

Review of the Applications of Botulinum Toxin and Tissue Fillers in Dental Practice

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The Dental Profession has a long and noble history of providing excellence in care through an elegant mixture of art and science. Advances in pharmacology and a better understanding of both the static and dynamic relationship of soft tissues on the oro-facial complex have opened new avenues in treatment. Through the judicious use of Botulinum toxins and tissue fillers, the oro-facial complex can be safely sculpted and functionally modulated. Their use as part of comprehensive dental treatment can relieve pain, restore function and help to create the perfect smile.

What are Botulinum Toxins?

Botulinum Toxin-A (BTX-A), is one of eight sub-types of a neurotoxin produced by the bacterium *Clostridium botulinum* (1). It behaves primarily as a blocking agent at the nerve level by temporarily preventing the release neurotransmitters such as acetylcholine. (Figure 1) In this way it can relax skeletal muscle as well as inhibit glandular secretions (2, 3). In muscle, it lowers maximum contractile force as well as resting tone. Reversal of the toxin's effect occurs through several mechanisms and takes from one to four months. (4, 5) There is no damage to either the nerves or the target tissues.

Are Botulinum Toxins Safe?

In Canada only the 'A' type toxin is available and sold as Botox^R (Allergan) and Xeomin^R (Merz). These products are slightly different in their formulation and therefore behave slightly differently in some clinical applications. (Figure 2) Dosing regimens are similar but not interchangeable between these two products. (6) Botulinum toxins despite their ominous name are extremely safe drugs. Their therapeutic margin (LD₅₀/ED₅₀) is in the order of 15:1 meaning that systemic toxicity does not occur until doses reach 15 times the effective therapeutic dose. (7) Lidocaine by comparison has TM of 3:1.(8) Most

unwanted effects result from the drug drifting to adjacent sites. (9) This can result in unwanted muscle weakness such as an asymmetrical smile or a dry mouth. Only rarely does the drug cause significant dysfunction such as an inability to swallow, which is why a clinician must have a thorough understanding of regional anatomy as well as injection protocols. Side effects just like desired therapeutic effects are temporary and typically require no supportive intervention. Local injection sequelae are the same as with any other percutaneous injection and include bruising, erythema and the possibility of infection.

Both Botox^R and Xeomin^R must be reconstituted with saline prior to use as described in the product monograph. (10) The measure of potency of these drugs is the 'mouse unit' or 'unit' which is an archaic reference to the dose needed to kill 50% of the mice it was tested on. Injection techniques and dosing protocols vary depending on the condition being treated. Most oro-facial injections can be safely and effectively carried out with a tuberculin syringe and a 1 inch 30 gauge needle. Adjunctive techniques such as EMG, Doppler and ultra sound guidance can be useful in select areas where the anatomy is complex such as the neck and larynx. (Figure 3)

Despite any specific regulations enacted by the Dental Colleges, very few of the many applications of BTX-A in the head and neck are Health Canada approved. Approved indications also known as 'on-label' include chronic migraine, eyelid spasm and glabellar wrinkles. (10) This means that almost all uses of BTX-A by dentists are 'off-label' or unapproved. This is not to say that a given therapy is ineffective or unproven but rather that the manufactures have elected not to spend the money on the clinical trials necessary for formal government approval. For a clinician it means that care must be taken in the consent process and that reimbursement for the drug or treatment may not be available from third party insurers.

Botulinum Toxins for Cosmetics

Botulinum toxin injections are most effective and predictable in blocking the release of acetylcholine. Therefore conditions which are primarily muscular or glandular are most responsive. BTX-A injected into the muscles of facial expression will effectively force them to relax. As a result any muscle induced wrinkling (hyperkinetic lines) will disappear for a period of 4 – 6 months. Small doses injected into the forehead will smooth creases without significantly inhibiting a patient's ability to create facial expressions. (Figure 4) Similarly, injections into hypertrophic masseter and temporalis muscles can

reduce their bulk, softening the jaw. In the hands of an experienced clinician, strategic placement of BTX-A will allow for facial sculpting. Brow lifts, altering the shape of the eyes from almond to more round, lowering the upper lip to reduce a 'gummy smile', turning up the corners of the mouth and smoothing jaw lines are just some of the possible interventions. (Figure 5) In combination with a more youthful and less stressed appearance created by smooth wrinkle-free skin, it is understandable why BTX-A treatment has become extremely popular. The success of these cosmetic applications relies not only on a thorough understanding of muscular anatomy but also on a thorough assessment of the patient's soft tissue. If there is insufficient elasticity to the tissue, or the dose is excessive, the resulting relaxation of the muscles will create sagging which is particularly troublesome around the eyes. The use of BTX-A as a stand-alone treatment for smoker's lines in the lips is generally not very effective and can cause significant lip incompetence with pronunciation problems.

