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Botulinum Toxin for Neurological Disorders in a Movement Disorders Clinic in Singapore

A K Y Tan

ABSTRACT

Aim of study: This study was done to examine the usefulness of botulinum toxin A injections in treating various neurological disorders such as hemifacial spasm, blepharospasm, focal dystonia and task-specific dystonia.

Methods: This was a prospective, open-labelled trial of patients seen in a Movement Disorders Clinic with dyskinesias potentially treatable with botulinum toxin. All patients were assessed before and after injections using clinical rating scales, and those with focal and task-specific dystonias were also recorded on videotape.

Results: There were 102 patients with hemifacial spasm, 3 with blepharospasm, 13 with neck dystonia, 6 with writer's cramp, 1 with musician's cramp, and 1 with jaw dystonia. All patients with hemifacial spasm and blepharospasm obtained good results, while 77% of those with cervical dystonia received substantial benefit. Only half of those with writer's cramp improved. Hemifacial spasm seems more prevalent in Singapore compared with Western populations.

Conclusion: Injections of botulinum toxin are useful in treating the various neurological disorders studied. This is an advancement in the treatment of these dyskinesias which respond poorly to oral medications.

Keywords: botulinum toxin, hemifacial spasm, focal dystonia, writer's cramp

INTRODUCTION

Botulinum toxin is produced by the bacterium *Clostridium botulinum*, the organism which causes food poisoning. There are seven immunologically distinct serotypes, but only types A, B, and E have been linked to botulism in humans[1]. It has become an established treatment for various neurological disorders such as blepharospasm, hemifacial spasm and neck dystonia, and shows promise in focal and task-specific limb dystonias, and spasticity following stroke or spinal cord lesions. We carried out a prospective open-labelled study to evaluate the efficacy of botulinum toxin injection in various disorders seen at our Parkinson's and Movement Disorders Clinic.

Department of Neurology
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433

A K Y Tan, MBBS, MRCP (UK), FAMS
Consultant

METHODS

Patient assessment

Patients with hemifacial spasm, blepharospasm, task-specific dystonias and torticollis/cervical dystonia were assessed and severity rated on a 0 to 4 scale (0 = no spasm; 1 = mild, barely noticeable; 2 = without functional impairment; 3 = moderate spasm, moderate functional impairment and 4 = severe, incapacitating spasm). Patients with writer's cramp were asked to write and draw Archimedes spirals. Those with torticollis, focal dystonia and task-specific dystonia were recorded on videotape before the botulinum toxin injections and again after two weeks.

All patients were reassessed two weeks after the injections. The improvement was rated again on a 0 – 4 scale (0 = no effect; 1 = mild improvement; 2 = moderate improvement, but no change in function; 3 = moderate improvement in severity and function and 4 = marked improvement in severity and function).

Injection technique

Botulinum toxin (Botox) as a freeze-dried lyophilised preparation was reconstituted with 0.9% sterile saline to a concentration of 2.5 U per 0.1 mL. The diluted solution was drawn into a tuberculin syringe for injection. The following dose schedule was used: 5 – 10 U for each eyelid, 5 U for each facial muscle such as levator labii superioris, temporalis, rissorius, submentalis, 25 – 100 U for neck or shoulder muscles, 10 – 25 U for each forearm muscle.

Patients with hemifacial spasm were seated and had their eyelids and eyebrows cleaned with alcohol, before the toxin was injected laterally and medially into the pretarsal orbicularis oculi. It is important to avoid the levator palbeprae and superior oblique to prevent ptosis and diplopia respectively. The other facial muscles such as levator labii, zygomaticus, rissorius, orbicularis oris and mentalis were also injected with the patient in a seated position.

Patients with torticollis (lateral rotation of the neck) had their ipsilateral trapezius and contralateral sternocleidomastoid injected while patients with retrocollis needed injections into both their splenius capitis muscles, trapezius muscles, and sometimes the deep paravertebral cervical muscles. Those with laterocollis has botulinum toxin injected into the ipsilateral splenius capitis,

trapezius and levator scapulae. We did not have any patient with anterocollis. For these neck muscles, the total dosage for each muscle was distributed into 3 – 4 sites for the larger muscles, and 1 – 2 sites for the smaller ones. Electromyogram (EMG) localisation was carried out in all these patients.

The muscles injected in patients with writer's cramp were determined by clinical examination, with the patient writing and drawing spirals. The forearm muscles were also palpated when the patients were writing, and the actively contracting muscles determined. The muscles involved were mostly the long flexor and extensor muscles of the fingers, and the wrist flexors and extensors.

RESULTS

In total, botulinum toxin was injected in 126 patients, of which, 102 had hemifacial spasm, 3 had blepharospasm, 13 had cervical dystonia, 6 had writer's cramp, 1 had musician's cramp, and 1 had jaw dystonia as a peak-dose complication of levodopa in Parkinson's disease (Tables I & II).

