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Chapter 6

Botulinum Toxin in Dentistry

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Abstract

Botulinum toxin (BT) is an injectable intermuscular medication that is used as a muscle relaxant. In this chapter, we explore the applications of botulinum toxin in dentistry for either cosmetic or therapeutic purpose, such as gummy smile (high lip line), parafunctional habits, temporomandibular disorders and facial pain. It is considered as a non-invasive, conservative and affordable alternative treatment in comparison to surgical procedures. Although, the effect of BT is temporary that lasts for 4–6 months, it is preferred by most of the patients as it gives positive significant results that meet their desires with minimal side effects.

Keywords: Botox, botulinum toxin, gummy smile, temporomandibular joint disorder, asymmetric smile, reverse smile, drooping mouth corners, facial nerve palsy, migraine, excessive salivation, trigeminal neuralgia, parafunctional habits, maxillofacial fracture

1. Introduction

Botulism toxins are exotoxins produced by anaerobic, Gram-positive, rod-shaped, motile bacteria of the genus *Clostridium*, which is called *Clostridium botulinum*, *C. butyricum*, *C. baratii* and *C. argentinense* [1], which are widely distributed in the surrounding environment, including the soil and dust. Also, some food products such as honey, canned and not well cooked food may contain amounts of these bacteria [2]. These bacteria are divided into four distinct phenotypic groups (I–IV) and is also classified into seven serotypes (A–G) based on the antigenicity of the botulinum toxin produced [3]. The most common ones are Botulinum toxin type A and B. However, Onabotulinumtoxin A is marketed under brand names Botox®, Vistabel® and Vistabex®, while Abobotulinumtoxin A is marketed under the brand names Dysport® and Azzalure®. In addition, incobotulinumtoxin A is marketed under the brand names Xeomin®, Xeomeen®, and Bocouture®. Whereas, botulinum toxin

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B has approval under the brand name Myobloc® and Neurobloc®. All of them are injectable intramuscular medications that are used as muscle relaxants. In 2007, British Columbia dentists were among the first to use botulinum toxin (BT) for cosmetic treatments, and to subsequently appreciate the potential in dental therapeutic treatments [4]. Now, A growing number of dentists are practicing botulinum toxin (BT) injections for their patients for oral and maxillofacial cosmetic and therapeutic uses.

2. Mechanism of action

When BT is injected into a target muscle, it creates a temporary dose-dependent effect that weakens muscles activity. It is a neurotoxin which produces transient chemical denervation of facial muscle by binding to glycoproteins structures and inhibiting the release of acetylcholine from the cholinergic nerve endplates, which leads to decrease in the contraction intensity, flaccid paralysis and muscle inactivity. When the target tissue is an exocrine gland, the glandular secretion is blocked as it inactivates the glands innervated. However, the neuromuscular transmission is re-established by restoration of the SNARE protein complex turnover, initiation of new acetylcholine receptors, sprouting of new axonal terminals and elongation of the endplate. The effect can usually last up to 3 months and gradually returns to its full function with no adverse effects. Therefore, the blockage is transient and not permanent which make this treatment considered as a palliative approach rather than a curative option [5].

3. Preparations

BT is shipped frozen and it is recommended to be kept in at frozen temperature −5°C before use as lower temperature may affect its potency. Doses of BT utilized for the treatment of a particular purpose depend on the certain brand/preparation as the unit of one product is not similar to the other [6]. The two most commercially available types of BT are Botox® and Dysport®. About 20–25 units of Botox® are equipotent to 80 units of Dysport®. Botox® is marketed as single-use, sterile 100 Units or 200 Units vacuum-dried powder while the vial of Dysport® contains 500 units. They are reconstituted only with sterile, non-preserved 0.9% sodium chloride (normal saline solution) [7]. However, there is no established method to calculate the equivalent doses between various products of BT. The potency per unit of a product is not interchangeable with other preparations, therefore it is important for a dentist to be aware of the different formulations before their use [8].

After drawing up of preservative-free saline by an appropriate sized needle and syringe, it is important to introduce the saline slowly into the vial, then mix by gentle rotating movement to avoid foaming and denaturation of the toxin. After that, storing of BT in a frozen vial (2–4°C) is recommended [9]. However, it has been reported that higher dilutions of BT can lead to an increase of its tissue diffusion, thus influencing the therapeutic and side effects. So far, no valid studies are available to evaluate the optimal dilution for different therapeutic situations [5]. The BT potency has been reported to be effective until the fourth week after reconstitution [10].

4. Injection procedures

The preferred syringe for BT injections is a calibrated 1.0 mL tuberculin syringe with a gauge preference of 26–30 [11]. The patient should be placed in upright raised position, the target facial muscle should be examined by inspection and palpation when the patient is making the facial expressions or just clenching to determine the exact area of the injections. The injectable areas should be sterilized with a non-alcohol cleanser such as Betadine. Topical anesthesia and ice could be applied before injection to control pain and bleeding the Botox is then injected into the desired areas. It is recommended to apply pressure to the injected area if there is bleeding. After finishing the procedure, the patient should lay upright for 2–5 min to assure his wellness and receive the postoperative instructions which are; avoiding lying down for 4 h, avoid strenuous activity for at least 24 h to avoid the risk of bruising, non-steroidal anti-inflammatory drugs will be prescribed if patients complained of pain or headache, ice packs are advisable after injection to reduce bleeding and edema. However, as the injection of BT is intramuscular, the dosage of BT injection varies between females and males, depending on the volume of muscle. Certainly, males have a larger muscle volume than females, so they require more units of BT during injection to achieve the same results as female patients [12].

