Botulinum Toxin Type A
Review and Its Role in the Dental Office

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KEYWORDS

• Botox • Botulinum • Toxin • Dentist • Dental • Oral • Mouth • Face

KEY POINTS

- For the general dentist, the use of BTA confers the ability to exert control over the soft tissues surrounding the mouth to better create a harmonious smile.
- Although not technically challenging, the injection of BTA into the facial musculature requires a level of finesse to achieve the desired outcomes.
- A sound understanding of the toxin's mechanism of action and the ability to manage potential complications are also necessary, as the dentist administering BTA must be competent to the same level as other providers who have traditionally been the gatekeepers of such agents.

Once firmly secured in the armamentarium of plastic surgeons, the use of botulinum toxin type A (BTA), perhaps best-known commercially by the household name Botox, has recently begun to see a diversification in the types of practitioners employing its use. Few could argue the impact that this and other neurotoxins have had on the practice of improving facial aesthetics. Although cosmetic purposes remain the most common application, this was actually not the original indication, and still several other indications continue to emerge.

For the general dentist, BTA can be an excellent practice builder when properly utilized. Because the perioral region contributes greatly to dental aesthetics, the ability to exert control over the soft tissues surrounding the mouth equips the dentist with additional tools to create a harmonious smile.

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MECHANISM OF ACTION

Prior to the advent of Botox and other subsequent neurotoxins used for therapeutic purposes, BTA was exclusively known as the causative agent in botulism poisoning. BTA is derived from the obligate anaerobe *Clostridium botulinum*. The earliest studied accounts of poisoning from this microbe date back to 1793, when an outbreak in Wildbad, Germany killed 6 people and affected 7 other people. The source was determined to be a contaminated batch of *Blutwurst*, or blood sausage—hence the name "botulism," after the Latin word for sausage, *botulus*. A larger outbreak in Belgium nearly a century later allowed Emile Van Ermengem to identify toxins produced by *C botulism* as the cause of botulism poisoning. This most commonly occurs when consuming food contaminated and stored under anaerobic conditions (eg, improperly canned). Per unit mass, botulinum toxin remains the most potent and lethal toxin known, with an LD50 of 1 to 3 ng/kg in people.[1]

Type A is the most potent of 8 serotypes of botulinum toxin that have been identified thus far (designated A–H, the latter being the most recently discovered in 2013).[2] Most variants cause paralysis at the neuromuscular junction by inhibiting the release of acetylcholine. Ordinarily, acetylcholine produced by the neuron remains contained in vesicles that upon depolarization of the neuron, fuse with the neuronal membrane to deposit the acetylcholine into the synaptic cleft. This process is facilitated by a complex of SNARE proteins: VAMP-2 and synaptobrevin on the vesicular surface, and syntaxin 1A and SNAP-25 on the neuronal membrane. When botulinum toxin is present, it binds to a separate class of surface proteins and becomes internalized by the neuron, subsequently cleaving the SNARE proteins that allow acetylcholine's exit into the synapse (**Fig. 1**). Owing to the storage vesicles of acetylcholine already within the motor endplate, the effect of paralysis is not manifested until 24 to 48 hours later, when these reserves are depleted. Paralysis would be permanent were it not for new axonal sprouts that are generated in 2 to 6 months, reestablishing the functional neuromuscular junction.

PREPARATION AND GENERAL CONSIDERATIONS

The first US Food and Drug Administration (FDA)-approved pharmaceutical preparations of BTA in the late 1980s were indicated for the treatment of strabismus and blepharospasm. The side effect of eliminating wrinkles in the lateral canthal region of the eye ("crow's feet") was quickly realized, and following extensive study, FDA approval for additional indications soon followed, including cervical dystonia (2000), glabellar rhytids (2002), and axillary hyperhidrosis (2004).

In the United States, BTA is available by the trade names Botox Cosmetic, Dysport, and Xeomin. All medications have similar FDA-approved indications, but Botox's *ona*botulinumtoxinA differs from Dysport's *abo*botulinumtoxinA and Xeomin's *inco*botulinumtoxinA primarily in regards to unit potency and nonprotein components that arise from different manufacturing processes.[3] Commercially available vials of any of the medications contain a given number of biologically active units. It is important for the clinician to realize that these units are essentially arbitrary quantities used for convenience in dosing. In general, most literature agrees on a potency equivalence of 2.5 to 3 units of Dysport to 1 unit of Botox.[4] Despite containing very similar toxins, this difference in potency can be attributed to the bacterial strain from which the toxin is sourced, the purification method, or differences in methods of testing potency.[5] For purposes of consistency, all doses in this article will refer to Botox units, with the understanding that an equivalent dose of Dysport or Xeomin would be anticipated to be equally effective.