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Toxin to Treatment; A Narrative Review of Botulinum Toxin Applications in Dentistry

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Abstract

The integration of Botulinum Toxin in treatment plans has become very essential in the field of dentistry. The purpose of this review is to examine the different numerous uses of Botulinum Toxin in the dental field. Data was obtained with keywords "Botulinum Toxin", "Botox"," Gummy Smile"," "Bruxism". A Literature search was conducted using PubMed, Scopus databases, and Google Scholar. A total of 122 published articles , including case reports, case series, observational and interventional clinical trials, and systematic reviews were included in this narrative review after reviewing the literature and including the relevant studies. Botulinum Toxin could be used as an adjunct treatment or as a treatment for; Bruxism, Facial Palsy, chronic facial pain, Excessive Gingival display, papilla reconstruction, salivary gland hypersecretion, TMJ disorders, some Maxillofacial traumas and with cancer treatments. Botulinum Toxin has given dentists a less invasive treatment modality for several conditions; however, dentists should make sure they have the full knowledge and expertise before incorporating botulinum toxin in their treatment plans.

1. Introduction

The journey of Botulinum Toxin from being a deadly poison to a prolific treatment has introduced a range of less invasive treatment options in the field of dentistry. The first well-documented incident of botulism food poisoning was about a century before it's discovery, when residents ingested improperly preserved meat and blood sausages that caused countless deaths throughout the kingdom of Württemberg in Southwestern Germany. The district medical officer Justinus Kerner (1786–1862), a well-known German poet, published the first accurate and complete description of the symptoms of botulism between 1817 and 1822, hypothesizing that a biological poison caused the intoxication [1]. Kerner was able to extract the toxin from infected sausages and use it in animal models displaying that it could cause paralysis of skeletal muscles and loss of parasympathetic function which led him to hypothesize in his reports that the toxin might be used for treatment of strabismus and hypersalivation in the future [2]. Kerner's vision was correct however it didn't come to pass until the late 20th century. Some reports of "Atropa belladonna" were reported in old medical literature much before the 18th century, but when examined by modern scientists and physicians, they concluded that the records were probably cases of food-borne botulism,

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because the described combination of dilated pupils and fatal muscle paralysis without clouding of consciousness cannot be attributed to atropine intoxication [3-7].

In 1895, an outbreak of botulism in a small Belgian village called Ellezelles the pathogen ''Clostridium botulinum'', a neurotoxin producing, rod-shaped, gram-positive bacterium was discovered by Emile Pierre van Ermengem. The bacterium was given that name because of its association with the sausages (Botulus means sausage in Latin) [5]. In 1944, Edward Schantz was able to culture Clostridium botulinum, isolate the toxin, and develop a bulk purification system for the toxin .In 1949, Arnold Burgen discovered that the neurotoxin produced by Clostridium botulinum' inhibits release of acetylcholine which is a neurotransmitter responsible for muscle contraction, thus inducing decreased muscle tone and causing symptoms such as diplopia, bulbar weakness, dysphonia, dysarthria ,dry mouth , generalized muscle weakness ,respiratory failure and death [6,8]. lan B. Scott and Edward J.Schantz pioneered modern botulinum toxin treatment in medicine with use of type-A serotype Botulinum Toxin to correct strabismus (Squint)[9,10]. This strain of botulinum Toxin was approved by the US Food & Drug administration in 1989 under the trade name – Botox (Allergan, Inc, Irvine, Calif) mainly to treat hemifacial spasms, strabismus , and blepharospasm .Type B was approved by the FDA to treat cervical dystonia in 2000 . Botulinum injections to treat severe frown lines between the eyebrows (glabellar lines) were approved in 2002. Over the years, Botulinum toxin was used to treat a wide variety of conditions associated with muscular hyperactivity, glandular hypersecretions and pain [6,11-14].

There are seven types of Botulinum Toxin from A to G of which only BT type A (BTA) and BT type B (BTB) are commercially available [15]. Botulinum toxin causes a dose-dependent temporary flaccid muscle paralysis in the injected muscle through inhibition of Acetylcholine production; however, neuromuscular transmission is re-established within 3-6 months by emergent new axonal terminals. Treatment with botulinum is considered a temporary treatment not a definitive curative option. The toxin also prevents acetylcholine release at parasympathetic nerve terminals [15,16]. Recently Botulinum toxin was introduced in the dental field by Polo in 2005 to treat excessive gingival display, since then many uses have been utilized in the field of dentistry [17].

