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CLINICAL USE OF BOTULINUM TOXINS IN ORAL AND MAXILLOFACIAL SURGERY

ORAL VE MAKSİLLOFASİYAL CERRAHİDE BOTULINUM TOKSİNLERİN KULLANIMI

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Abstract

Botulinum toxin (BTX), widely recognized as Botox, is generated by the gram-positive anaerobic bacterium Clostridium botulinum. The administration of BTX toxin has become one of the most prevalent cosmetic procedures worldwide. Over the past three decades, the clinical applications of BTX have expanded markedly, with numerous novel indications emerging. Primarily, botulinum toxin A (BTX-A) has been employed in the management of temporomandibular joint disorders (TMD) and in addressing the hypertrophy and hyperactivity of masticatory muscles, thereby facilitating pain relief and functional recovery following dental and oral-maxillofacial surgical interventions. Moreover, BTA is extensively utilized for cosmetic purposes, including the reduction of facial wrinkles and asymmetries. Although the therapeutic effects of BTA are temporary and generally considered safe, a comprehensive understanding of the relevant anatomical structures, as well as the potential systemic and local adverse effects associated with its facial applications, is essential. This article presents a thorough literature review detailing the historical development of BTX, its structural characteristics and mechanisms of action, available market formulations, guidelines for dilution and storage, toxicity considerations, indications and contraindications, the potential for resistance development, and its applications in dentistry and oral-maxillofacial surgery, accompanied by a discussion of associated side effects.

Keywords: *Botulinum toxin; dentistry; oral and maxillofacial surgery.*

Özet

Botulinum toksini (BTX), yaygın olarak Botox olarak bilinir, gram-pozitif anaerobik bakteri Clostridium botulinum'dan üretilir. Botulinum toksini enjeksiyonları, dünya genelinde en yaygın uygulanan kozmetik prosedürlerden biridir. Son otuz yılda, botulinum toksininin klinik uygulamaları önemli ölçüde genişlemiş ve birçok yeni alan bildirilmiştir. Öncelikle, botulinum toksini A, temporomandibular eklem bozukluklarının (TME) yönetiminde ve çiğneme kaslarının hipertrofisi ve hiperaktivitesinin tedavisinde kullanılmış, dental ve oral ve maksillofasiyal cerrahi sonrası ağrı semptomlarının yönetiminde ve fonksiyonel iyileşme sağlamak için terapötik bir müdahale olarak hizmet etmiştir. Ayrıca yüz kırışıklıklarının ve asimetrilerin azaltılması gibi kozmetik amaçlarla yaygın bir şekilde kullanılmaktadır. Botulinum toksinin terapötik etkileri geçici ve genel olarak güvenli olarak kabul edilse de, bu ajanın yüz uygulamaları ile ilişkili potansiyel sistemik ve lokal yan etkilerinin bilinmesi, ilgili anatomik yapılar hakkında kapsamlı bir bilgiye sahip olunması önemlidir. Bu makale, botulinum toksininin tarihi gelişimi, yapısal özellikleri ve etki mekanizması, mevcut formülasyonları, seyreltme ve depolama yöntemleri, toksisitesi, endikasyon ve kontraendikasyonları ile diş hekimliği ve oral ve maksillofasiyal cerrahide uygulama alanları ve yan etkileri hakkında kapsamlı bir literatür incelemesi sunmaktadır.

Anahtar Kelimeler: *Botulinum toksini; diş hekimliği; ağız, diş ve çene cerrahisi.*

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OVERVIEW / GENEL BAKIŞ

Introduction and History of Medical Use of Botulinum Toxin (BTX)

Botulism derives its nomenclature from the Latin term "botulus," signifying "black sausage," and pertains to food poisoning resulting from the consumption of decomposed meats harboring the neurotoxin produced by the rod-shaped, gram-positive bacterium Clostridium botulinum. Purified botulinum toxin (BTX) was the inaugural bacterial toxin utilized as a therapeutic agent. Over the past 30 years, its application in clinical settings has expanded significantly, establishing it as a versatile drug across various medical fields (1). Historical accounts reveal that BTX poisoning has long impacted humanity; however, the first documented case of foodborne botulism emerged only in the 18th century, linked to the consumption of contaminated meat and blood sausages in the Kingdom of Württemberg, Southwest Germany. Between 1817 and 1822, Justinus Kerner (1786-1862), a regional medical officer of health and notable German poet, provided the first comprehensive descriptions of foodborne botulism symptoms, attributing the poisoning to a biological toxin. Kerner also proposed the therapeutic potential of this toxin. In 1895, a botulism outbreak in the small Belgian village of Ellezelles resulted in the identification of Clostridium botulinum by Emile Pierre van Ermengem. The modern therapeutic application of botulinum toxin (BTX) was pioneered in the early 1970s by Alan B. Scott and Edward J. Schantz, who initially employed the type A serotype for the correction of strabismus. Subsequently, various preparations of type A toxin have been developed and manufactured in the United Kingdom, Germany, and China, while the therapeutic type B toxin is produced in the United States. Currently, BTX is utilized to address a wide range of disorders associated with muscular hyperactivity, glandular hypersecretion, and pain (2).

