Botulinum Toxin and Dentistry

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Commercially available botulinum toxin is the purified exotoxin of the anaerobic bacteria, Clostridium botulinum. This same neurotoxin is the cause of the rare but serious paralytic illness, botulism. Seven types of botulinum toxin have been isolated but only two, types A and B, have been made commercially available. Initially, only botulinum toxin A was available commercially on prescription but more recently, type B also came on the market. The Food and Drug Administration (US) has only approved botulinum toxin type A for treatment of cervical dystonia (severe neck muscle spasm), severe primary axillary hyperhidrosis (excessive axillary sweating), blepharospasm (spasm of the eyelids) and temporary improvement in the appearance of moderate to severe glabellar lines (wrinkles). Food and Drug Administration has provided a similar list of approved applications for botulinum toxin A, thus far the only product approved in Canada. The most publicized application has been for the elimination of facial wrinkling. The latter is accomplished by paralysis of the subcutaneous mimetic muscles.

The toxin acts by preventing the release of acetylcholine from presynaptic vesicles at the neuromuscular junction resulting in an inhibition of muscular contraction. This blockade is temporary, varying from three to four months, after which sprouting of new axon terminals result in a return of neuromuscular function. Therefore, treatment with botulinum toxin cannot be considered curative but a palliative and symptomatic approach to the management of a problem. The toxin has also been shown to block acetylcholine release at parasym pathetic nerve terminals.

More recently, botulinum toxin has been suggested as part of the armamentarium for the management/treatment of various orofacial conditions and a considerable body of literature has been developed describing or investigating its efficacy and safety. To date, most of the reports relate to botulinum toxin A and there are few well controlled double blind studies.

**Safety and Adverse Effects**

In general, adverse reactions are uncommon and relatively mild and transient. They are more common at or near the site of injection. These include dry mouth, dysphagia, dysphonia, transient muscle paralysis, headache, urticaria and nausea. Often, but not always, these side effects are noted when the dose exceeds that recommended. In 2008/2009, both Health Canada and the FDA revised the prescribing information for the commercially available botulinum toxin A products to include a “Boxed Warning” highlighting potentially adverse reactions related to distant spread of the toxin effect from the injection site. These highlight botulism-like symptoms such as muscle weakness, hoarseness or dysphonia, dysarthria, loss of bladder control, difficulty breathing, difficulty swallowing, double or blurred vision and drooping eyelids. These effects can occur anywhere from a day to several weeks after treatment at unrelated sites. Although rare, deaths have been reported. Children treated for spasticity seem particularly susceptible but adults have also been affected. Serious adverse reactions have occurred at therapeutic or lower doses.

**Temporomandibular Disorders**

The term “temporomandibular disorders” refers to an often poorly understood collective of clinical problems involving the masticatory musculature, the temporomandibular joints and associated structures or some combination. The disorders are often intermingled with other chronic pain disorders including fibromyalgia, chronic fatigue syndrome or tension type headache. Treatment is dependent on a thorough history and examination of the patient with a view to developing a clinical diagnosis and attempting to establish the basis for the patient’s complaints. These symptoms can originate from the tissues of the joints themselves or the related musculature. There is evidence that botulinum toxin is a valuable clinical tool in the management of the myofascial component of temporomandibular disorders. The first line treatment approach for temporomandibular disorders includes physiotherapy, exercises, behavioural type therapy, oral appliances (most often stabilizing type), anti-inflammatory medications, muscle relaxants, analgesics or some combination of these. Rarely surgical intervention is indicated. Botulinum
toxin can be a useful adjunct, particularly when these have failed to provide adequate relief, particularly in cases involving muscular hyperactivity. There is evidence that it has a place in the treatment of dystonia, masticatory muscle hyperfunction, myofascial pain and, to some extent, bruxism.8,10-15 Similarly, it may have a place as an adjunct to appropriate physical therapy in some cases of whiplash injury.16 Although there is a paucity of supportive research, there is a suggestion that botulinum toxin may also have a supportive role in temporomandibular joint surgery.17,18 These applications are off-label uses and patients should be so informed.

Other Orofacial Pain Disorders
There is still inadequate, well controlled research on the effectiveness of botulinum toxin in most other orofacial and related conditions. In some cases, the results are in conflict. Although research is still ongoing, there may be a place for it in the management of some forms of headache, migraine and tension type in particular where the more common therapeutic modalities have been unsuccessful.19,20,21 Its value in orofacial neuropathic conditions is yet unproven. Again, patients should be informed of these off-label applications before making an informed decision.

Other Applications
Botulinum toxin has been shown to be effective in the management of sialorrhea.22,23 This involves injection into the salivary glands, usually with electromyographic guidance. It has been suggested as a means of reducing the load on newly placed implants but there is no strong scientific evidence that there is any significant effect of the success or survival of the implant.

It has been well demonstrated that botulinum toxin will reduce facial wrinkles. Some have suggested its use to treat high lip lines or perioral age related changes. The scientific evidence in support of much of this is weak and the application is once again an off-label use.

Summary
Botulinum toxin has certainly been demonstrated to have significant value in the management of some types of orofacial pain, particularly myogenous temporomandibular disorders in cases where the patient is unresponsive to the less invasive therapeutic modalities or, at times, in conjunction with them. Similarly, it has been proven effective in cases of severe sialorrhea but the administration is more complex. The benefits of botulinum toxin for some forms of headache are strongly suggested but unproven scientifically as yet. Cosmetic applications of the toxin have been well demonstrated in some areas. Although the drug is considered generally safe, there are a number of uncommon, relatively mild adverse reactions but more recently, some severe, potentially life threatening side effects, distant from the site of injection have been described. Most of the conditions for which a dentist might use botulinum toxin are not amongst the approved applications (off-label use). Therefore patients should be properly informed prior to consenting. The practitioner must ensure that the treatment is within his or her scope of practice and that he or she has the appropriate training, not only to administer the drug but to deal with potential adverse effects.
References

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