2. Review of Literature

2.1 Excessive Gingival Display:

With the introduction of Botulinum toxin in the field of dentistry, a more conservative and immediate nonsurgical treatment modality became available for excessive gingival display. In cases of excessive gingival display due to hyper mobility of the muscle, injecting the overactive muscles with measured quantities of botulinum toxin can result in a decrease of muscle activity relaxing the lip muscles and decreasing upward pull on the lip thus reducing the excessive gingival display [18]. Usually an average of 5 units of botulinum toxin A is injected superficially just lateral to the nasal alar cartilage, at a point where levator labii superioris, levator labii superioris alaeque nasi and zygomaticus minor muscles converge together [19,20]. Botulinum toxin type A is known to be the most effective botulinum toxin in treatment of excessive gingival display [21,22].

The improvement achieved with botulinum toxin is almost immediate but lasts only for a period of 3–6 months, before slowly fading away[10]. This relatively short duration is the major disadvantage of this technique in management of excessive gingival display, necessitating constant reapplication. Moreover, the short- and long-term effects of injecting Botulinum toxin into the tissues have not been adequately researched. A Systematic review and meta-analysis by Zengiski et al., 2021 found a mean decrease of 3.42 mm of gingival display, with maximum effect reached after 2 weeks, persisting effect for up to 12 weeks & increased gingival display values at 24 weeks but a return to initial values after approximately 29 weeks [23].

When compared to other techniques described in literature, some authors stated that Botulinum toxin might be considered the gold standard for the treatment of excessive gingival display caused by hypermobile or short lip because it is less invasive, has minimal side effects when used in small doses, and shows immediate effects after application [17,23,24]. Botulinum toxin is indicated for excessive gingival display caused by hyperactive upper lip muscles, short lip, and as a form of masking for minor vertical maxillary excess cases that refuse to undergo orthognathic surgery. Moreover, Botulinum toxin may be used alone or in conjunction with hyaluronic acid fillers, and the combination may be more effective in reducing excessive gingival display [25]. Despite being considered safe and effective, a review by Bellows and Jankovic, 2019 reported production of antibodies that impair the effect of botulinum toxin mainly with short intervals between doses, and use of higher doses [26].

The greatest pitfall of Botulinum toxin treatment of excessive gingival display is that it has a reversible effect & hence must be repeated to maintain results [27].Despite this disadvantage, a randomized controlled trial performed by Hexsel et al., 2021 evaluated patient satisfaction with botulinum toxin treatment of excessive gingival display as a secondary outcome, and found that even after 12 weeks, 80% of patients were satisfied or very satisfied with the treatment, that they would like to repeat the treatment again [28].

2.2 Temporomandibular disorders

Botulinum Toxin was found to be effective in resolving pain and tenderness in temporomandibular joint disorders that have a myofascial component. The toxin is now used as an adjunct in managing temporomandibular joint disorders, particularly in cases involving muscular hyperactivity, bruxism and psychomotor component [29-34].Conditions treated by Botulinum Toxin injections include ; Bruxism and clenching, myofascial pain, trismus, masseter and temporalis hypertrophy,

and chronic headaches [30,35- 37].

Up till now, there is no consensus on the specific treatment protocol or the precise amount of injected material but, Botulinum Toxin significantly decreased pain, improve function and mouth opening with intramuscular injection into temporalis and masseter muscles. The toxin has also been used in patients suffering from recurrent mandibular dislocations by injection into lateral pterygoid muscle and has shown effective results in reducing the occurrence of mandibular dislocation [38-42].

Some clinicians inject Botulinum toxin in muscles post-orthodontic treatment to prevent relapse that may occur in patients with strong muscle activity such as that of mentalis muscle. Botulinum toxin can be used to reduce the intensity of muscle contractions and then gradually the muscles are trained post-treatment to a more physiologic movement [24,,13].

