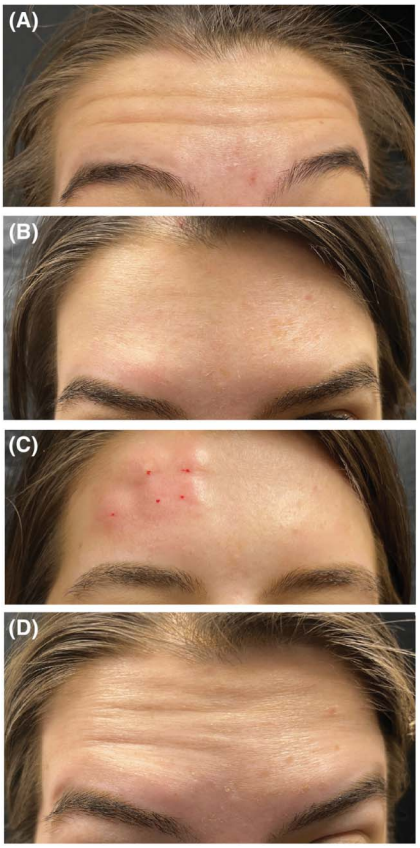

Figure 1. (A) Baseline movement before BTXA injection. (B) 2 weeks after BTXA injection, no movement or wrinkles noted. (C) The location of bacteriostatic saline injection (total 1cc injected). (D) 1 week after bacteriostatic saline injection, visible movement has been regained in the area injected with BS. BS, bacteriostatic saline; BTXA, botulinum toxin type A

spontaneous improvement. The controls also confirm that, when injected within 1 week of injecting BTXA, BS acted faster (1 week) than spontaneous recovery. Of interest, BS also had a positive impact for the 1 patient case the authors encountered using the newest daxibotulinum toxin A.

Possible Mechanism of Action of BS

The current understanding of the recovery of BTXA denervation is that of a gradual regrowth of nerve terminals.[2] The quick timing of these case reports suggests a different mechanism. The controls suggest that only bacteriostatic saline (BS), which contains 9 mg of benzyl alcohol (BnOH) and 9 mg of saline, exerted an effect that neither NS nor SW could. This eliminates the theory that core neurotoxin dilution was the mode of action.[3] The effect of BS on expediting the recovery of neuromuscular transmission to manage ptosis complications is a novel observation that may be explained by the previously reported effects of BnOH on cell membranes. One could theorize that BnOH, as a nonpolar solvent, dissolves nonpolar substances such as lipids, an essential component of cell membranes.[4] Several studies have reported that benzyl 18 alcohol is a bilayer-fluidizing agent that increases cell membrane permeability.[5] The saline component of BS may also create a localized gradient that allows a net flow of cytosolic fluid (with any light chain) out of the cell through a cell membrane that is more permeable, thereby decreasing the intracellular concentration. In addition, BnOH has also been found to inhibit endosomal trafficking. Therefore, BnOH may also prevent additional endosomal transport of the neurotoxin core. Further studies are needed to confirm the potential mechanism of action of BS hypothesized in this study. The paradoxical observation that the same agent being used to reconstitute botulinum toxin, can also be used to manage ptosis adverse events, is counterintuitive. However, the BS volumes the authors have injected to successfully manage these cases are much larger and more localized than those commonly used for aesthetic treatments.

References

1. Klein AW. Complications, adverse reactions, and insights with the use of botulinum toxin. *Dermatol Surg* 2003;29:549–56.
2. Nigam PK, Nigam A. Botulinum toxin. *Indian J Dermatol* 2010;55:8–14.
3. Shumaker PR, Rao J, Goldman MP. Treatment of local, persistent cutaneous atrophy following corticosteroid injection with normal saline infiltration. *Dermatol Surg* 2005;31:1340–3.
4. Coster HG, Laver DR. The effect of benzyl alcohol and cholesterol on the acyl chain order and alkane solubility of bimolecular phosphatidylcholine membranes. *Biochim Biophys Acta* 1986;861:406–12.
5. Friedlander G, Le Grimellec C, Giocondi MC, Amiel C. Benzyl alcohol increases membrane fluidity and modulates cyclic AMP synthesis in intact renal epithelial cells. *Biochim Biophys Acta* 1987;903:341–8.

Peter P. Rullan, MD, FAAD*†
Jennifer M. Rullan, MD, FAAD†
Jacqueline McKesey, MD, FAAD†
Juan Velazquez, PhD‡
Julia Szeremeta, BS†
*Department of Dermatology, Volunteer Clinical Faculty, UCSD, San Diego, CA
†Dermatology Institute, Chula Vista, CA
‡BeautyHealth, Los Angeles, CA

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the full text and PDF versions of this article on the journal's Web site (www.dermatologicsurgery.org).

The authors have indicated no significant interest with commercial supporters.