Results will be conspicuous within 4–14 days and lasts for 4–6 months, depending on the muscle thickness and anatomy. Some authors [13, 14] conducted that several injections of BT could prolong its effect. One explanation of this process is that the extended muscle paralysis that occurs after numerous injections can cause partial muscle atrophy and permanent weakness in the contraction ability later on, even after the evanescence of the BT toxic effect [15]. It is important to avoid BT injections before the complete disappearance of the BT effect to prevent the antibodies formation against the toxins, which can lately lead to disappointing results [16].

5. Contraindications

1. Pregnant or lactating woman as it may harm the baby (Botox is classified as pregnancy category C drugs) [7].
2. Neuromuscular disorders as patients will be at risk of muscle weakness, diplopia, ptosis, dysphonia, dysarthria and severe dysphagia [7].
3. Patients under Ca channel blockers, cyclosporine and aminoglycosides medications as it may cause arrhythmia and myocardial infarction [7].
4. Patients with a history of allergy to any of the constituents of BT or saline solution as it may cause immediate hypersensitive reactions including anaphylaxis, serum sickness, urticaria, edema and dyspnea [7].
5. Psychological unstable patients [7].

6. Side effects and complications

Generally, the Botox treatment is safe when it is administered in proper doses and techniques. The complications of BT are divided into systemic, local, and reduced therapeutic effects due to antibody formation. The systemic complications include nausea, loss of appetite, diarrhea, abdominal pain, fatigue, malaise, flu-like symptoms such as fever and running nose, increased blood pressure, sore throat, modification of salivary consistency, difficulty in swallowing and ringing in ears [17]. While local complications vary regarding the injection site, involving infection, headache, pain at the injection site, bruising, inflammation, orofacial edema, loss of muscle strength, nerve palsy, rash, itching, ptosis, dry eye syndrome and dysphonia. In addition, improper injection technique or dose may result in asymmetrical appearance of a face or smile, some difficulties in speech, chewing and/or drinking, alternation in salivary consistency and drooping or ptosis of the lip causing obstruction of visible teeth on full smile [16].

In some cases, BT action may diffuse to sites beyond the local application site, presenting generalized muscle weakness manifesting as diplopia, dysphagia, dysphonia, ptosis or even breathing difficulties. The probability of this spread of toxin effect is considered to be high in the face as well as head and neck region due to facial planes and spaces.

The lethal dose of BT injections is not known yet, but it has been estimated to be about 3000 U [18]. The maximum dose recommended for dental applications at an injection session is about 80–100 U. Therefore, more doses could have a potentially lethal outcome.

7. Uses and indications of Botox in dentistry

Certainly, BT treatments have been amplified in popularity over the last two decades, it is getting much more attention in dentistry and frustrated many dentists, where they use BT injections for dental esthetic and therapeutic purposes. It was proven that BT injections can improve cosmetics, reduce pain and relax retrain muscles which in turn enhance the dental treatment plans.

The applications of BT injections have been classified into:

I. Cosmetic uses

1. Gummy smile
2. Asymmetric smile
3. Sad/reverse smile (Marionette lines)
4. Perioral rhytides (Smoker lines)
5. Masseteric hypertrophy (bulky jaws)

II. Therapeutic uses

1. Tempomandibular joint disorder
2. Migraine

3. Trigeminal neuralgia
4. Facial nerve palsy
5. Bruxism and parafunctional habits
6. Salivary gland secretory disorders (excessive salivation/drooling)
7. Maxillofacial trauma and fractures
8. As adjunctive treatments in dental clinics

7.1. Cosmetic uses

7.1.1. Gummy smile

Although, displaying a small amount of gingiva is esthetically acceptable and gives a youthful appearance, a smile with more than 2 mm exposed gingiva is known to be gummy smile (GS). It is one of the most common variations among the people, with predominance of females than males. The etiological factors of GS can extensively vary, including altered passive eruption of teeth, dentoalveolar extrusion, vertical maxillary excess, short or hyperactive upper lip muscles (levator labii superioris, levator labii superioris alaeque nasii, levator anguli oris, depressor septi and the zygomaticus muscles), or combinations of one or more of them (**Figure 1**). Accordingly, proper diagnosis of the etiology will lead to the proper treatment [16]. In case of altered passive eruption, crown lengthening is the choice treatment, whether with or without bone reduction. Also, surgical lip repositioning techniques were reported to give satisfactory results. In addition, some cases need orthognathic surgery or orthodontic appliances, especially if the cause is skeletal in origin.