Botulinum Toxins for Hypersalivation

Although the use of BTX-A for cosmetics is the most well known application, it is only the tip of the iceberg. The number of therapeutic uses throughout the body now numbers in the hundreds. Since glandular secretions are modulated by acetylcholine as well, injection into the major salivary glands can effectively inhibit hypersalivation. This can be a life-saving therapy in Parkinson's and Cerebral Palsy sufferers who are at risk of aspirating. (11) These injections can be done intra or extra orally and will reduce salivary flow for a period of up to a year without creating a dry mouth. (12, 13)

Botulinum Toxins for Parafunction

Parafunctional conditions such as clenching and bruxing also respond well to the relaxing effects of toxins. Pathologic bruxers such as patients with traumatic brain injuries can benefit greatly as it unloads the teeth and jaw joints reducing the risk of dental fracture. (14) In patients who simply clench or have a very heavy bite, reducing clenching force is an excellent adjunct for enhancing integration of immediately restored implants. (15) (Figure 6) Similarly, the technique is used in adult orthodontics to allow for tooth movement where dental intercuspation may inhibit re-alignment.

Relaxation of the masticatory muscles can also be beneficial in fracture healing and orthognathic surgery. If muscular pull threatens to create instability or malalignment then temporarily weakening selected muscles will allow for more effective fixation and therefore more predictable healing. (16) As with all forms of therapeutic intervention a thorough assessment of the patient is a must. Injecting a

large dose of muscle relaxant into an individual who suffers from sleep apnea can worsen the condition. However, this is not any different from prescribing narcotics or another respiratory depressant to such a patient.

Botulinum Toxins for TMD and Headache

BTX-A has also been used to advantage in conditions associated with pain. Within sensory nerves there are other neurotransmitters (CGRP, NGF₁, and NP-Y) which are associated with pain and also susceptible to blockade by BTX-A. By preventing their escape the toxin can modulate pain appreciation in peripheral tissues. (17) These drugs are now the primary therapy for dystonias which have components of spasticity and pain. (18) Temporomandibular disorders (TMD) may also respond well. The difficulty with TMD, unlike bruxism or dystonia, is that it can be complex. If the TMD is primarily muscle centered (usually an early intermittent presentation), injection of the masseter and temporalis will bring relief for 2 – 4 months. (19, 20) (Figure 7) This is particularly useful in patients such as pilots where the cognitive dysfunction associated with oral muscle relaxants is unacceptable. If the TMD has myofascial, neuropathic or arthritic components, BTX-A can still be effective, but should be part of a more comprehensive, multimodal treatment plan. Since chronicity is most often associated with a multifactorial form of TMD, early intervention by the GP dentist has significant potential advantages. Headaches may also form part of a complex involving TMD. Primary headaches, such as chronic migraine have been shown to be responsive to BTX-A, but their long-term resolution depends on comprehensive treatment which generally falls outside of the scope of dentistry. (21) However, headaches induced by hyperactivity of the temporalis muscle secondary to clenching, whether associated with other TMD symptoms or not, will respond to toxin injections. (22)

Botulinum Toxins for Pain

Other forms of pain such as trigeminal neuralgia, post herpetic neuralgia, atypical dental pain and scar pain may also respond to toxins. The mechanism is believed to be related to inhibition of neurotransmitters in peripheral sensory nerves. (17) Since these forms of pain often involve central as well as peripheral components, they are not nearly as responsive to BTX-A injections as muscular conditions are. (23, 24) The injections themselves are also different in that they target intra-dermal or intra-mucosal sensory nerve fibres rather than muscles. Injections are very superficial (intra-dermal or submucosal) and follow a grid-like pattern. (Figure 8)

It is critical that injectors have a thorough understanding of the anatomy of the muscles of facial expression and cosmetic injection protocols even if they are not injecting for cosmetic reasons. Intradermal and sub-dermal injections in the V1, V2 and V3 dermatomes will diffuse into the muscles potentially creating significant functional or cosmetic deficits. (Figure 9)

What Are Dermal Fillers?