Structure and Types of Toxin

Neurotoxins synthesized by *Clostridium botulinum*, a Gram-positive anaerobic bacterium, are recognized as some of the most powerful toxins known to humanity and are the primary agents responsible for botulism. Botulinum toxin (BTX) operates by inhibiting the release of acetylcholine from the presynaptic terminal at the neuromuscular junction (3). To date, researchers have identified seven distinct antigenic botulinum toxins—BTX-A, B, C, D, E, F, and G—each produced by various strains of the bacterium. The human nervous system exhibits sensitivity to five of these serotypes (BTX-A, B, E, F, and G), while two others (BTX-C and D) do not affect it (4).

While BTX-A and BTX-B spores are heat-stable, the neurotoxin itself is not. Additionally, the toxin is alkaline-intolerant but acid-stable, meaning it does not break down under acidic conditions (5). Both BTX-A and BTX-B have clinical applications, with therapeutic effects achieved by adjusting their concentrations. The most commonly used BTX-A products include BOTOX® (Allergan, Inc., Irvine, CA, USA) and Dysport® (Ipsen Ltd., Maidenhead, Berkshire, UK), while MYOBLOC® is the

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primary formulation for BTX-B (Elan Pharmaceuticals, Inc., South San Francisco, CA, USA). MYOBLOC®, unlike BTX-A, is available in solution form and is primarily utilized in neurology. BOTOX® and Dysport® are supplied as white powders and must be diluted prior to use. Given its strength, BOTOX® is 3 to 6 times and 50 to 100 times more effective than equivalent doses of Dysport® and MYOBLOC®, respectively, highlighting the importance of meticulous dose selection based on the specific product employed (6).

Mechanism of Action

Different serotypes of BTX exhibit varying toxicities, durations of action, and potencies; however, all effectively inhibit acetylcholine release at the neuromuscular junction (NMJ). While high doses may affect autonomic cholinergic ganglia, therapeutic doses are generally not associated with significant adverse effects on autonomic functions, making BTX a safe option for various medical and cosmetic applications (7).

BTX causes muscular paralysis at the NMJ by blocking the calcium-mediated release of acetylcholine, a neurotransmitter essential for muscle contraction. Upon injection, the heavy chain of BTX binds to presynaptic cholinergic motor nerve terminals and enters the neuron through endocytosis. Inside the neuron, the light chain is released from the endosome into the cytoplasm, where it cleaves synaptosome-associated protein of 25 kDa (SNAP-25). This cleavage disrupts the process of acetylcholine exocytosis, preventing its release from presynaptic nerve fibers and inhibiting the depolarization of postsynaptic terminals, leading to muscular relaxation. Crucially, BTX does not impede the synthesis of acetylcholine; thus, motor function can ultimately be restored as the nerve terminals undergo regeneration. This recovery transpires through the growth of new axons at the motor end plate, which enables the reestablishment of neuromuscular transmission (8). The neurotoxic process involves three key steps (9,10):

1. **Binding:** The process begins with the irreversible binding of BTX to presynaptic cholinergic receptors via the heavy chain's 50-kD carboxy-terminal. While distinct receptors for different BTX serotypes have been suggested, recent findings indicate that a conserved protein, synaptotagmin, binds to multiple serotypes, including BTX-A, BTX-B, and BTX-E (11,12).

2. **Internalization:** The second step is the internalization of the neurotoxin via receptor-mediated endocytosis. This process is calcium-independent and partially reliant on nerve stimulation. Following internalization, a disulfide bond is cleaved, allowing the heavy chain to facilitate the translocation of the light chain into the neuronal cytoplasm (13,14).