However, in cases of hyperactive/hyper-functional elevator labial muscles, BT injections have progressed to be popular in the correction of the gummy smile (GS) compared to other surgical procedures. The advantages of these injections are the increase of the patient self-esteem and

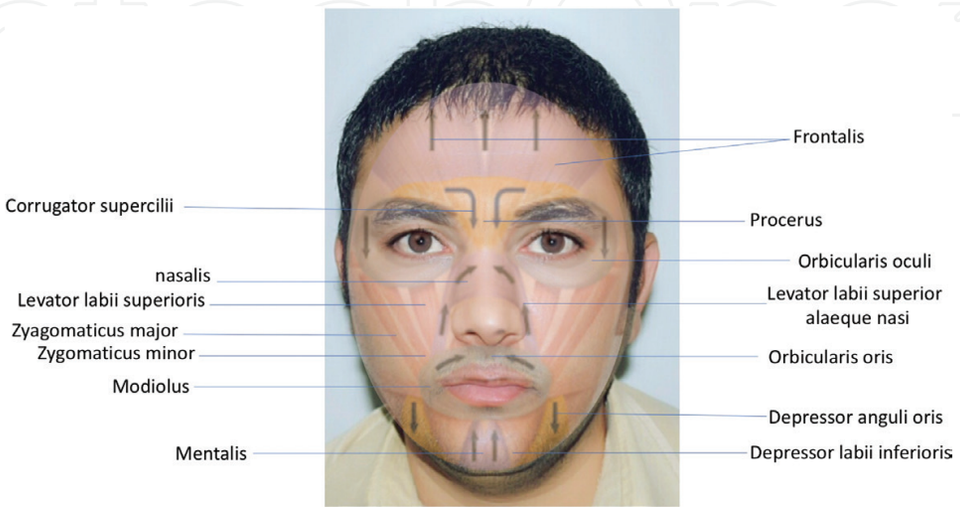

Figure 1. Facial muscles and the direction of their action (depression or elevation).

their preference because their technique is less invasive, reasonable cost and requires less time despite its short-term effect. The purpose of the BT injections is to relax the hyperactive elevator muscles, blocking excessive contractions that are excessively pull up the lip while smiling.

Injection technique: during smile, there are 2 stages in its development, the first stage happens when the upper lip raises to the nasolabial fold, the medial muscle bundles pull up the lip at the anterior teeth and the lateral muscle groups raise the lips at the posterior teeth. However, buccal fats resist the lips at the nasolabial fold while during the second stage, the lip raise superiorly by three muscle groups which are levator labii superioris, zygomaticus major and superior fibers of buccinators [19]. First, gummy smile should be diagnosed according to the classification of the exposed gingival area; anterior, posterior, mixed and asymmetrical or by Goldstein classification as low, moderate and high based on the amount of exposure of gingiva during smiling. These classifications are essential to identify the involved muscle, dose and technique of Botox injections. The muscles of injection are levator Labii superioris, superioris alaeque nasi, zygomaticus minor and major muscle, depressor septi nasi muscle and risorius muscle. The sites of injection should be determined first by palpating the muscles during smiling and relaxing movements to ensure the accurate locations of injections. There is an appropriate and effective point of intramuscular Botox injection introduced by Hwang et al., at Yonsei University College of dentistry, Seoul, Korea have where elevator lip muscles pass by, it is called Yonsei point as shown in **Figure 2** [20]. This point is located at the center of the triangle formed by levator labii superioris, levator labii superioris alaeque nasi and

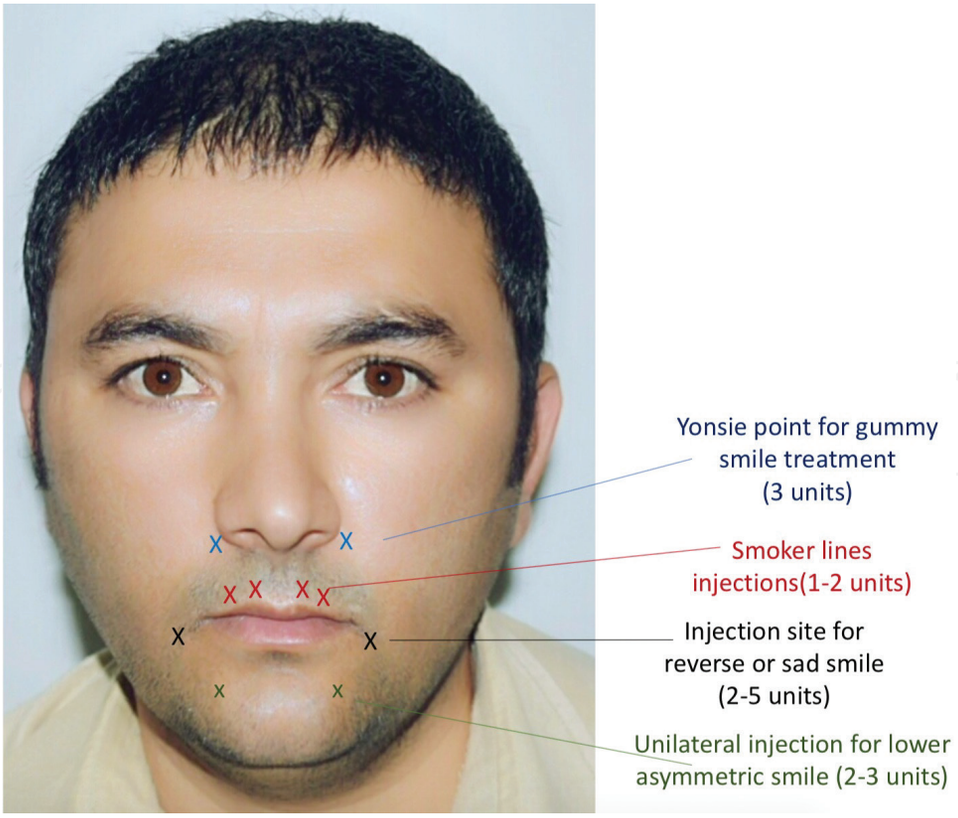

Figure 2. Sites of botox injections for the cosmetic uses.

