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Maxillofacial use of botulinum toxin: a series of three unusual cases

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Abstract

Background: Botulinum toxin is a neurotoxin produced by the bacterium Clostridium botulinum. A commercial version of the toxin has been available for medical use since the 1980s; one version is known as Botox®. When injected into a target muscle botulinum toxin causes localised partial paralysis. Famous for cosmetic applications, it is also used in oral and maxillofacial surgery for treatment of conditions such as masseteric hypertrophy, mandibular spasm, bruxism, pathologic clenching, chronic migraines, and hypersalivation. Three unusual maxillofacial cases are presented here in which botulinum toxin has been used to good effect.
Findings: Patient one suffered significant trismus following a fractured mandible and scarring of his masseter muscles. Physiotherapy had a limited benefit. Botulinum toxin was used to provide an immediate and lasting improvement in mouth opening.

Patient two suffered two instances of an unusual repetitive, semi-voluntary movement of his mandible for several weeks. He experienced significant pain and multiple medical interventions were attempted to arrest the movement. Botulinum toxin applied to the masseter and temporalis muscles ceased the movement. He has not suffered further recurrence.

Patient three suffered a number of long-term chronic pain issues centred on the temporomandibular joints (TMJ) and neck. She underwent usual TMJ dysfunction interventions such as medication and bite splints, with no improvement. Botulinum toxin injected into the masseter and temporalis muscles provided an immediate benefit.
Conclusion: These cases reflect the varied applications for botulinum toxin in the head and neck. With proper case selection, and care with administration, botulinum toxin is a safe and effective intervention with minimal complications.

Introduction

'Botulism' is a potentially fatal illness first described in 1820. Clostridium botulinum is a usually harmless bacterium which produces a powerful neurotoxin when subjected to anaerobic conditions. Early cases of botulism resulted from consumption of improperly-canned foods (Erbguth, 2008).

Botulism can be contracted by ingestion of wound infection by botulinum toxin; the result is reduced nerve transmission. In some cases, full body paralysis can result preceding respiratory arrest. Treatment of botulism is focused on early recognition and intervention, both of which improve outcomes significantly (Sobel, 2009).

Although identified as one of the most acutely lethal known toxins, the potential for small doses to be employed for therapeutic benefit was recognised early by researchers. Development throughout the 19th century has resulted in the commercial availability of the toxin for medical use. When used in therapeutic doses, partial nerve activity is preserved. This function has found several applications in modern medicine in treatment of conditions where weakening of hyperactive muscles or control of hypersecretory glands is beneficial (Münchau et al. 2000).

Perhaps most well recognised by the general public is the use of botulinum toxin in cosmetic applications for treatment of facial wrinkles (a commercial variant is known as Botox). However, well established usages are recognised in a range of conditions from treatment of ophthalmological disorders (strabismus or nystagmus); movement disorders (focal dystonia, Parkinson's disease, tremor or hemifacial spasm); pain (headache, back pain, myofascial pain) and to control hypersecretion of glands (e.g. hyperhidrosis) (Münchau et al. 2000; Azam et al. 2015).

Uses in oral and maxillofacial surgery are well documented and include the treatment of temporomandibular joint (TMJ) disorders, salivary gland secretion disorders (pytalism) and myofascial pain amongst others (Park et al. 2016). A series of three unusual cases are discussed in which botulinum toxin was used to good effect.

Case One

A 30-year-old male with a non-contributory medical history presented to the Emergency Department of Tauranga Public Hospital. He had suffered a workplace accident which resulted in a splinter of wood passing through both angles of his mandible. He underwent removal of the foreign body under general anaesthetic with primary closure of the soft tissues with no significant tissue loss. His mandibular fracture was repaired conventionally by open reduction with internal fixation. The patient was discharged home after two days of monitoring and pain control. Conventional post-operative advice and follow-up were instigated. Trismus developed during early healing with an inter-incisal distance of 25 mm recorded. This was managed with physiotherapy and analgesia but failed to show significant improvement at a 6 week post-operative review. A further 6 weeks of intensive physiotherapy failed to increase mouth opening.

It was noted that both masseter muscles were scarred and felt 'tight' to palpate. Application of botulinum toxin to the masseter muscles was discussed with the patient. Then 50U of Botox® was administered to each masseter muscle and the patient instructed to continue to encourage mouth opening by placing increasing numbers of wooden spatulas into the inter-incisal space. Two weeks showed a marked improvement in mouth opening with an inter-incisal distance of 37 mm recorded.