3. **Neuromuscular Blockade:** The final step involves neuromuscular blockade, during which protein isoforms in the synapse create a platform necessary for the docking, fusion, and release of acetylcholine vesicles. The light chain, equipped with zinc-endopeptidase activity, cleaves a specific

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protein isoform, disrupting neurotransmitter release. Notably, BTX-C cleaves two proteins instead of one (15).

Clinically, the effects of BTX typically become noticeable within 3 to 7 days after administration, with maximum effects usually observed 1 to 2 weeks post-injection. After reaching this peak, the effects gradually level off and eventually resolve as full nerve recovery occurs over a period of approximately 3 to 6 months, with recovery often expected around the 3-month mark (16).

Contraindications and Complications

BTX is generally considered safe when administered correctly, with appropriate technique and dosage. Nevertheless, infrequent localized side effects may occur, including pain, infection, bruising, inflammation, edema, loss of muscle strength, nerve palsy, and hematoma. Inadequate injection techniques can lead to complications such as asymmetrical smiles and challenges in speech, chewing, or drinking. Furthermore, excessive administration may cause drooping (ptosis) of the lip, which can hinder the visibility of teeth when smiling broadly (17).

Systemic complications primarily arise from an overdose of BTX-A injections and may manifest as nausea, fatigue, malaise, flu-like symptoms (such as fever and chills), increased blood pressure, diarrhea, abdominal pain, and, in some cases, anaphylaxis due to allergic reactions (26).

To prevent the development of antibodies against the toxin, it is crucial not to administer BTX injections before the effects have completely worn off, as this can lead to unsatisfactory results in the future. BTX is contraindicated for certain individuals, including pregnant or lactating women, patients with neuromuscular disorders (such as Lambert-Eaton syndrome and myasthenia gravis), and those undergoing treatment with calcium channel blockers, cyclosporine, aminoglycoside antibiotics, quinidine, magnesium sulfate, succinylcholine, and polymyxin.

In Lambert-Eaton syndrome, antibodies targeting tumor antigens mistakenly attack voltage-gated calcium channels, disrupting acetylcholine release and impairing neuromuscular transmission. Myasthenia gravis results in muscle weakness due to antibody-induced internalization and degradation of acetylcholine receptors, further complicating muscle function. Additionally, individuals with a history of hypersensitivity to BTX or its saline solution should avoid this treatment (1,10,17).

Dosage Recommendations

For adult patients receiving BTX for various indications, it is essential to adhere to specific dosage and administration guidelines. The maximum cumulative dose should generally not exceed 360 units within a three-month period. BTX is available in single-use vials containing 50, 100, or 200 units (18).

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Injection Procedure

When preparing for injection, draw slightly more than the intended dose into a sterile syringe, ensuring to expel any air bubbles. A new sterile needle and syringe must be used each time BTX is accessed. The reconstituted solution should be clear, colorless, and free of particulates, and must be visually inspected prior to administration.

Reconstitution and Preparation

Prior to injection, botulinum toxin (BTX) must be reconstituted using sterile, non-preserved 0.9% Sodium Chloride Injection USP. The correct volume of diluent is drawn into a syringe and carefully injected into the vial. If the vacuum does not draw the diluent in, the vial should be discarded. After gently mixing the solution, it should be labeled with the date and time of reconstitution. The reconstituted BTX should be stored in a refrigerator at 2° to 8°C and utilized within 24 hours.

In addition to these instructions recommended by the FDA, research indicates that no evidence of bacterial contamination has been reported after cold storage of reconstituted BTX for periods ranging from 5 days to 10 months (19,20,21,22). Based on multiple studies, it is recommended to use reconstituted BTX within 2 weeks after preparation, as efficacy is preserved during this timeframe (23,24).

Clinical Application of Botulinum Toxin in Dentistry and Oral and Maxillofacial Surgery

The clinical application of botulinum toxin A (BTX-A) in dentistry and oral and maxillofacial surgery addresses a range of conditions that significantly affect patient comfort and quality of life. BTX-A is commonly used to manage bruxism, effectively reducing the intensity of teeth grinding and associated jaw pain. In cases of masseteric hypertrophy, BTX-A can decrease muscle size, enhancing facial aesthetics. It is also beneficial for temporomandibular joint (TMJ) dislocation and dysfunction syndrome, alleviating pain and improving joint function. Additionally, BTX-A helps control sialorrhea by reducing excessive saliva production and is effective in treating Frey's syndrome, chronic facial pain, and hemifacial spasm, showcasing its versatility and efficacy in improving the overall well-being for patients with these conditions (25).