zygomaticus minor. The doses depend on the dilution of BT with saline. However, there are different techniques for gummy smile injections, all of them have a common site of injection which is Yonsei point, where the recommended dose is 3 U at each injection site. The depth of administration should be intramuscular with the needle perpendicular to the skin surface and bevel facing upwards [16].

7.1.2. Asymmetric smile

Asymmetrical smiles (AS) are due to unilateral hyperkinetic of either lip elevator muscles or lip depressor muscles, where lip rises or depressed more on one side than the other due to the imbalance of the muscle intensity or activity between the left and right sides during smiling. Lip elevator muscles are the muscles responsible for upper AS while the depressor labii inferioris and depressor anguli oris are the muscles responsible for lower AS. However, injections of BT into the muscles of the side where the upper lip pulled to the highest side or the lower lip retracted to the lower side, shown to be effective and give positive results [20, 21].

Injection technique: for upper AS, patient should be in the right position and asked to smile, 2–3 U at the Yonsei point should be injected unilaterally to the most elevated side. While for the lower AS, patient should be asked to smile to determine which side has pulled lip down then, 2–3 U of Botox injections into one of depressor labii inferioris muscles as shown in **Figure 2** and 2 U in one of depressor anguli oris. For both techniques, the needle should passed perpendicular to the skin and enter the thickest part of the muscle. It is advisable to give small doses to correct AS, otherwise, excessive weakening and over correction may result.

7.1.3. Sad or reverse smile (Marionette lines)

The presence of the cervical commissures of the lips in combination with the rest of facial anatomical features are responsible for the old or sad appearance. This happens due to age changes as skin loses the consistency of collagen and elastic fibers and also due to the hyperactive of depressor anguli oris (triangularis muscle) that is located bilaterally (**Figure 1**), adjacent to the lip corners which causes the drooping mouth corners and gives the Marionette line appearance. However, BT injections has proved its effectiveness and give satisfactory outcomes in such cases, it relaxes the depressor muscles which in turn lift the lip corners precisely through their antagonists, improving the depressed and aged facial appearance [22, 23].

Injection technique: Botox injections are indicated for patients with horizontal and vertical platysma muscle bands and with downturned oral commissures, without the existence of submental lipodystrophy or excessive skin laxity [22]. Before injection, patient should be asked to frown, then muscles should be palpated to detect the exact sites of injection. Also, muscle can be detected by bimanual palpation at angle of mouth when the patient says "iii". The site of injection is on the trajectory of nasolabial fold to the jaw line. Bilateral superficial injections in doses of about 2–5 U of Botox is the norm (**Figure 2**). However, it is difficult to inject the depressor anguli oris muscle because its medial border overlaps with the depressor labii inferioris, and its lateral border is adjacent to the risorius, zygomaticus major, and platysma muscles. Therefore, precautions should be taken as if Botox is injected with improper

dose, possible negative outcomes may result including drooling, slurred speech and lack of facial expressions [22]. In addition, if it is injected medially, Botox may diffuse into the depressor labii inferiors causing a lower lip protrusion appearance, known as a Gomer Pyle look and if it is injected too laterally, it may reach Buccinator muscle, causing the patient to bite and traumatize the buccal mucosa.

7.1.4. Perioral rhytides (smoker lines)

These are vertical rhytides which are present in the upper lip and the lower lip region. It is caused by hypertrophic or repetitive contractions of orbicularis oris (circles the mouth) increased with age, sun exposure, strawing and smoking. Their treatment choices are Botox injections or dermal filler or both of them together. Although, BT injections will treat the vertical wrinkles around the lips, they give more eversion results and more lip fullness appearance which make them, the first choice [24].

Injection technique: ask the patient to close his lips and push them forwards, injections should be very superficial of 1–2 U at 2–4 spaced sites along the vermilion border to assure symmetry (**Figure 2**). Results do not last too long because of the repeated action of same muscles, but after injection patient may complain of difficulty in swishing, spitting, strawing, whistling, kissing and pronouncing. In addition, asymmetry may result during taking and smiling [24].

7.1.5. Masseteric hypertrophy (bulky jaws)

Masseteric hypertrophy is an asymptomatic unilateral or bilateral enlargement of the masseter muscles due to congenital cause, chronic clenching habits, asymmetric chewing habit, TMJ dysfunction and focal dystonia. Thus, causing the bulk of mandibular jaw and square appearance of the face. The traditional treatment is partial resection surgery of masseter muscle under general anesthesia, which make this choice have several complications, including hematoma, nerve paralysis, infection, mouth opening restriction and sequel from general anesthesia [25]. Botox injections of masseter muscle reported to be safe as it causes weakening in its intensity and reduction of its bulking appearance which in turn give more tapered face and jaw line contouring [26].

