Clinical Procedures

Botulinum toxin injections for cerebral palsy and post-stroke spasticity: an overview

Brent Mollon, Meds 2010

Introduction

Botulinum Toxin Type-A (BTX-A) has received much attention by both medical and non-medical individuals. Clinical preparations of BTX-A such as Botox® (Allergan Inc, Irvine, CA) are available for cosmetic use by family physicians providing additional education is obtained. When injected intramuscularly, this toxin prevents the release of acetylcholine from presynaptic vesicles in the neuromuscular junction, thus temporarily and reversibly blocking muscle fibres. This ultimately leads to weakened muscular contractions. Although commonly associated with cosmetics, BTX-A is becoming an accepted pharmacologic treatment for other conditions, as injections for focal spasticity secondary to upper motor neuron disorders such as cerebral palsy or stroke have been utilized in medicine for some time and have been covered by OHIP since 2003. Nonetheless, the evidenced based support for such treatments does not always extend as far as randomized controlled trials (RCTs). It is the purpose of this article to explore the techniques for administering BTX-A to treat spastic muscular conditions, specifically cerebral palsy or post-stroke, while also exploring the clinical evidence associated with their use.

Muscular Spasticity

Spasticity, one component of the upper motor neuron syndrome, has been previously defined by J.W. Lance as “a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon jerks resulting in hyper-excitability of the stretch reflex”. Physical trauma to the central nervous system, stroke, multiple sclerosis, cerebral palsy, and hereditary spastic paraparesis are all common causes of spasticity. As noted by O’Brien, spasticity can be viewed as having either ‘negative’ or ‘positive’ symptoms. Negative symptoms, such as loss of dexterity, decreased coordination, or muscle fatigue and weakness can be treated conservatively through physical therapy or living aids. On the other hand, positive symptoms such as hyperactivity, muscle spasm, exaggerated deep tendon reflexes and the persistence of primitive reflexes need to be treated conservatively through physical therapy or living aids. Thus, it is by addressing the positive symptoms of spasticity that BTX-A exerts its effects, aiming to reduce exaggerated or spastic muscle activity to help allow for stretching and antagonistic muscle activity. Physically, the aim of these injections is to restore balance to affected joints, while preventing contractures and bony deformities from forming. However, physicians should gauge clinical benefit by evaluating functional improvement, relief of symptoms (i.e. pain), decreasing the burden of care or facilitating other therapies (i.e. postponing surgical intervention in paediatric patients until the skeleton becomes more mature). Nonetheless, it is important to emphasize that pharmacotherapy must be combined with physiotherapy and other forms of conservative management (such as orthoses or casting) to achieve the best improvement of patient outcomes.

As noted above, clinicians must aim to restore functional deficit while mitigating negative side effects such as excessive muscle weakness when administering BTX-A for spasticity. Thus, the muscular target of the injection must be considered, the appropriate dose of toxin must be gauged, and accurate injection of BTX-A must be ensured. Physical exams should reveal the affected muscles, and dosing regimens have been developed to guide toxin use (see O’Brien for adult dosing by muscle). For children, total dose of toxin should be less than 400 units or 12 units/kg of body weight for BOTOX®, although significant heterogeneity exists within the literature regarding the units/kg/muscle used.

In terms of localizing the appropriate muscle for injection, anatomic knowledge and palpation is an accepted technique providing the muscle is large and subcutaneous, while the use of electromyographic guidance or electrical stimulation is seen as superior for smaller muscles like those in the forearm or hand due to improved accuracy over anatomic knowledge alone. However, the above techniques may require special training and can be painful to the patient, thus they are of limited use in paediatric populations.
BTX-A injections do not appear to be associated with any major side effects, with only focal weakness or nausea being reported more often in the BTX-A groups when compared to control. However, it is known that some patients (<1%) do not respond to BTX-A while up to 10% of patients may lose their response to therapy, potentially due to the production of neutralizing antibodies. Thus, it is recommended that physicians limit the doses to no more than once every 3 months while using the lowest effective dose possible. In the event a patient develops resistance to therapy, a clinician might consider switching botulinum toxin serotypes (i.e. BTX-A to BTX-B) as they are antigenically distinct.

Clinical Evidence

In adult populations, the majority of research has centered around post-stroke or multiple sclerosis patients. In post stroke populations, it is believed that BTX-A is effective at managing muscular tone. It is less clear if these decreases in tone translate into measurable clinical benefits for the patients. For example, of the six completed RCTs published in peer reviewed journals and listed in the Stroke Trials Registry (www.strokecenter.org), all four studies that gauge the impact of BTX-A injections on muscle tone/spasticity report statistically significant benefits in the intervention relative to the control group, although one study required 1500U doses to achieve significance and another did not report consistent results over time. Only three of the five studies examining functional improvements report significant results, of which two did not report consistent results over time (i.e. significance noted at weeks 1, 4 and 6 but not 8 and 12). Thus, while it appears studies are able to confirm the neurotoxic effect of BTX-A, the functional impact of this therapy is still uncertain.

In paediatric populations, BTX-A injections for spasticity is primarily provided to patients with spastic cerebral palsy, a population where BTX-A’s effects have been used since the early 1990s. The use of BTX-A for lower limb spasticity is generally accepted in the literature. For example, one recent RCT evaluating gastrocnemius BTX-A injections for spasticity noted a statistically significant decrease in spasticity at 8 weeks, an increase in dorsiflexion range and performance goals at 12 weeks, and an maximum voluntary torque and gross motor function at 24 weeks. However, despite measurable gains in performance, patients and their families were not significantly happier about their performance goals when compared to the placebo group. The impact of BTX-A injections on upper-limb spasticity is far less agreed upon, as a recent systematic review found that there is insufficient Level I evidence to support or refute its use to impact spasticity/tone, range of motion, or short to medium functional gains. Thus, it appears that the literature should continue to define the benefits of BTX-A for upper limb spasticity in CP, while also seeking to determine what therapies adjunctive to BTX-A injections will benefit CP outcomes.

Impressions

BTX-A as a pharmacotherapy appears capable of reducing spasticity in post-stroke and cerebral palsy patients. This therapy includes the alleviation of painful muscle spasms, along with postponing surgery in pediatric populations by preventing prolonged contractures which could deform a joint over time. Much heterogeneity exists regarding the muscles selected for injections, the dose of the injections and the means by which muscles are identified, which reflects the patient centered approach of this therapy. While evidence confirms BTX-A is able to reduce muscle tone or spasticity in these populations, the overall functional impact for the patient is still unclear.

References