The patient experienced no severe side effects. Some minor difficulty in eating hard and chewy foods was reported together with early fatigue duringmastication. The patient was discharged from care. He was interviewed 10 years later for this report and still experiences some difficulty with chewing hard foods, however, his mouth opening has remained stable.

Case Two

An otherwise healthy 12-year-old boy presented to the Emergency Department of Tauranga Public Hospital suffering from an unusual rhythmic translocation of his jaw. He demonstrated an involuntary movement of the mandibular condyles down the articular eminence symmetrically, with a 1-2 second periodicity. After persisting for several hours, the movement elicited increasing pain. With teeth clenched the patient could prevent movement, however, upon relaxation the pattern returned immediately. A number of interventions were instigated in a step-wise manner and included the use of non-steroidal anti-inflammatories, midazolam, and patient controlled analgesia with Fentanyl, amitriptyline and orphenadrine. These had limited impact. Ultimately the patient was sedated which arrested the movements. He was transferred to a tertiary children's hospital (Starship Children's Health, Auckland) where he underwent investigation by several specialties. This included a CT of his head and review by the maxillofacial, neurology, endocrinology, paediatrics, psychiatry and pain management teams. No abnormal findings were reported. TMJ dysfunction, dystonia, jaw tremor, epilepsy, and involuntary/voluntary muscular spasm secondary to TMJ or other non-specific pain, with a psychosomatic component were considered. No pathology was identified and he was referred to an outpatient team for psychiatric assessment and counselling.

The patient presented again with the same issue 18 months later. He reported minor trauma as an initiating factor. After consideration of his previous history, treatment focused on arresting the movements and botulinum toxin was administered to the masseter and temporalis muscles bilaterally. This immediately resulted in a reduction in amplitude of the movements, although minor muscle contraction continued for 24 hours following administration. After 24 hours the patient was no longer using analgesia, had no contractions, and was comfortable to be discharged home. He underwent a subsequent MRI scan and review by the Child and Adolescent Mental Health Service in the community. No further findings were made and he was discharged.

The patient was followed up eight years post operatively whilst writing this report. He has suffered no further episodes and has not required application of further botulinum toxin. No clear aetiology for his symptoms was discovered. It is assumed he was suffering from a semi-voluntary response to TMJ or other poorly-defined pain. Botulinum toxin clearly played a minimally invasive role in breaking the pain-contraction cycle at his second presentation. We are unaware of any similar cases reported in the literature. If further cases are described this may warrant further investigation.

Case Three

A 27-year-old female was referred by her general medical practitioner to the private practice of author JB. She had a two-year history of pain in her mandible, TMJs and neck. She experienced near-constant headaches. She was also affected by chronic pain at other sites including a burning abdominal pain and neuropathic pain in her ankles. She had a diagnosis of fibromyalgia. She was aware of clenching her teeth during the day and of a nocturnal bruxism habit. Her discomfort was worse when she slept poorly or was stressed. Her symptoms were debilitating and it was suggested that she may be suffering from central sensitisation resulting in chronic pain. There was also concern that she may be suffering from serotonin syndrome. She was using a number of medications; venlafaxine, amitryptyline, lorazepam, zopiclone, gabapentin, mesalazine, tramadol, ibuprofen, codeine and fentanyl patches, with limited benefit.

For control of her facial pain she was provided with a soft bite splint and instructed to wear this as often as possible, but various designs of splint served only to worsen her symptoms. Bilateral arthrocentesis with steroid injections was undertaken with no measurable relief. Ultimately injection of botulinum toxin to the temporalis and masseter muscles bilaterally was discussed with the patient and 25U applied to each muscle.

Review was completed at one-week post and the patient reported better quality sleep and a 'miraculous' relief of her symptoms. Pain was significantly reduced with cessation of bruxism. She reported feeling more relaxed and without headaches and this had reduced her tendency to clench her teeth during the day. She felt it was easier to tolerate her other chronic pain conditions and was confident to reduce her analgesia. She was able to increase her levels of exercise, which was an important milestone for her return to normal life.