Injection technique: the patient should be asked to clench his teeth to determine the most bulky and prominent area in the masseter muscle for Botox injections, the injections are equally given into three points at the center of the lower third of the masseter muscle with a distance 1 cm from each other, 5–15 U in each point total of 15–45 U per side (**Figure 3**) depending on the bulk of the muscle [26].

7.2. Therapeutic uses

7.2.1. Tempomandibular joint disorder

TMJ disorder is a term used to describe orthopedic and myofascial disorders that cause disharmony in the temporomandibular joint (TMJ), masticatory muscles, and associated structures. It is associated with oromandibular dystonia, periauricular pain, cervicogenic headaches, chronic low back pain, decreased jaw excursion, jaw locking, and noise at the

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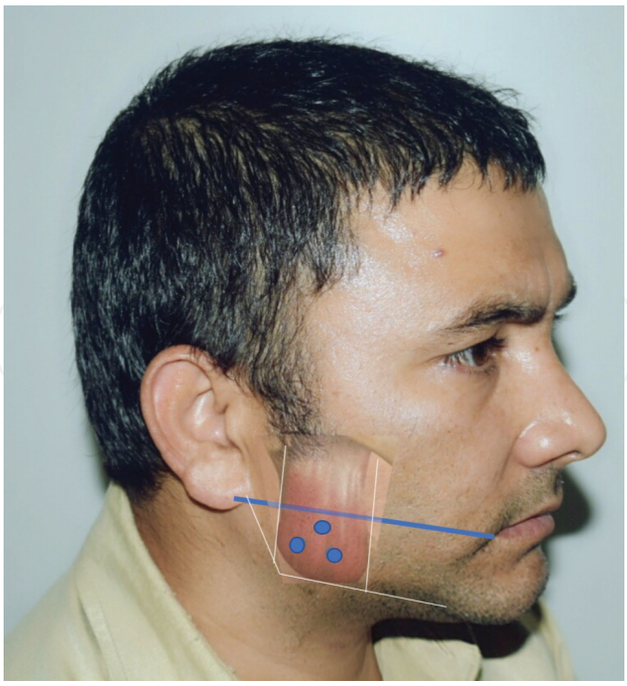

Figure 3. Injection points of Masseteric hypertrophy (5–15 U for each point).

joint with movement. The etiological factors include excessive masticatory muscle activity, parafunctional habits, trauma, psychological factors, and diseases such as arthritis [27]. In general, TMJ disorders are divided into myofacial TMJ disorder or arthrogenic TMJ disorder. The myofacial TMJ disorder is manifested by a pain from hyperfunctioning masticatory muscles causing chronic myositis. While, arthrogenic TMJ disorder is associated with pain due to intracapsular pathology [28].

The diagnosis of TMJ disorders is based on history, physical findings and clinical examination. Patient should be asked about bruxism, gum chewing, jaw soreness, morning headaches and history of trauma [26]. However, there are several therapeutic modalities for TMJ disorders, which are occlusal equilibrations, full mouth reconstructions, orthotic devices, jaw repositioning, psychological therapy, neuromuscular therapy, physiotherapy and laser. In addition, systemic pharmacological medications can play a role in its management, such as corticosteroids injections, anti-inflammatory agents, non-narcotic and narcotic pain medications, muscle relaxants and in some cases tricyclic antidepressants [29, 30]. However, some patients with arthrogenic TMJ disorder may be treated by intra-articular corticosteroid injections, arthrocentesis, arthroscopic surgery or TMJ open surgeries such as arthroplasty [28].

Some dental practitioners solve the occlusion problem and achieve ideal occlusion without treating the spasm of the masticatory muscles. Thus, will lead to the recurrence of sign and symptoms of TMJ disorders and failure of the treatment. Hereby, muscle spasm should be relieved first to reduce facial pain, then achieve the proper occlusal equilibration. However, the use of Botox is considered to be an effective supportive treatment of the myofacial TMJ disorder, especially with patients who did not achieve complete remission by conservative and pharmacological modalities. It decreases the intensity, frequency and duration of recurrent attacks [28].

Injection technique: the involved muscles are temporalis muscle and masseter muscle which are manifested as direct muscle pain while lateral pterygoid muscle involvement usually is manifested as buccal pain [31]. To identify the injected sites, first ask the patient to clench his teeth to make the injection muscles more prominent and easily detected. Injections are performed bilaterally using the proper dose of BT to reduce the contractions of these muscles as well as the facial pain. Identification of the lateral pterygoid muscle is done intraorally where needle placed between the pterygoid plate and the coronoid process of the mandible. The starting dose of Botox 10–25 U for a temporalis muscle, 25–50 U to a masseter muscle (**Figure 4**) and 7.5–10 U for the lateral pterygoid [28]. It is recommended to give low concentrations in different sites to increase the areas of injections and avoid incomplete effect. Higher doses may increase the risk of diffusion of Botox to undesired neighboring areas causing brow ptosis, blepharoptosis or diplopia if the temporalis muscle is injected too close to the orbit and if the masseter muscle is injected too close to the zygomaticus major, asymmetry may result. Also, dry mouth may occur if BT is injected into the parotid gland [32].