1. Therapeutic Use of Botulinum Toxin

Temporomandibular Disorders (TMD) and Bruxism

Temporomandibular disorders (TMDs) are a prevalent cause of pain in the orofacial region and can be categorized into two main types: myofascial, involving the muscles surrounding the

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temporomandibular joint (TMJ), and arthrogenic, pertaining to issues directly affecting the joint itself. Key symptoms of TMDs include joint noise, pain, and limited range of motion in the jaw (26).

One promising treatment for TMDs is the use of botulinum toxin A (BTX-A). This therapy has demonstrated effectiveness in relieving pain associated with muscle hyperactivity, particularly in patients who experience non-spastic clenching or bruxism. BTX-A injections are typically administered into the masticatory muscles, such as the masseter and temporalis, alleviating symptoms and improving muscle function (27).

The term 'bruxism' originates from the Greek word "brychein," which translates to 'to grind or gnash the teeth' (28). Bruxism is characterized by rhythmic grinding and clenching of teeth, affecting a significant portion of the adult population, with prevalence rates ranging from 8% to 31% (29). It can lead to complications such as headaches, fractured dental restorations, and hypertrophy of the masseter muscle. Although the exact causes of bruxism remain unclear, factors such as emotional stress, neurological disorders, and occlusal interferences are believed to contribute (30).

Various treatment modalities for bruxism have been explored, including occlusal splints, medications, and cognitive-behavioral therapy. However, these approaches often focus on managing symptoms rather than addressing underlying issues. In this context, BTX-A therapy has emerged as a valuable option, offering a therapeutic approach that alleviates symptoms while targeting the muscle activity contributing to TMDs and bruxism. Overall, BTX-A shows significant potential in improving outcomes for patients suffering from these conditions (26,31).

Salivary Secretory Disorders

Sialorrhea, or excessive salivation, is a common issue in various neurological disorders, particularly in conditions such as cerebral palsy, Parkinson’s disease, and amyotrophic lateral sclerosis (32). The use of BTX-A for treating drooling has yielded consistently positive outcomes, with preliminary results indicating significant improvement in up to two-thirds of patients after targeting both parotid glands or a combination of parotid and submandibular glands. Serious complications are rare, and treatment primarily focuses on the parotid gland, with less emphasis on the submandibular gland and infrequent injections into the sublingual gland (1). Botulinum toxin type A (BTX-A) can reduce uncontrolled salivation through autonomic denervation, although optimal dosages and application methods require further research involving larger clinical trials. Additionally, Botulinum toxin type B (BTX-B) has shown high efficacy and safety for treating sialorrhea across different diseases, though it necessitates higher doses and has a slightly shorter duration of action compared to BTX-A. Overall, more studies are needed to refine injection techniques and establish ideal treatment protocols (33,34).

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BTX-A has proven effective in treating auriculotemporal (Frey's) syndrome by inhibiting sweat glands that have been abnormally reinnervated via the cholinergic pathway, thus reducing gustatory sweating in affected skin areas (35). This syndrome often arises from surgical trauma to the parotid gland. BTX-A is typically injected into the preauricular and temporal regions to prevent sweating, with an average effective dose of 25-40 units via intradermal injection, providing relief for up to 12 months (36).

Facial Nerve Palsy

While most studies on the use of BTX-A for facial paralysis are case series, some approaches show promise. Injecting BTX-A into the levator palpebrae superioris can induce temporary ptosis, helping to prevent corneal dryness when the eyes cannot close due to facial nerve palsy. Additionally, BTX-A injections into the normal side of the face may promote facial symmetry by inducing paralysis. Administering BTX-A through an orbital route or skin crease effectively creates protective ptosis, which is beneficial for intensive care patients (27). BTX-A is also commonly used to relieve symptoms of synkinesis, leading to significant improvement. In cases of hyperlacrimation, often caused by aberrant nerve connections post-facial palsy, injecting BTX-A into the lacrimal gland can effectively reduce excessive tearing (37).

