Botulinum toxin type A in the healing of chronic lesion following bilateral spasticity of gluteus muscle

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Abstract
Use of botulinum toxin is expanding as the clinical studies demonstrate new potential therapeutic applications. In rehabilitation, botulinum toxin is above all used as adjunct therapy for the treatment of spasticity, but it may prove useful for other atypical clinical situations. A 17-year-old man had a sub-arachnoid haemorrhage following the rupture of cerebral aneurism. The patient presented gluteus maximus and medius bilaterally spasticity that produced a chronic lesion in the intergluteal cleft, a flexed wrist and a flexed elbow. As treatment for this spasticity, a total of 100 U botulinum toxin type A were injected into the glutei muscles. This treatment allowed for application of topical medication and subsequently, chronic lesion healing. Botulinum toxin A may be an important therapeutic aid for clinicians faced with treating persistent pathological conditions caused by spasticity.

Introduction
The potential for a therapeutic use of botulinum toxin was first recognised by Justinus Kerner who in 1817 provided the earliest account of food-borne botulism (1). He correctly recognised that the toxin paralysed skeletal muscles and parasympathetic function, and proposed that botulinum toxin could be used as a therapeutic agent. In 1895, an investigation into an outbreak of food poisoning in Ellezelles, Belgium, led to the discovery of Clostridium botulinum and its toxin by van Ermengem (2). The most potent poison known (it can be lethal at doses as low as 0.05 mg), botulinum toxin has been feared as a possible biological weapon (3). It was not until the 1981 report of botulinum toxin injections into eye muscles to correct strabismus that the therapeutic potential of this agent became recognised (4). In 1989, after extensive laboratory and clinical testing of botulinum toxin type A (BotoxH, Allergan Inc, Irvine, CA), the Food and Drug Administration (FDA) approved it as a therapeutic agent in patients with strabismus, blepharospasm and other facial nerve disorders, including hemifacial spasm. In 2000, the FDA approved BotoxH and botulinum toxin type B (MyoblocTM, Elan Pharmaceuticals Inc, Morristown, NJ) as treatments for cervical dystonia, and Botox Cosmetic for the treatment of glabellar (frown) lines. Although its widest application is still in the treatment of disorders manifested by abnormal, excessive or inappropriate muscle contractions, its use is rapidly expanding to include treatment of a variety of ophthalmological, gastrointestinal, urological, orthopaedic, dermatological, secretory, painful and cosmetic disorders (5,6).

A new indication for BTX-A, as described in this case report, is in the treatment of a glutei muscles spasticity that had led to a chronic, untreatable ulcer. This treatment allowed for the healing of the ulcer in the intergluteal cleft.

Case report
A 20-year-old man presented with a lower limb spasticity (gluteus maximus and medius bilaterally spasticity) and deformities associated with upper limb spasticity, including a...
flexed wrist and a flexed elbow with the right arm and elbow held close to the chest.

The spasticity of glutei muscles produced a circular skin chronic lesion located in the intergluteal furrow (Figure 1). The lesion had slightly irregular borders, of $2 \times 3$ cm in diameters, 1 cm depth, hot to the touch, painful and characterised by erythematous periwound skin. Because of this glutei spasticity, all efforts in treating the ulcer by topical medication had failed. Treatment of spasticity, by injecting botulinum toxin inside the glutei muscles was attempted in order to reduce their contraction and to allow for medication of the lesion.

The gluteus maximus and medius bilaterally were treated with a total of 80–100 IU BTX-A (Figure 2).

A month from the first BTX-A treatment, the glutei contraction was reduced. It was then possible to apply topical products for the treatment of ulcer. A second infiltration with the same BTX-A dosage 100 IU was performed every 4 months to maintain weakness of glutei muscles and to promote complete healing of the lesion (Figure 3).

Discussion

Inappropriate muscle contraction often occurs after cerebrovascular events (stroke, cerebral palsy and head injury) (7). The rehabilitation of these patients involves a multidisciplinary approach (8). The present case history describes the successful use of BTX-A in the treatment of a chronic, untreatable lesion caused by a spasticity of glutei muscles resulting from a cerebral haemorrhage.

The use of BTX-A is increasing with the publishing of studies that demonstrate new clinical indications for the treatment of several muscle-contracted-based pathologies (9).

The therapeutic value of botulinum toxin derives from its ability to inhibit the release of acetylcholine from the presynaptic nerve terminal, causing local chemodenervation (10).

There are seven immunologically distinct toxins; types A and B have been studied most intensively and used most widely, but the basic pharmacology and clinical applications of other types of toxins, particularly C, D and F, are also being explored (11).

Synthesised as a single-chain polypeptide (molecular weight of 150 kDa), botulinum toxin has relatively little potency until it is cleaved by trypsin or bacterial enzymes into a heavy chain (100 kDa) and a light chain (50 kDa). Three-dimensional structure shows that the neurotoxins contain a binding domain (heavy chain), a catalytic domain (light chain) and a translocation domain (12). The action of botulinum toxin involves a four step process such as (1) high affinity, serotype-specific binding by the heavy chains to acceptors on presynaptic...
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precluded topical application of medication. However, the spasticity produced an intergluteal ulcer that did not heal following rehabilitation. In conclusion, BTX-A might be a useful adjunct in the treatment of gluteal spasticity that evokes difficult to treat pathological sequelae.

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