7.2.2. Migraine

The migraine headache is a common neurological condition that is characterized by unilateral pulsatile throbbing pain, photophobia, phonophobia, feeling of nausea or vomiting and disabling intensity, its effect lasts from 4 to 72 h and may be longer [33]. It was reported that migraine has a relation to family history and its incidence in women is three times that in men with the highest prevalence among those aged 30–39 [34]. Treatment of migraine includes abortive and preventive therapy. The treatments for mild to moderate episodes are nonsteroidal anti-inflammatory drugs (NSAD) and analgesics containing acetaminophen or aspirin. While, for severe migraine, Triptans are indicated. Not only, some patients with migraine respond poorly to triptans, but also it is contraindicated in some cases such as cardiovascular co-morbidities [35, 36]. Intravenous administration of some combination of dopamine receptor agonists (e.g., prochlorperazine), dihydroergotamine (DHE), and intravenous (IV) NSAIDs (diclofenac or ketorolac) is recommended for more severe attacks [37].

In 2000, Binder found that individuals who had cosmetic facial injections reported a pain reduction of the headache [38]. After that, they discovered that the relief of the pain often happened before the decrease in muscle contractions [39]. Botox blocks the release of peripheral nociceptive neurotransmitters, modulating the peripheral sensation and also suppresses indirectly the central pain processing systems responsible for migraine [40]. In 2010, the FDA approved intramuscular BT injections as a prophylactic treatment of migraine [41].

Injection technique: muscles to be injected by BT are procerus, corrugator, frontalis, temporalis, occipitalis and posterior cervical muscles. The FDA has approved 31 sites with total 165–195 U at which BT can be injected for treating migraines. The injections are given to corrugator in 10 U divided into 2 sites, procerus 5 U is given in one site, frontalis 20 U divided into 4 sites, temporalis 40 U divided into 8 sites (**Figures 4** and **5**), occipitalis 30 U divided into 6 sites, cervical paraspinal muscles 20 units divided into 4 sites and finally trapezius 30 U divided into 6 sites [42]. Cautions should be taken during injection of frontal sites as droopy eyelids, dry eyes and vision problem may result.

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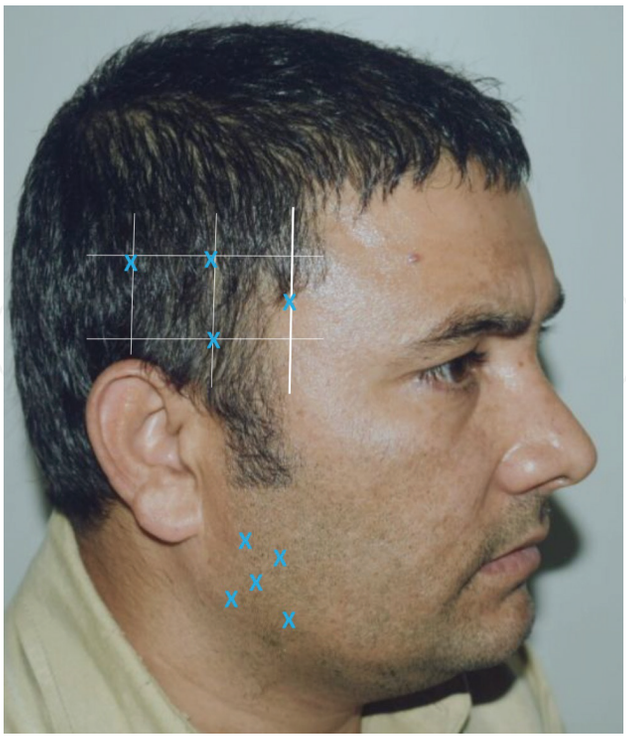

Figure 4. Botox injection points for temporalis and masseter muscles in treatment of TMJ disorders.

7.2.3. Trigeminal neuralgia

Trigeminal neuralgia (TN) is known as sudden, usually unilateral severe recurrent stabbing pain involving the distribution of one or more branches of the trigeminal nerve [43]. It is caused by compression of the nerve near its origin. The pain is usually triggered by stimuli such as chewing, washing of the face, speech and tooth brushing [33]. It occurs more in the old patient rather than younger ones. Its management based on the prophylactic pharmacological treatment with anti-epileptics including Carbamazepine, Oxcarbazepine, Bacloten, Lamotrigine, Gabapentin and ropivacaine. In case of unsatisfactory response or undesirable adverse effects, neurosurgical treatments are recommended which include peripheral techniques (cryosurgery, neurectomy, laser, acupuncture, thermocoagulation, injections of streptomycin, alcohol and phenol), Gasserian ganglion radiofrequency thermocoagulation, glycerol, balloon compression, Gamma knife and microvascular decompression. All of these surgical treatments may cause damage to the nerve except microvascular decompression, which limits the consideration of these techniques [44]. However, BT has been found to be minimally invasive and effective treatment of pain in the maxillofacial region over other invasive therapies especially, in cases of trigeminal neuralgia presenting no adverse effects [45, 46].