Headache Disorders

Randomized, double-blinded, placebo-controlled trials have demonstrated that BTX-A is effective for chronic migraine prophylaxis, although the improvement compared to placebo is modest. Despite this, its excellent tolerability makes it an attractive alternative for patients who struggle with traditional oral prophylactics. The precise mechanisms by which BTX-A provides relief remain unclear, yet it represents a valuable addition to treatment options for chronic migraines, which can be debilitating and difficult to manage. The U.S. FDA approved BTX-A for chronic migraine treatment in 2010, recognizing its potential benefits (36).

Furthermore, BTX has been utilized in the treatment of chronic daily headaches, encompassing both migraines and tension-type headaches (38). The proposed mechanisms behind pain alleviation from BTX injections include muscle relaxation and reduced tension on the trigeminal nerve, which may help diminish headache pain and intensity. This comprehensive approach enhances the management of chronic headache disorders, providing promising prospects for improved patient quality of life (39,40).

Oromandibular Dystonia

Primary oromandibular dystonia (OMD) is a rare form of dystonia that affects the mouth, jaw, and tongue, with a prevalence of approximately 70 per million and a higher incidence in females. OMD is among the most debilitating types of dystonia, leading to visible deformities and social

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embarrassment that may result in withdrawal and associated psychiatric issues. In clinical settings, BTX injections are recognized as the most effective treatment for OMD, supported by numerous studies that demonstrate significant benefits. Successful outcomes rely on proper injection techniques, a solid understanding of oral anatomy, and the appropriate serotype, often resulting in remarkable improvements with only minor, self-limiting side effects (41).

Dysphagia

Dysphagia, characterized by uncoordinated muscle contractions during swallowing, shows improvement following intramuscular BTX injections. The cricopharyngeus muscle is the primary target for these injections, which can be performed using electromyography guidance, either through the skin or endoscopically (42). Additionally, BTX injections can serve as a diagnostic tool to predict the success of surgical outcomes following cricopharyngeal myotomy (43).

Neuropathic Pain Treatment

Neuropathic pain may result from nerve irritation due to damage in either the peripheral or central nervous systems, often associated with lesions or disorders affecting the somatosensory system. BTX injections are employed to address a range of conditions linked to neuropathic pain, including post-herpetic neuralgia, diabetic neuropathy, post-traumatic neuralgia, phantom limb pain, trigeminal neuralgia, occipital neuralgia, and complex regional pain syndrome. The mechanism of action involves the inhibition of neurotransmitter release that plays a role in pain signaling and inflammation (44).

For post-herpetic neuralgia, BTX has demonstrated efficacy in two class 1 studies, with intradermal injections ranging from 20 to 190 units resulting in pain improvement within 3 to 5 days (45). Trigeminal neuralgia can also be effectively treated with BTX, with intradermal or submucosal injections leading to a reported 50% reduction in pain frequency and intensity. BTX is particularly useful for patients who do not respond to medical treatments, cannot undergo surgery, or have failed surgical interventions. Doses of 20-50 units applied to trigger points are often sufficient, with pain relief beginning within 2-3 days and lasting for 2-6 months (46). Furthermore, BTX injections have shown effectiveness for post-traumatic and post-surgical neuralgia, with reductions in pain and allodynia typically starting two weeks after administration. Further research is necessary to validate these findings (43).

Cosmetic Use of Botulinum Toxin

Wrinkle Therapy

The predominant cosmetic application of botulinum toxin A (BTX-A) lies in wrinkle therapy, specifically targeting glabellar lines, platysmal bands, and perioral aesthetic treatments for conditions

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such as gummy smiles and facial asymmetry. The administration of BTX-A for wrinkle correction is typically straightforward, involving perpendicular injections that account for the relevant anatomical structures of the treatment area. Given that BTX-A diffuses approximately 10 mm from the injection site, care is taken to administer the toxin at a safe distance from significant anatomical landmarks, such as the bony orbit (47).

Clinical outcomes have demonstrated efficacy not only in managing glabellar lines but also in addressing vertical lip rhytids, mentalis wrinkling, lower eyelid orbicularis hypertrophy, and excessive gingival display (gummy smile). These conditions can effectively be treated through targeted injections into the lip to facilitate muscle elevation (25,47).

Gummy Smile

Botulinum toxin (BTX) is frequently used in the treatment of "gummy smile," characterized by an excessive gingival display exceeding 3 mm during smiling. Mazzuco and Hexsel classified gummy smiles into four distinct categories: anterior, posterior, mixed, and asymmetric. In moderate cases, the levator labii superioris alaeque nasi (LLSAN) muscle elevates and everts the upper lip, while the depressor septi nasi muscle pulls the nasal tip inferiorly (48). In more severe cases, both the levator labii superioris (LLS) and, to a lesser extent, the zygomaticus minor (ZMi) also contribute to upper lip elevation. Targeted injection of 2 units at a single point on each side, located 1 cm laterally from the nostril ala (the “Yonsei point”), can effectively modulate the activity of these muscles (49,50).