Botulinum Toxin has shown success when used as an adjunct to the treatment of bruxism [43-46] .Interestingly some authors suggested the prophylactic use of Botulinum toxin injection into the muscles of mastication when placing implants to decrease the load on implants and guarantee uninterrupted osseointegration, particularly in cases of basal or zygomatic implants in severe bone atrophy and in cases that are immediately loaded [47-49] or post periodontal surgeries to decrease the load on treated area[50]. Botulinum toxin injections for muscles were also suggested to be used in edentulous patients struggling to adapt to a new set of dentures, especially patients who have been edentulous for a long period of time, to correct irregular and uncoordinated muscle activity [51,52]. Botulinum Toxin can be used to manage muscle hypertrophy of Temporalis and Masseter muscle and the associated chronic facial pain due to masticatory hyperactivity or parafunctional habits. Injection sites are identified by palpation during clenching and the thickest part of the muscle is injected percutaneously [54- 58].

Botulinum Toxin can be used as adjunct in Prosthetic Rehabilitation in Bruxer patients. Bruxism, poses significant challenges particularly for patients with removable dentures. To accurately diagnose bruxism, participants must exhibit at least one sign or symptom defined by the American Academy of Sleep Medicine [59,60]. The diagnosis can be further supported by the use of an ambulatory electromyography and electrocardiographic, which records sleep bruxism events per hour. This device correlates well with findings from polysomnography, the gold standard for diagnosing sleep bruxism [61]. Participants are instructed to place the device electrodes on their bodies before bed [62] and a specific software program is used for automatic evaluation. Additionally, bruxers with overdentures are questioned about how often they wear their overdentures, particularly during sleep, and their overdentures are examined for signs of wear on artificial teeth [63].

Bruxism is associated with reduced patient satisfaction and impaired sleep quality. For patients with implant-supported or tooth-supported overdentures, removing the denture during sleep can result in loss of retention and increased wear on attachments due to contact with the opposing arch [64,65]. Although the traditional practice of removing overdentures at night is intended to allow time for tissue rest, it may unintentionally lead to harmful contact between attachments and opposing teeth, soft tissues, or prostheses in bruxers. This contact can cause discomfort and may result in wear or damage to teeth, implants, or attachment components [66- 68]. Effective management of bruxism is crucial, especially for overdenture wearers, as it increases the risk of mechanical and technical complications [62,66,68-70].

Various treatment options for bruxism exist, including physical therapy, behavioral management, and occlusal splints. However, these modalities often lack consistent effectiveness and can introduce undesirable side effects [71-75]. Occlusal splints are commonly used to manage the harmful effects of sleep bruxism, but they do not provide definitive solutions and are limited by issues of patient compliance and fabrication complications [76-80].

Botulinum Toxin injection offers a promising alternative by reducing muscle contraction through the interruption of acetylcholine neurotransmission. Studies have indicated that Botulinum Toxin therapy may effectively treat sleep bruxism [44, 81]. A significant advantage is its ability to function independently of patient compliance, providing a sustained effect for up to 24 hours. Despite concerns regarding injection-related complications, such as facial asymmetry and reduced chewing power [82, 83], the therapeutic potential of Botulinum Toxin remains compelling.

2.3 Drooping of Corners of Mouth

Hyperactivity of depressor anguli oris can lead to drooping of the corner of the mouth. Injection of Botulinum Toxin has shown positive results in such cases [84]. The site of injection is on the trajectory of nasolabial fold to the jaw line. Facial palsy causing facial asymmetry due to weakening of facial muscles can also be corrected by botulinum toxin injection on the unaffected side to weaken it and restore facial symmetry [85].

2.4 Black triangles/Papilla Reconstruction

Recently, Botulinum Toxin has been used in conjunction with hyaluronic acid or other dermal fillers to provide immediate volume to black triangles formed due to loss or inadequate interpapillary tissue by direct injection into the interdental tissues [86, 87 ,88]. However further research is needed in this area to develop exact treatment protocols, and establish more consistent results.