Injection technique: for the injection to the maxillary root, a dental needle of 0.40 × 50 mm is used through the upper edge of the zygomatic arch, midway between the external ear and the orbital rim, the needle should be pointed toward the zygomatic bone on the other side of the skull (forming obtuse angles to the front and below) at a depth of 50 mm around the pterygopalatine ganglion. For the injection to the mandibular root, through the lower edge

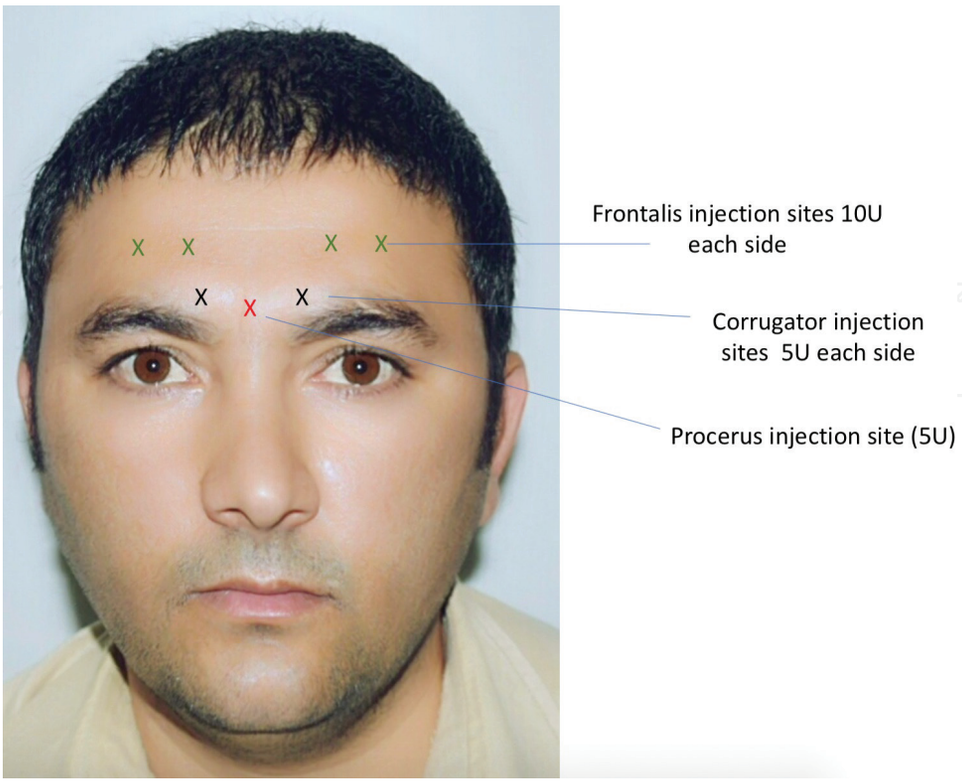

Figure 5. Injection sites of Botox into Frontalis, Corrugator and procerus muscles.

of the zygomatic arch, the position should be the same. The needle should be pointed transversely along the base of the skull toward the middle, then to be inserted below the middle of the zygomatic arch. After striking the pterygoid process, the needle should be withdrawn slightly craniodorsally about 5–10 mm where the solution is administered around the trigeminal ganglion [47].

7.2.4. Facial nerve palsy

It is a facial paralysis with resultant paresis and synkinesis of muscles on the affected side of the face, causing loss of forehead creases, loss of the nasolabial fold, lagophthalmos, brow droop, and drooping of the corner of the mouth. In contrast, muscles on the unaffected side of the face have no opposing forces [48]. Thus, lead to articulation difficulty, eating and drinking problems, asymmetry of the face and unacceptable facial esthetics causing psychological and physical disturbance in a patient's life. Treatments of facial palsy involve nerve grafts, muscle transfers, myofunctional approaches, and microsurgical patches. Although there are many treatment modalities, facial symmetry may persist. However, BT injection treatment was reported to be effective in reducing facial synkinesis, thus improving facial expression symmetry both at rest and involuntary movements [49]. One of the complications of facial nerve palsy is hyperlacrimation (crocodile tears) associated with salivation due to the abnormal connection between secretomotor fibers of salivary gland to lacrimal gland. Injection of BT into the lacrimal gland has been successfully reported in managing this condition too [50].

Injection technique: the areas of injection that are usually considered are levator labii alaeque nasi to reduce the visibility of the upper teeth; depressor labii inferioris to reduce the

visibility of the lower teeth and orbicularis oculi and frontalis to match the contralateral rhytides (**Figure 1**). Patient should be seated in an upright position with the head supported and asked to smile widely, Then, sites of injection are examined clinically, the area exhibiting the maximum pull on movement of the lower face are marked and is injected at an angle of 45° intramuscularly. The unaffected side is also injected to make balance, improve hyperkinesis and give more symmetry at rest. Titration is needed to reduce the effect of the intentional muscle function while increasing the treatment of unintended motion [51].

7.2.5. Bruxism and parafunctional habits

Parafunctional habits such as bruxism, clenching or grinding interfere with the normal occlusion causing generalized attrition, masticatory muscle disharmony, TMJ disorder, facial pain and headache. Traditionally, oral appliances such as oral splint and night guard are indicated for such cases and give good success results as to relieving some or all of the symptoms. Also, BT has been introduced successfully to reduce these symptoms. However, in comparison of BT injections to oral splint modality, both of them are equally effective and safe on bruxism [52, 53] but use of BT in sleep bruxism is more encouraging and comfortable, also a single injection has been shown to be effective for at least a month [54].