Masseter Hypertrophy

The use of BTX in the management of masseter hypertrophy constitutes a noteworthy advancement in both aesthetic and therapeutic dentistry. The masseter muscle, one of the four primary masticatory muscles, plays an essential role in chewing and the closure of the jaw. Anatomically, it is characterized as a superficial quadrangular structure, originating from the zygomatic arch and inserting onto the lateral aspect and angle of the mandible (49).

For effective management of masseter hypertrophy, injections should be administered both superficially and at deeper levels. This dual approach is essential, as the deep inferior tendon (DIT) can impede toxin diffusion, potentially leading to paradoxical masseteric bulging. A typical dosage of 25 to 30 units of BTX is injected bilaterally into the masseter muscle. In individuals with a more slender musculature or lower body mass index, it may be necessary to adjust the injection points to minimize anterior diffusion, preventing a “sunken cheek” appearance. Improper injection techniques, such as positioning the needle too anteriorly or superiorly, may also contribute to this aesthetic concern.

Injections should be administered below an imaginary line drawn from the oral commissure to the tragus and at least 1 cm away from the anterior border of the masseter muscle. Beyond its role

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in aesthetic enhancement, BTX injections in the masseter have been shown to alleviate symptoms associated with bruxism, muscle clenching, and myofascial pain. However, caution is essential, as excessive dosages may temporarily impair chewing function (51).

SUMMARY / SONUÇ

In conclusion, the application of BTX in oral and maxillofacial surgery represents a promising advancement in both therapeutic and cosmetic interventions. Its efficacy in treating conditions such as masseter hypertrophy, bruxism, and various forms of facial pain highlights its versatility and potential benefits for patient quality of life. However, the current body of evidence predominantly comprises level 4 studies, including case reports and expert opinions, indicating a need for more rigorous research. Randomized controlled trials and larger cohort studies are essential to further elucidate mechanisms, optimize dosages, and establish standardized protocols for BTX applications in this field. Such efforts will enhance the understanding of its long-term efficacy and safety, ultimately contributing to improved clinical outcomes and patient care in oral and maxillofacial practice.

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References / Referanslar

1. O. W. Majid. Clinical use of botulinum toxins in oral and maxillofacial surgery. International journal of oral and maxillofacial surgery 2010;39(3):197-207.

2. F. J. Erbguth. From Poison to Remedy: The Chequered History of Botulinum Toxin. Journal of Neural Transmission 2008;115(4):559-65

3. Shone CC. Clostridium botulinum neurotoxins, their structures and modes of action. In:Watson ED, editor. Natural toxicants in foods. Chichester: Ellis Harwood Ltd; 1986;11-57.

4. Coffield JA, Bakry N, Zhang RD, Carlson J, Gomella LG, Simpson LL. In vitro characterization of botulinum toxin types A, C, and D action on human tissues: combined electrophysiologic, pharmacologic, and molecular biologic approaches. J Pharmacol Exp Ther 1997;280:1489-98.

5. Osako M, Keltner JL. Botulinum-a toxin (oculinum) in ophthalmology. Surv Ophthalmol 1991; 36: 28-46.

6. Carruthers A, Kiene K, Carruthers J. Botulinum a exotoxin use in clinical dermatology. J Am Acad Dermatol 1996;34:788-97.

7. Niemann H. Molecular biology of clostridial neurotoxins. In: Alouf JH, Freer JH, editors. A sourcebook of bacterial protein toxins. London: Academic Press; 1991;303-48.

e-ISSN 2667-7288 Vol 6, Issue 3, (2024) Review Article / Derleme Makale

8. Kao I, Drachman DB, Price DL. Botulinum toxin: Mechanism of presynaptic blockade. Science 1976; 193:1256-8.

9. Simpson LL. Molecular pharmacology of botulinum toxin and tetanus toxin. Annu Rev Pharmacol Toxicol 1986;26:427-53.

10. Huang W, Foster JA, Rogachefsky AS. Pharmacology of botulinum toxin. J Am Acad Dermatol 2000:43:249–259.

11. Black JD, Dolly JO. Interaction of 125I-labeled botulinum neurotoxins with nerve terminals. I: ultrastructural autoradi- ographic localization and quantitation of distinct membrane acceptors for types A and B on motor nerves. J Cell Biol 1986;103:521-34.