Dermal fillers were designed to replace or enhance the volume of subcutaneous tissues. These filler products are generally classed as either 'permanent' (PMMA, calcium hydroxyl apatite and e-PTFE) or 'non-permanent' (collagen or hyaluronic acid). Most Dentists prefer to use hyaluronic acid products such as Juvederm^R (Allergan) and Restylane^R (Medicis). These products come in various viscosities, are easy to use, antigenically safe and can be dissolved after inadvertent injection with hyaluronidase. Juvederm and Restylane come in pre-loaded syringes for ease of use and treatments last from 6 – 12 months depending on the location.

Filler for the Face & Lips

Popular areas for Dentists to fill include the lips, naso-labial folds and cheek bones. There are different techniques which address both functional as well as cosmetic concerns. Lip injections are among the simplest and safest to do. (Figure 10) Whether 'plumping' for better lip competence or as part of crafting an exceptional smile, complications are uncommon. Sequelae include bruising and short term difficulty pronouncing consonants. The injections are uncomfortable and best done with local anaesthesia. Smoker's lines can be obliterated with a combination of filler and BTX-A. The incompetence created by relaxing the orbicularis oris muscle is compensated for by increasing lip volume.

Improving deep nasolabial folds is best accomplished by injecting filler over the cheek bones to create more tissue tone above the fold, as opposed to injecting only the fold itself. The object of the procedure is to reduce the shadowing created by a deep fold rather than to eliminate it. Both the cheek bone and nasolabial fold areas can be reached either through the maxillary vestibule or percutaneously. Complications in these areas are infrequent; however, inadvertent intravascular injection has caused local tissue necrosis and thrombo-embolic events resulting in blindness and death. (25) Again, a thorough and realistic patient assessment is a necessity as fillers can only partially compensate for age-induced tissue sagging. These products are not a substitute for a face lift.

Fillers for Black Triangles

There are very few applications for fillers within the mouth, although they have been successfully used to enhance deficient interdental papillae. By 'puffing up' the interdental tissue between teeth or implants, the black triangle can be made much less obvious.⁽²⁶⁾ The technique is simple but temporary as filler in this location also resorbs with time.

Records & Consent

The innovative use of both Botulinum toxins and tissue fillers in dental practice has addressed therapeutic and cosmetic needs that could not otherwise be easily satisfied. Although rigorous scientific testing of treatment protocols is for the most part lacking, anecdotal evidence endorsing the safe application of these agents is overwhelming. Given the off-label nature of many of the described applications, clinicians must ensure that they are treating within their scope of practice, have been adequately trained and have kept meticulous records. Record keeping as part of the informed consent process should include photographs where appropriate. It is remarkable how many patients discover that they have naturally asymmetric features only after they have been treated.

Conclusions

The introduction of Botulinum toxins and dermal fillers into dental practice has brought with it exciting new treatment options for many previously difficult to treat clinical situations. Neuromuscular dysfunction can be effectively controlled, pain can be eased and soft tissues can be aesthetically and functionally optimized. Although generally simple and safe to use these products must be respected. Each Dental College has or will define limitations on the usage of BTX-A and dermal fillers as well as training requirements. Dentists are already adept at using needles which is often a hurdle for many health professionals. Training by expert individuals or organizations is readily available and your College can guide you as to whether a particular training course meets its educational standards. Ideally, Dentists should consider taking their own patient(s) to a hands-on course. This will allow them to get experience with particular protocols that are most suited to their practice, get an honest evaluation of the procedure as well as being able to follow functional and aesthetic changes as they evolve. It is also an excellent idea to bring staff to a course since they are often responsible for patient education and

treatment coordination. Product monographs, scientific articles and information on acquiring products is available from the respective pharmaceutical companies.

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Figure 1 After being injected, the toxin is taken up by nerve cells where it cleaves the proteins that allow storage vesicles to discharge neurotransmitters such as acetylcholine.