2.5 Sialorrhea

Excessive salivation/drooling known as sialorrhea is a common problem caused by poor oral and facial muscle control. Treatment options before the introduction of botulinum toxin ranged from a medication to surgery. Botulinum toxin has shown success in controlling excessive salivation when injected into

parotid and submandibular glands. A reduction in salivary flow is observed within 4 weeks of injection, however, the effects last for about 3 months, and injections must be repeated afterward to maintain results. Better results were reported with repeated treatments than with the first treatment. Botulinum toxin is also effective in managing gustatory sweating; facial flushing and excessive sweating after smelling or eating certain foods (Frey's syndrome) [89-98].

2.6 Oral and Maxillofacial Trauma

Botulinum Toxin is often used to treat injuries of the maxillofacial bones including maxilla, mandible, zygoma, nasal bone, and orbital bone. Temporary paralysis by Botulinum toxin injection in masseter muscles allows for fewer mini plates/microplates in the treatment of zygomatic fractures [99]. Botulinum toxin use in the management of condylar fracture has also been recommended in various reports [100,101]. Botulinum toxin injections in the anterior belly of the digastric muscle have shown success in the correction of post-traumatic anterior open bite [102].

2.7 Head & Neck Cancers

Botulinum toxin injections can improve movement disorders after major reconstructive surgery in patients with cancers of the parotid gland and can be used as palliative care for severe pain. The use of Botulinum toxin helps improve the quality of life of patients with head and neck cancers of different etiologies with minimal side effects [40,103]. Botulinum toxin is sometimes used as an adjunctive treatment to potentiate the effect of anti-cancer radiotherapy or chemotherapy. More superior results were reported when the patient was given Botulinum toxin injection 3 days before start of cancer treatment regimen [104].At first injections were administered to reduce pain associated with radiotherapy, chemotherapy, or surgical treatment of cancers; they also have shown effectiveness in cases of salivary gland tumors to alleviate associated fistula, gustatory sweating, gustatory hyperhidrosis, functional hypersalivation, sialorrhea,& sialocele[103,105-111] .In addition, some studies have reported that the toxin briefly opens tumor vessels, allowing a chance for more effective destruction of cancer cells by radiotherapy and chemotherapy thus increasing their efficacy [104 ,112-114].

2.8 Possible Applications in Odontogenic Pain

Pain that first presents as dental pain, oftentimes turns out to be nonodontogenic pain from surrounding muscles, joints, maxillary sinuses, or cranial nerves (trigeminal nerve particularly). Furthermore, nonodontogenic pain sometimes occurs simultaneously with odontogenic pain which puts the clinician in a very puzzling situation[115- 118]. Additionally, dental treatment, particularly root canal is known to cause flare up of some chronic nonodontogenic conditions. Use of Botulinum toxin as an adjunct post-root canal has shown some success in reducing postoperative discomfort, especially if there is another causative of facial pain present as well. When about 3700 Endodontists were asked a little over 50% of them saw that Botulinum Toxin was useful when nonodontogenic pain conditions overlapped with endodontic pain ; however ,nearly 60% agreed when asked if the toxin improved patient satisfaction , and whether it should be included in residency training and about 65% estimated that more endodontists will be using Botulinum Toxin as an adjunct treatment in the future [113,114,119- 121] .Better outcomes were reported with Botulinum toxin treatment in cases of Atypical Odontalgia (Phantom Tooth Syndrome) and persistent dentoalveolar pain [122].

3.Conclusion

The use of Botulinum toxin as a therapeutic agent has broadened the prospects of dentistry; whether as a treatment for minor cases or as an adjunct to other treatments in more complex cases. Botulinum toxin provides a minimally invasive approach with minor side effects; its only disadvantage is the need for repeated treatments every 3 months to maintain results. Treating dentist must be sure that he/she has the full knowledge regarding the use of Botulinum toxin and be ready to deal with any possible complication before using it with his/her patients. Future research should assess the possibility of long-acting Botulinum Toxin that lasts more than 3-6 months.

Authors' Contributions

LA: conception and design of the study; data acquisition and analysis; interpretation of data; manuscript draft and revision; personal accountability NZ: conception and design of the study; data acquisition and analysis; interpretation of data; manuscript draft and revision; personal accountability, DE: data acquisition, revision of the manuscript. All authors reviewed and approved the manuscript.

Conflict of interest

The authors declare that they hold no competing interests.

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