12. Schiavo G, Benfenati F, Poulain B, Rossetto O, Polverino de Laureto P, DasGupta R,etal. Tetanus And Botulinum-Neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin. Nature 1992;359:832-5.

13. Brin MF. Botulinum toxin: chemistry, pharmacology, toxicity, and immunology. Muscle Nerve Supply 1997;6:S146-68.

14. Montecucco C, Schiavo G, Tugnoli V, de Grandis D. Botulinum neurotoxins: mechanism of action and therapeutic applications. Mol Med Today 1996;2:418-24.

15. Sollner T, Whiteheart SW, Brunner M, Erdjument-Bromage H, Geromanos S, Tempst P, et al. SNAP receptors implicated in vesicle targeting and fusion. Nature 1993;362:318-24.

16. Sadick NS, Matarasso SL. Comparison of botulinum toxins A and B in the treatment of facial rhytides. Dermatol Clin 2004: 22: 221–226.

17. Diana Mostafa. A successful management of sever gummy smile using gingivectomy and botulinum toxin injection: A case report. International Journal of Surgery Case Reports 42 2017:169-74.

18. FDA BOTOX (onabotulinumtoxinA) for Injection, for Intramuscular, Intradetrusor, or Intradermal Use Initial U.S. Approval: 1989. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103000s5302lbl.pdf

19. Mark A. Jabor vd. Efficacy of Reconstituted and Stored Botulinum Toxin Type A: An Electrophysiologic and Visual Study in the Auricular Muscle of the Rabbit. Plastic and Reconstructive Surgery 2003:11(7):2419-26

20. Doris Hexsel vd. Blind Multicenter Study of the Efficacy and Safety of Injections of a Commercial Preparation of Botulinum Toxin Type A Reconstituted up to 15 Days before Injection. Dermatologic Surgery: Official Publication for American Society for Dermatologic Surgery [et Al.] 2009 Jun;35(6):933-9

21. J. Menon ve A. Murray. Microbial Growth in Vials of Botulinum Toxin Following Use in Clinic. Eye (London, England) 2007:21(7):995-7

22. Murad Alam vd. Sterility Assessment of Multiple Use Botulinum A Exotoxin Vials: A Prospective Simulation. Journal of the American Academy of Dermatology 2006:55(2):272-5.

23. R. R. Sloop, B. A. Cole, ve R. O. Escutin. Reconstituted Botulinum Toxin Type A Does Not Lose Potency in Humans If It Is Refrozen or Refrigerated for 2 Weeks before Use. Neurology 1997:48(1):249-53.

24. George C. Yang, Robert J. Chiu, ve Grant S. Gillman. Questioning the Need to Use Botox within 4 Hours of Reconstitution: A Study of Fresh vs 2-Week-Old Botox. Archives of Facial Plastic Surgery 2008:10(4):273-9.

25. Preetpal Sing Bhogal, Alison Hutton, ve Andrew Monaghan. A Review of the Current Uses of Botox for Dentally-Related Procedures. Dental Update 2006:33(3):165-68.

26. Okeson JP. Orofacial Pain: Guidelines for Assessment, Diagnosis and Management. Chicago: Quintessence Co. 1996:45–52.

27. Kyung-Soo Park, Chi-Heun Lee, ve Jung-Woo Lee. Use of a botulinum toxin A in dentistry and oral and maxillofacial surgery. Journal of Dental Anesthesia and Pain Medicine 2016:16(3):151-57.

28. S. C. Miller ve J. M. Firestone. Psychosomatic Factors in the Etiology of Periodontal Disease. Journal of Dental Research 1947:26(2):173.

29. Daniele Manfredini vd. Epidemiology of Bruxism in Adults: A Systematic Review of the Literature. Journal of Orofacial Pain 2013:27(2):99-110.

30. F. Lobbezoo vd. Bruxism Defined and Graded: An International Consensus. Journal of Oral Rehabilitation 2013:40(1):2-4.

31. Alexander Saletu vd. On the Pharmacotherapy of Sleep Bruxism: Placebo-Controlled Polysomnographic and Psychometric Studies with Clonazepam. Neuropsychobiology 2005:51(4):214-25.