Regular follow up over five years has been undertaken and repeat administration has been required every three to six months, with a maximum interlude of nine months. She reports most relief in the weeks following injection, followed by a slow return of her symptoms. There is some suggestion that the efficacy of each application is reducing with time, which may indicate development of resistance.

Discussion

Botulinum toxin acts by inhibiting release of acetylcholine (a key neurotransmitter) at the neuromuscular junction. This prevents nerve signaling, resulting in paralysis (Huang et al. 2000). The blockage of acetylcholine release is irreversible, however, the synapse is not

damaged and function recovers as the nerve regenerates and new synaptic contacts develop. Following injection, the peak of the paralytic effect is four to seven days (Nigam et al. 2010). Nerve function, and therefore normal muscle function, typically returns to previous levels after two or three months (Münchau et al. 2000).

In the above cases the masseter and temporalis muscles were targeted with therapeutic doses of botulinum toxin to induce weakness and manage the varying clinical symptoms. The unit of botulinum toxin is the 'mouse unit' (MU) which is a unit of biologic activity and relates to the lethal dose in a specific breed of mouse. The effects of administration cannot be seen for at least 24 hours, but in some cases up to 5 days is required. The maximum benefit is often seen at 10 days (Nigam et al, 2010).

Case One experienced trismus secondary to trauma and spasm of the masseter muscles bilaterally; there was no mechanical restriction of mouth opening. The rationale for use of botulinum toxin was to induce partial or total paralysis of the masseters, enabling the other muscles of mastication to take over normal jaw movements, overriding the restricted movement of the masseters. In contrast to this, Case Two was experiencing hyperactivity of the muscles of mastication and judicious application of botulinum toxin to the affected muscles produced sufficient paralysis to arrest the parafunctional movements.

The use of botulinum toxin in the management of myofascial pain as in Case Three is well documented. The aim is that by temporarily and selectively weakening muscles which display 'trigger points' eliciting pain on palpation, the spasm and pain cycle is broken. This gives conservative measures such as a bite raising appliance or diet and stress modification an opportunity to have an impact (Borodic, 2001).

One important consideration when planning use of botulinum toxin is that nerve activity returns to normal over an 8 to 12-week period and so repeated applications are required in chronic conditions. The toxin is a foreign protein and the immune system treats it as such, sometimes developing neutralising antibodies (Brin, 1997). Although antibody formation is rare (BNF 2018), reduction in efficacy can be seen with repeated use of botulinum toxin.

There are a number of recognised side effects. Injection site reactions are common and include bruising, bleeding, pain, redness, swelling or infection. It is also common for influenza-like symptoms to be experienced. Excessive doses can cause paralysis in distant muscles and misplaced injections may paralyse nearby muscle groups other than the intended target (BNF 2018). Patients should be specifically warned of this risk when used in the head and neck as temporary facial asymmetry because partial or total loss of movement or muscle tone may result. Atrophy of the target muscle can also occur, but this is usually reversible if treatment is discontinued.

Rarely reported side effects include tingling, nausea and palpitations. These symptoms usually resolve within one to two days (Cote et al. 2005). Care should be taken when considering use in those with chronic respiratory disorders, dysphagia, neurological disorders or neuromuscular disorders as it is possible to exacerbate these conditions (BNF 2018).

Treatment is contraindicated if there is history of allergy to the toxin, or if there is infection at the proposed site of injection. Use should be avoided during pregnancy and lactation as Botulinum toxin it is currently a category C drug. This means safety during pregnancy is yet to be established (Huang et al. 2000). It has been reported that use in patients with myasthenia gravis can result in prolonged effects of the toxin beyond the usual 8-12 week period (Patel et al, 2011).

Alongside the well-known cosmetic purposes, use in the orofacial region is well described and highly effective. Successful treatment of mandibular spasm, bruxism, trigeminal neuralgia, pathologic clenching, chronic migraines and hypersalivation are reported (Srivastava et al. 2015).

Conclusion

In these cases, targeted use of botulinum toxin has proven a safe and effective adjunct to traditional management techniques in a variety of situations. The risks should be weighed against benefits. Consideration should be given to non-invasive interventions where possible. The cases were atypical and not adequately managed prior to administration of botulinum toxin. They emphasise the unique and effective therapeutic benefit of this drug and highlight uses in the management of pathology associated with abnormal facial muscle function.

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