Injection technique: injection sites identified by palpation during clenching, then receive bilateral injections of Botox in three sites in the thickest parts of the masseter muscles [55] with dose range of 25–100 U per side. Exceeding the dose will paralyze the muscles of mastication and interfere with the patient's ability in chewing and talking. Also, too small doses will have no effect at all [56].

7.2.6. Salivary gland secretory disorders (excessive salivation/drooling)

The salivary gland secretory disorders cause excessive salivation, such as sialorrhea and Frey syndrome, they are due to poor oral and facial muscle control. They are common in patients with cerebral palsy or neurologic disorders, also patients have post-traumatic sialoceles and cysts, which commonly developed during cancer resection surgery. These disorders may cause perioral dermatitis, or dehydration which leads to problems in the hygiene and the psychosocial status [57]. Their treatment methods vary from a conservative medical modality to a more aggressive surgical approach, including oral motor therapy, intraoral devices, anticholinergic medications, and surgery. However, anticholinergic medications are poorly tolerated due to their adverse effects on the body, such as constipation, urinary retention, orthostatic hypotension, bradycardia, irritability and drowsiness. In addition, surgery is considered to be an invasive procedure that has complications, including increased dental caries, gingival problems, parotitis, and postoperative cysts and fistulae [58].

The secretion of saliva is under parasympathetic autonomic control with acetylcholine working as the specific neurotransmitter. Therefore, down regulation of acetylcholine by BT injections will lead to the decrease of the salivary production [59]. Lately, BT injections have been utilized to manage sialorrhea in adults with Parkinson's disease, head and neck cancer, neurodegenerative disorders and strokes without any noticeable side effects [57].

Injection technique: the injection of Botox into the parotid and submandibular glands is effective in controlling drooling [60, 61]. Botox is administered in a dose range of 30–70 U into parotid

gland. However, the significant reduction in salivary flow is usually observed at 4 weeks and fades in about 3 months, so repeated injections are necessary for such cases [61, 62].

7.2.7. Maxillofacial trauma and fractures

To avoid inappropriate muscle movements during healing period of fractured bones, BT have been introduced to be effective in this mission when there is a injury or fracture in the maxillofacial region such as the maxilla, mandible, nasal bone, zygoma and orbital bone. Also, BT injections are used as a temporary splint during fracture healing period. BT injections into the masticatory muscles in cases of jaw fractures, have been reported to prevent bone displacement and facilitate healing [63]. In 2003, Kayikçioglu et al. conducted a study in temporary paralysis of masseter muscles, to allow application of mini plates/microplates in the management of zygomatic fractures [64]. Also, some reports recommended the use of BT injections in masseter and anterior fibers of temporalis muscles as an adjunctive modality in treatment of condylar fracture [63, 65]. In addition, BT injections in the anterior belly digastric have been used successfully in the correction of post-traumatic anterior open bite [66].

7.2.8. Adjunctive to dental treatments

7.2.8.1. Implantology

BT injections have been postulated to increase the therapeutic benefits in patients with implants who have excessive functional force or have parafunctional habits. When Botox relaxes the masticatory muscles, especially the masseter and temporalis muscles, it weakens the muscles movement in immediate or delayed implant loading. Hereby, relief the abnormal forces on implants leading to successful osseointegration and good prognosis of the treatment. However, studies supporting the use of BT in implantology is rare and warrants further research [7, 67].

7.2.8.2. Orthodontic therapy

The relapse of orthodontic treatment is a common problem because not only teeth are responsible for the treatment relapse, but also the hyperactivity of facial muscles acts as a risk factor. Hereby, the BT injection of mentalis muscle and other muscles will decrease their strength and contractions which in turn avoid their disrupting to teeth alignment.

7.2.8.3. Removable prosthodontics

Some patients may suffer from difficulty in retention of their removable dentures due to hyperactivity or hypertrophy of their masticatory muscles such as masseter, lateral and medial pterygoid muscles. Therefore, weakening the contractions of these muscles by BT injections, increases the retention of the removable dentures.

7.2.8.4. Periodontal and dental health

As it is well known that there is a relation between stress and periodontal diseases as it decreases the immunity affecting the host inflammatory response to local factors, in turn increasing

the inflammation and periodontal destruction. However, a recent study has reported that BT injections improve the psychological status and release stress as Botox injections improve the facial appearance, causing increase in the immunity and health of periodontium [4]. In addition, decreasing stress and relief of grinding and bruxism habits will prevent the traumatized occlusion leading to the improvement of the dental and periodontal health.

7.2.8.5. Mandibular trismus

After a prolonged time of dental procedures, patient may complain of pain and limitation of mouth opening due to spasm of masticatory muscles. Thus, may affect the compliance of dental treatment, restrict the oral hygiene regime, difficulty in drinking and eating. Botox injections into masticatory muscles will reduce pain, paralysis the muscles and diminish the spastic activity.

7.2.8.6. Diagnostic application for toothache

In cases of chronic intermittent toothache, BT injections can be used to identify the origin of the pain and distinguish if the pain is due to muscles or teeth. The pain of pulpal origin will not be relieved when Botox is injected into the muscles [9].

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