32. Alexander KC Leung ve C. Pion Kao. Drooling in Children. Paediatrics & Child Health 1999:4(6):406.

33. A. García Ron vd. Efficacy and safety of botulinum toxin in the treatment of sialorrhea in children with neurological disorders. Anales De Pediatria 2003) 2012:77(4):289-91.

34. Arianna Guidubaldi vd. Botulinum Toxin A versus B in Sialorrhea: A Prospective, Randomized, Double-Blind, Crossover Pilot Study in Patients with Amyotrophic Lateral Sclerosis or Parkinson's Disease. Movement Disorders: Official Journal of the Movement Disorder Society 2011:26(2):313-19.

35. Peter D. Drummond. Mechanism of Gustatory Flushing in Frey's Syndrome. Clinical Autonomic Research. Official Journal of the Clinical Autonomic Research Society 12, sy 3 2002: 144-46.

36. Sheng Chen. Clinical Uses of Botulinum Neurotoxins: Current Indications, Limitations and Future Developments. Toxins 2012:4(10):913-39.

37. F. J. Montoya vd. Treatment of Gustatory Hyperlacrimation (Crocodile Tears) with Injection of Botulinum Toxin into the Lacrimal Gland. Eye (London, England) 2002:16(6):705-9.

38. Ricardo Persaud vd. An Evidence-Based Review of Botulinum Toxin (Botox) Applications in Non-Cosmetic Head and Neck Conditions. JRSM Short Reports 2013:4(2):10.

39. W. J. Schmitt vd. Effect of Botulinum Toxin A Injections in the Treatment of Chronic Tension-Type Headache: A Double-Blind, Placebo-Controlled Trial. Headache 2001:41(7):658-64.

40. Mia Oliver, Joanna MacDonald, ve Moez Rajwani. The Use of Botulinum Neurotoxin Type A (Botox) for Headaches: A Case Review. The Journal of the Canadian Chiropractic Association 2006:50(4):263.

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41. Muhammad Atif Ameer ve Danish Bhatti. Chemodenervation for Oromandibular Dystonia Utilizing Botulinum Toxins. Cureus 2021:13(10)e18425.

42. S. F. Ahsan, R. J. Meleca, ve J. P. Dworkin. Botulinum Toxin Injection of the Cricopharyngeus Muscle for the Treatment of Dysphagia. Otolaryngology--Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery 2000:122(5):691-95.

43. Shilpadevi Patil vd. Botulinum Toxin: Pharmacology and Therapeutic Roles in Pain States. Current Pain and Headache Reports 2016:20(3):15.

44. Hyun-Mi Oh ve Myung Eun Chung. Botulinum Toxin for Neuropathic Pain: A Review of the Literature. Toxins 2015:7(8):3127-54.

45. Martin Taylor, Sachin Silva, ve Constance Cottrell. Botulinum Toxin Type-A (BOTOX) in the Treatment of Occipital Neuralgia: A Pilot Study. Headache 2008:48(10):1476-81.

46. Wei Cheong Ngeow ve Rekha Nair. Injection of Botulinum Toxin Type A (BOTOX) into Trigger Zone of Trigeminal Neuralgia as a Means to Control Pain. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics 2010:109(3):47-50.

47. Joseph Niamtu. Botulinum Toxin A: A Review of 1,085 Oral and Maxillofacial Patient Treatments. Journal of Oral and Maxillofacial Surgery: Official Journal of the American Association of Oral and Maxillofacial Surgeons 2003:61(3):317-24.

48. Rosemarie Mazzuco ve Dóris Hexsel. Gummy Smile and Botulinum Toxin: A New Approach Based on the Gingival Exposure Area. Journal of the American Academy of Dermatology 2010:63(6):1042-51

49. Kim H.-J., Seo K.K., Lee H.-K., Kim J. Clinical Anatomy of the Face for Filler and Botulinum Toxin Injection. Springer; Singapore: 2016. Clinical anatomy for botulinum toxin injection; pp. 55–92.

50. Woo-Sang Hwang vd. Surface Anatomy of the Lip Elevator Muscles for the Treatment of Gummy Smile Using Botulinum Toxin. The Angle Orthodontist 2009:79(1):70-77.

51. Sung Ok Hong. Cosmetic Treatment Using Botulinum Toxin in the Oral and Maxillofacial Area: A Narrative Review of Esthetic Techniques. Toxins 2023:15(2):82.