Table I – Types of movement disorders treated with botulinum toxin

Diagnosis	Number of patients Sex (M:F)	Mean age of onset	Range
Hemifacial	102 (1:1.3)	46.2	19 – 72
Blepharospasm	3 (1:2)	52.1	45 – 58
Cervical dystonia	13 (1:3.3)	43.2	23 – 68
Writer's cramp	6 (5:1)	42.5	38 – 58
Musician's cramp	1	24	
Jaw dystonia	1	63.5	

Table II – Injection doses and degree of response

		Percentage of improvement			
Diagnosis/muscles injected	Mean dose	Marked	Moderate	Mild	None
Hemifacial spasm	15.9	80.4	19.6	-	-
Orbicularis oculi	10.5				
Lower facial muscles	6.2				
Blepharospasm		100			
Orbicularis oculi (bilateral)	40.6				
Cervical dystonia	152.3	30.8	46.2	23.0	-
Trapezius	82.5				
Sternocleidomastoid	25.0				
Splenius capitis	50.6				
Levator scapulae	26.7				
Writer's cramp	52.6	16.7	33.3	-	50
Flexor carpi ulnaris	18.2				
Flexor pollicis longus	15.6				
Flexor digitorum profundus	12.1				
Flexor digitorum superficialis	13.2				
Extensor carpi ulnaris	20.1				
Extensor carpi radialis	19.3				
Extensor digitorum	14.8				
Extensor indicis	13.2				
Musician's cramp	20				100
Flexor pollicis longus	10				
Flexor digitorum superficialis	10				
Peak-dose jaw dystonia		100			
Masseters	50				

Eighty-two (80.4%) patients suffering from hemifacial spasm experienced a marked improvement. The injection dose ranged from 12.5 to 35.2 U (mean 15.9 U). All 3 patients with blepharospasm also experienced marked improvement of their spasms. The mean dose of botulinum toxin used was 40.6 U. Eight patients developed the complication of transient partial ptosis, which lasted a mean of 8.1 days. Nine patients had a slight facial weakness which was also transient. Five patients complained of eye irritation which was relieved with artificial tears.

Of the 13 patients with cervical dystonia, 9 patients had mainly lateral rotation, 3 had neck extension (retrocollis) and 1 had purely lateral tilt (laterocollis). The total dose of botulinum toxin used ranged from 100 – 200 U (mean 137.7 U) per patient. Four (30.8%) patients obtained a marked improvement, 6 (46.2%) a moderate improvement both in severity and function, and 3 (23.1 %) with only a mild improvement. Therefore, a total of 77% had substantial improvement of their neck dystonia. Three patients developed mild dysphagia after botulinum toxin injections and they were advised to consume soft food until the effect of the toxin wore off. Eight patients with cervical dystonia complained of significant neck pain before the injections. All 8 of them had improvement of neck pain after injection. Most of the patients had atrophy of their previously hypertrophied actively contracting muscles.

The 6 patients with writer's cramp were treated with botulinum toxin in doses ranging from 20 – 80 U (mean 35.3 U). One had marked improvement, 2 with moderate improvement, while 3 patients did not benefit at all from the injections in terms of their writing. These 6 patients had complained of pain in their forearm muscles, and these symptoms improved after botulinum toxin injection. Four patients complained of finger weakness which affected their grip slightly. The patient with musician's cramp (a guitarist), did not experience any response after the injection. The patient with levodopa peak-dose jaw dystonia improved significantly with botulinum toxin.

DISCUSSION

Oral medications such as anticholinergics, baclofen and benzodiazepines can offer patients with focal dyskinesias some symptomatic relief, but the majority failed to obtain satisfactory response. Patients with hemifacial spasm usually respond poorly to medications such as carbamazepine and benzodiazepines, and the only effective therapy before the advent of botulinum toxin was Jannetta's microvascular decompression of the facial nerve[2].

This prospective open-labelled trial confirms that botulinum toxin is highly effective in treating hemifacial spasm, blepharospasm and cervical dystonia, and provides a significant measure of benefit in writer's cramp, with few complications. The majority of patients with hemifacial spasm

obtained an excellent response with botulinum toxin. It is not known why there is such a high prevalence of hemifacial spasm in Singapore and Southeast Asia compared with the Western countries. A possible reason is that Southeast Asian people have a smaller body habitus and bony cranial structures, and the facial nerve is more liable to compression in the posterior cranial fossa.

All patients with blepharospasm and 77% of those with cervical dystonia benefitted substantially from the injections. Only half of those with writer's cramp benefitted from botulinum toxin. Results varied for writer's cramp from no objective improvement[3] to a high response rate of 83.5%[4]. Experience and skill in selecting involved forearm muscles probably accounted for the great difference in efficacy of botulinum toxin in writer's cramp and other focal task-specific dystonias.

Electromyographic guidance in writer's cramp is invaluable in the precise localisation of the small phalangeal muscles located in the forearm. In cervical dystonia, EMG may not be necessary. Some investigators have proposed a quantitative EMG method for determining the actively contracting muscles responsible for the dystonic spasms[5].

Side effects encountered with the use of botulinum toxin injections were few and transient. The most common complications were partial ptosis, mild facial weakness for hemifacial spasm; dysphagia in cervical dystonia; and grip weakness in writer's cramp. Muscle atrophy was clinically evident in the hypertrophied neck muscles in cervical dystonia. This chemical denervation occurred because botulinum toxin was internalised in the presynaptic terminal and cleaved various synaptosomal membrane-associated proteins, thereby preventing the fusion and release of acetylcholine vesicles[6]. Muscle atrophy usually reverses after 3 – 6 months.

Injections of botulinum toxin should be administered only by clinicians with a thorough knowledge of the physiologic and clinical effects of the toxin. Being familiar with the local anatomy is essential to ensure proper and safe administration. When indicated, botulinum toxin adds significantly to the treatment options of a movement disorder neurologist.

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