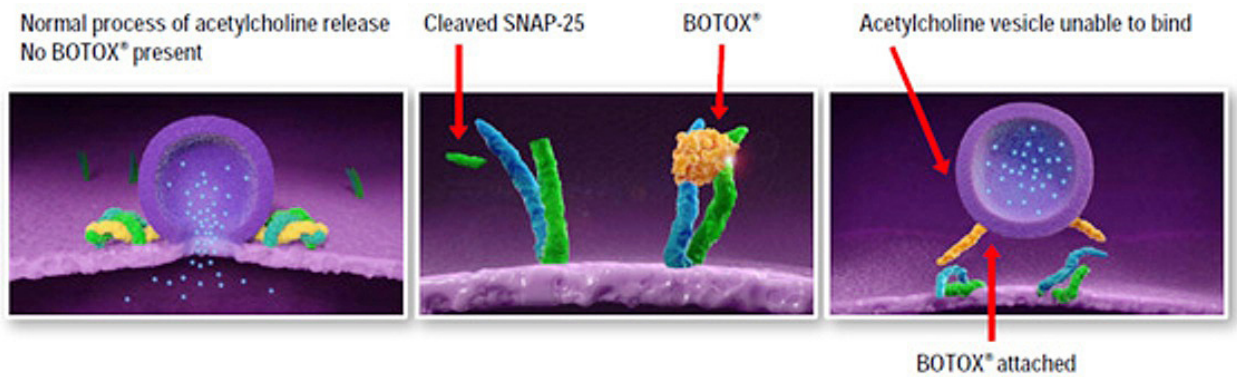


Figure 2 Botulinum type-A products share the same 'core molecule' but differ in the surrounding 'accessory proteins'. It is the accessory proteins which alter the clinical behavior of products such as tissue diffusion. The illustration below is of Botox^R which has 750 kD (kilo Daltons) of accessory proteins.

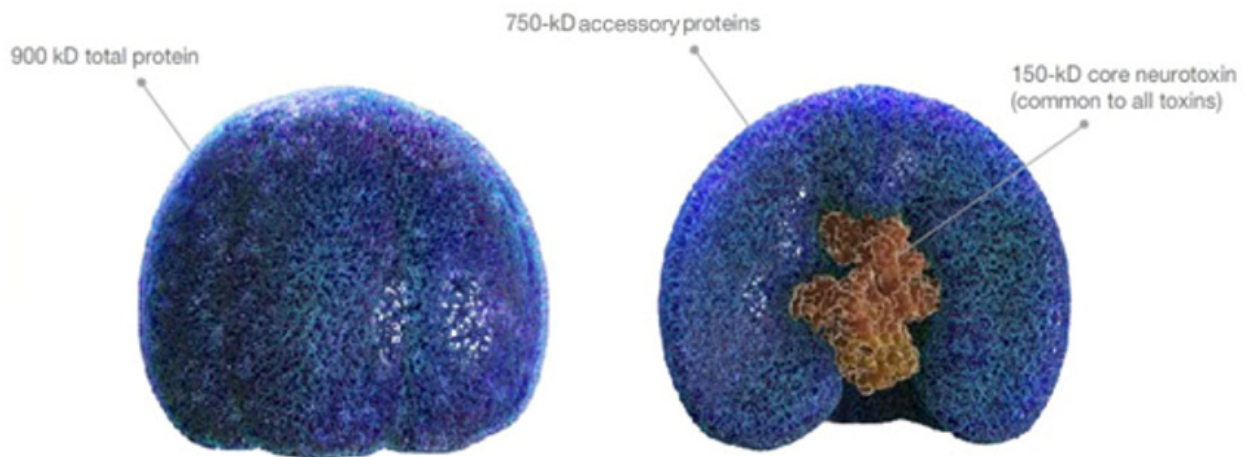


Figure 3 Techniques such as EMG guidance (illustrated below) can be used to improve injection localization for difficult to palpate muscles such as Lateral Pterygoid.



Figure 4 Many injections in the oro-facial complex will affect the muscles of facial expression. It is crucial that injectors be familiar with 'cosmetic' injection protocols even if they are not injecting for cosmetic reasons. Forehead injections are the most popular cosmetic injections practiced by dentists. They are safe and predictable. Injections in this region will reduce muscular activity that creates dynamic furrows and wrinkles without eliminating the ability to be expressive. Deep long-standing wrinkles will not be completely eliminated.



Figure 5 The 'Gummy Smile' can be improved with small amounts of BTX injected in the maxillary vestibule over the tips of the cuspids, similar to placing local anesthetic. The top photograph shows smile before injection, the lower 7 days post injection.



Figure 6 When injected into the Masseters and Temporalis muscles, bite force can be reduced in proportion to drug dose. This technique can reduce loading and improve healing after fractures, dental avulsions or subluxations, in orthodontics and after placing immediately restored implants. Below is a graph that shows temporal reduction in bite force after BTX injection.

