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REVIEW ARTICLE

Toxin yet not toxic: Botulinum toxin in dentistry

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Abstract Paracelsus contrasted poisons from nonpoisons, stating that "All things are poisons, and there is nothing that is harmless; the dose alone decides that something is a poison". Living organisms, such as plants, animals, and microorganisms, constitute a huge source of pharmaceutically useful medicines and toxins. Depending on their source, toxins can be categorized as phytotoxins, mycotoxins, or zootoxins, which include venoms and bacterial toxins. Any toxin can be harmful or beneficial. Within the last 100 years, the perception of botulinum neurotoxin (BTX) has evolved from that of a poison to a versatile clinical agent with various uses. BTX plays a key role in the management of many orofacial and dental disorders. Its indications are rapidly expanding, with ongoing trials for further applications. However, despite its clinical use, what BTX specifically does in each condition is still not clear. The main aim of this review is to describe some of the unclear aspects of this potentially useful agent, with a focus on the current research in dentistry.

Contents

Abbreviations: BTX, botulinum neurotoxin; SNARE, soluble N-ethylmaleimide-sensitive factor attachment protein receptor; SNAP-25, synaptosomal-associated protein; MPDS, myofacial pain dysfunction syndrome; EMG, electromyography; TGF-β1, transforming growth factor β-1

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1. Introduction

Botulinum neurotoxin (BTX) is a neurotoxic protein produced by the Gram-positive, rod-shaped, spore-forming, and strictly anaerobic bacterium *Clostridium botulinum* and, rarely, by *Clostridium butyricum* and *Clostridium baratii*, commonly found on plants and in soil, water, and animal intestinal tracts. Although once considered lethal, BTX is now used as a therapeutic drug. BTX exhibits transient, nondestructive, dose-dependent, and localized actions, with minimal systemic side effects (Marchese et al., 2008), underlying its wide use in various orofacial and dental disorders. The exact mechanism of action, dosage, and delivery procedure of BTX are very important. In addition to conditions for which BTX is currently used as a therapeutic agent, evidence supports the expansion of its indications in dentistry. The purpose of this review is to provide insights into the current indications of BTX, highlight its expanding use, and review recent advances in the use of BTX in dentistry.

2. Sites and modes of action of BTX

Modes of action of BTX are summarized in Table 1 (Muthane and Panikar, 2003). BTX induces muscle weakness by inhibiting transmission of alpha motorneurons at the neuromuscular junction. Release of acetylcholine (ACh) is mediated by the assembly of synaptic fusion complexes—a set of soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins, including synaptobrevin, synaptosomal-associated protein (SNAP), and syntaxin. Seven BTX serotypes have been identified. BTX types B, D, F, and G cleave synaptobrevin; types A, C, and E cleave SNAP-25; and type C cleaves syntaxin (Kant et al., 2009; Davis, 1993).

2.1. Forms of BTX

Commercially available various forms of BTX are summarized in Table 2 (Rao et al., 2011). Forms of BTX range in weight

Table 1 Action of botulinum toxin.

Absorption via the GI tract or through tissue
↓
Reaches the lymphatic channels and the blood stream
↓
Circulates in the blood until it reaches cholinergic synapses
↓
Binds with the help of binding domain
↓
Cholinergic neuronal cell membrane at nerve terminal
↓
Enters neuron by endocytosis
↓ light chain of the toxin
Crosses the membrane of the endocytic vesicle
↓
Enters cytoplasm of the pre synaptic terminal
↓ cleaves to sites on SNARE proteins
Prevents assembly of synaptic fusion complex
↓
Blocks docking, fusion and acetylcholine release