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Review

Botulinum toxin: Clinical use

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Abstract

Since its development for the use of blepharospasm and strabismus more than 2.5 decades ago, botulinum neurotoxin (BoNT) has become a versatile drug in various fields of medicine. It is the standard of care in different disorders such as cervical dystonia, hemifacial spasm, focal spasticity, hyperhidrosis, ophthalmological and otolaryngeal disorders. It has also found widespread use in cosmetic applications. Many other indications are currently under investigation, including gastroenterologic and urologic indications, analgesic management and migraine. This paper is an extensive review of the spectrum of BoNT clinical applications.

Keywords: Botulinum toxin; Dystonia; Blepharospasm; Cervical dystonia; Spasmodic dysphonia; Writer's cramp; Oromandibular dystonia; Tourette's syndrome; Spasticity; Hyperhydrosis; Cosmetic; Hyperreflexive bladder; Detrusor sphincter dyssynergia; Urethrism; Achalasia; Anal fissure; Levator ani syndrome; Pain; Parkinson's disease; Headache

Contents

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0. Introduction

In 1897, Emile van Ermengem investigated an epidemic in Ellezelles, Belgium, where several people who had gathered at a funeral music festival developed botulism after consuming raw ham [1]. After isolating the bacteria from the ham, van Ermengem produced the disease in laboratory animals by injecting the toxin produced by the organism. Botulism can develop not only from ingestion of foods, but also as intestinal colonization in infants or, rarely, adults. Wound botulism or inadvertent botulism has also been documented. Inadvertent botulism has been reported in patients treated with intramuscular injections of botulinum neurotoxin (BoNT), even in therapeutic doses or doses below the maximum recommended doses [2,3]. In these reports, patients demonstrated moderate to marked clinical weakness, autonomic nervous system effects or electrophysiological abnormalities consistent with botulism [4].

In the late 1970s, the toxin was introduced as therapeutic agent for the treatment of strabismus [5]. Since then, its therapeutic applications have expanded into many different fields, often with innovative treatments and surprising results.

1. Preparations

A number of botulinum toxin preparations have been approved in different countries. Currently, there are five different botulinum toxins available on the market in one or more countries. Four of them contain BoNT serotype A (Botox®, Dysport®, Xeomin® and CBTXA) and the other contains BoNT type B (Myobloc®/NeuroBloc®). Approval procedures are very complex and vary from preparation to preparation and from country to country. CBTXA is currently available only in China and there is little information about this product. Xeomin® was recently approved in Germany. The only approved BoNT/B preparation (Myobloc®/NeuroBloc®) has only been licensed for cervical dystonia (CD), and only in a few countries. Its use is limited to patients who develop neutralizing antibodies to BoNT/A preparations. Botox® has garnered the most approvals worldwide, followed by Dysport®, although Dysport® is not yet licensed in the US.

Doses of BoNT used for the treatment vary depending on the particular brand of toxin used. Although two of the widely available products contain type A (Botox® and Dysport®), a unit of one product is not the same as a unit of the other. Various studies put the dose ratio (Botox®). Dysport® differently, with many in the range of 1:3 to 1:5 [6–9]. At the 1:3 ratio, Dysport has an adverse event profile different from Botox® [8]. The dose ratio for Botox®:Xeomin® is estimated as 1:1 [10]; however, the US type A product (Botox®) is estimated to be about 50 times more potent than the type B product [11–13]. It is therefore important to remember that the dose given for any particular toxin refers only to that particular preparation and does not readily transfer to doses of other products, even if they are of the same