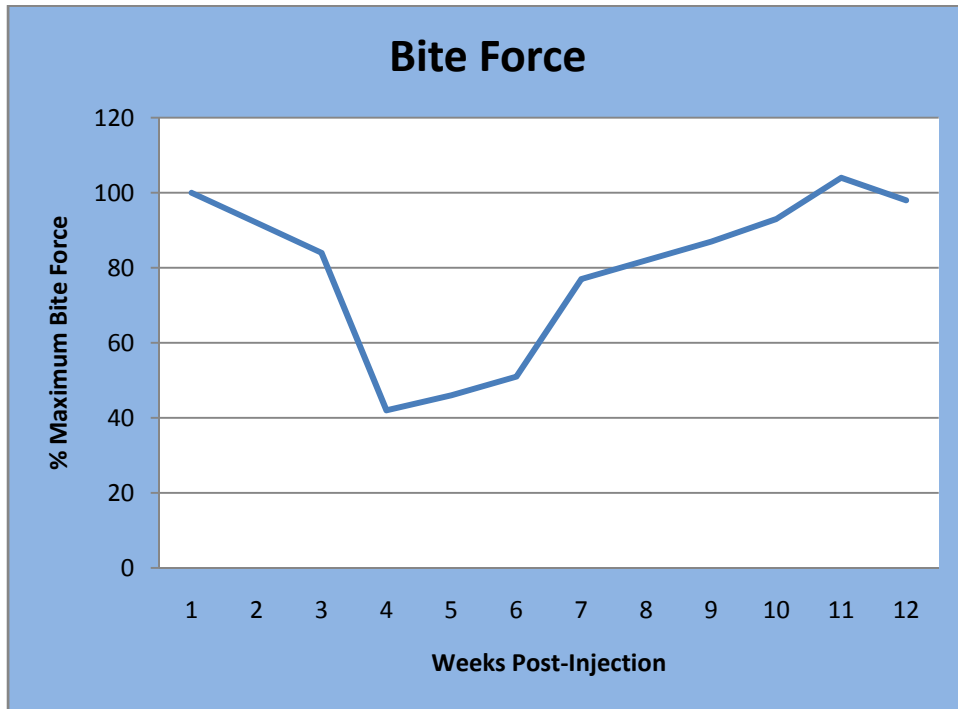


Figure 7 Injections for TMD are done by placing 3 – 5 injections into the bulkiest parts of the Masseter and Temporalis muscles.



Figure 8 Neuropathic pain such as Post Herpetic Neuralgia or Trigeminal Neuralgia is often responsive to Botulinum Toxin injections. The injections are intra-dermal or subcutaneous and follow a grid pattern covering the painful dermatome. Below is an illustration of injections for PHN.

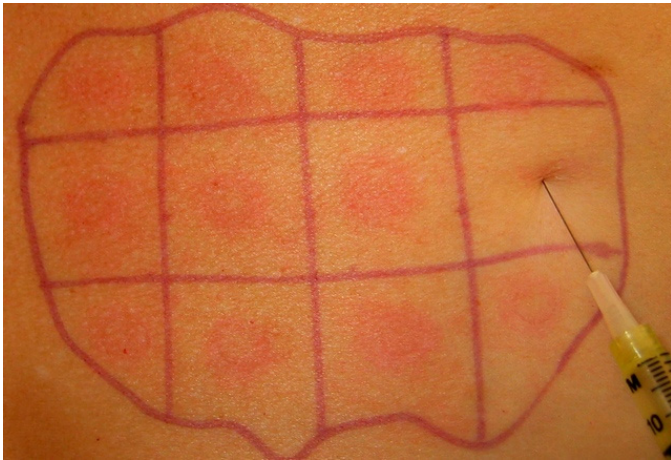


Figure 9 Five days after left forehead (V1 dermatome) injections. Note eyelid ptosis, brow ptosis, forehead asymmetry and bruising. Injections for pain anywhere in the oro-facial complex should follow cosmetic protocols as much as possible to avoid needless complications.



Figure 10 Injection of dermal filler into the lips can provide both esthetic and functional improvements. There are several techniques, all of which give safe and predictable results which last 6 – 8 months. The technique illustrated below employs a punctuate approach which gives better control of filler volume. Before (above) and after (below) demonstrate subtle volume enhancement with improved lip competence.

