Complications in the Cosmetic Use of Botulinum Toxin Type A: Prevention and Management

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Abstract

Botulinum toxin type A (BTX-A) has become the most frequently requested nonsurgical procedure performed around the world. The use of BTX-A in cosmetics has expanded greatly since its approval by the Food and Drug Administration for reduction of glabellar rhytids. Experienced clinicians have been using BTX-A in other areas off-label to improve the appearance of rhytids and facial harmony. Adverse effects associated with BTX-A are rare and tend to be mild and temporary, such as bruising, swelling, and pain at injection sites. More serious complications, such as brow ptosis or eyelid ptosis, can occur. These complications can be minimized by a thorough understanding of the anatomy of the face and careful injection technique, which will be outlined in this article.

12.1 Introduction

Photoaging, volume loss, and rhytids all contribute to the stigmata of the aging face. Nonsurgical treatment of the aging face is most effective when it addresses all contributing factors. Hyperdynamic rhytids, most notable in the upper third of the face, contribute to the appearance of the aging face. Over time, contraction of the muscles of facial expression can contribute to dermal atrophy and lead to static rhytids [1–3].

Botulinum toxin type A (BTX-A) has become the most frequently requested nonsurgical procedure performed around the world [4–6]. In 2015, there were 6.7 million treatments with BTX-A performed, which is up 1% from 2014, and up 759% from 2000 [5]. BTX-A was initially

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approved by the US Food and Drug Administration (FDA) in 1989 for the treatment of strabismus and blepharospasm associated with dystonia [4, 6, 7]. In 1992, Carruthers and Carruthers published their findings that patients injected with BTX-A for blepharospasm also had improvement in the appearance of glabellar rhytids [8]. In 2002, BTX-A was approved for the temporary improvement in the appearance of moderate to severe glabellar lines in adult patients [4, 6, 7]. Since then, BTX-A has been widely used for the treatment of glabellar rhytids as well as other off-label locations in the head and neck. Currently, BTX-A is FDA approved for a wide variety of conditions, including glabellar rhytids, migraine headaches, hyperhidrosis, strabismus, hemifacial spasm, blepharospasm, cervical dystonia, and upper limb spasticity [4, 6, 7, 9].

There are three formulations of BTX-A that are FDA approved for cosmetic use and available commercially: onabotulinum-toxin A (Botox; Allergan Inc), abobotulinum-toxin A (Dysport; Galderma Laboratories), and incobotulinum-toxin A (Xeomin; Merz Pharmaceuticals, LLC). These formulations are FDA approved for the temporary improvement in the appearance of glabellar rhytids in patients aged 18–65 [9–11]. Onabotulinum-toxin A (Botox) is the only product that is also FDA approved for the treatment of lateral canthal lines [9]. It should be noted that all other uses of these formulations for cosmetic purposes are considered off-label. The effects of BTX-A generally last 3–6 months [9–11].

There are variations between these three products in their potency, onset time, and duration [12]. The unit dosing for all three formulations are not interchangeable, with the most notable difference between Dysport and the other two formulations (Botox and Xeomin) [9–11]. Botox and Xeomin are dosed in comparable unit values, whereas Dysport requires 2.5–3 times of its own unit value (Speywood units) to achieve the same result [9–11]. It should be noted that the recommended doses of BTX-A listed in this article will apply to units of Botox and Xeomin. The clinician should make the appropriate adjustment in the number of units used for Dysport.

12.2 Patient Selection and Education

Patient selection and patient education are important factors in avoiding complications with neurotoxin use. There are few contraindications to the use of BTX-A. Patients with neuromuscular disorders, such as myasthenia gravis, amyotrophic lateral sclerosis, Eaton-Lambert syndrome, and motor neuron diseases can be worsened by administration of BTX-A [9–11]. Certain medications (i.e., some antibiotics such as aminoglycosides, calcium channel blockers, neuromuscular-blocking agents, anticholinesterases) can also interfere with neuromuscular transmission and should be avoided as they can enhance the paralytic effect of BTX-A [13, 14].

Relative contraindications include anticoagulant use. If possible, patients are asked to discontinue aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) 7–10 days prior to treatment to avoid excessive bruising [1]. BTX-A is a category C medication for pregnancy and lactation and should be avoided in patients who are pregnant or actively breast-feeding [9–11].

It is important to educate patients how neurotoxins work. Many patients do not understand how neurotoxins work, how they differ from fillers, and what are the limitations of these modalities. In our practice, patients are asked to point out in a mirror which lines bother them. The practitioner can evaluate which of these areas can be improved with neurotoxin use, specifically dynamic versus resting lines. Patients should be educated that neuromodulators will improve dynamic lines in the forehead, glabella, and lateral canthal region mainly. However, static lines, which are made worse by the actions of muscles of facial expression, will not be treated entirely by neurotoxin use. These lines should also be addressed with skin resurfacing or volume replacement (i.e., fillers or fat transfer) [1, 3, 4].

Any asymmetries should be pointed out to the patient and documented in the medical record. New patients should be photographed at rest and in animation prior to treatment. In addition, they should be encouraged to return to the clinic at 2 weeks posttreatment for an evaluation for the

need for touch-up, as well as for photographs. This allows the injector to determine the number of units and location of injections that work best for that particular patient next time. There is a range of units of BTX-A recommended; however, this must be tailored for each patient to improve outcomes and patient satisfaction. This 2-week follow-up can be particularly useful for the novice injector.

12.3 Safety

While patients must be informed about potential adverse effects of BTX-A, patients should be reassured of the long history of safety [1, 2, 4, 15]. Adverse effects associated with BTX-A are rare and tend to be mild and temporary. Common side effects include bruising, swelling, pain around the injection site, headache, and flu-like symptoms [1, 2, 4, 15]. More serious complications, such as brow ptosis or eyelid ptosis, can occur and can be quite disconcerting to both the patient and the practitioner [1, 2, 4]. These complications can be minimized by a thorough understanding of the anatomy of the face and careful injection technique, which will be outlined in this article [1, 2, 4].

The likelihood of bruising can be decreased by advising patients to avoid anticoagulants 7–10 days prior to treatment, if possible [1, 2]. Prominent veins should be noted and avoided to minimize excessive bruising. Vein illumination devices can be helpful in identifying smaller veins, especially in patients with dark complexion.

12.4 Injection Technique for the Upper Face

12.4.1 Glabella

The glabellar complex is responsible for vertical frown lines, which is the most common site for BTX-A injections. Contraction of corrugators, depressor supercilii, and medial orbicularis oculi produces the vertical dynamic lines between the eyebrows, known as "11's." The procerus and depressor supercilii produce the horizontal lines over the bridge of the nose. Together, these frown lines can cause a person to look angry or worried and can project advanced age [1, 2]. The product inserts for Botox injections recommend five injection points (one in the procerus and two in the corrugators bilaterally) (Fig. 12.1) [9]. Some injectors prefer more injection sites along the length of the corrugator supercilii (Fig. 12.2). The recommended dose for the glabellar complex is approximately 20 units. However, most clinicians will tailor the injection technique depending on the gender of the patient, the strength of the muscles, the pattern of rhytids, and the symmetry. Women typically need a lower dose of neurotoxin than men [2]. It is also important to understand if a patient wants to soften the movement of these muscles or eliminate movement of the muscles. Most patients are moving away from the "frozen" look and do want to be able to use these muscles for expression [1, 2].

Care must be taken to inject at least 1 cm from the superior orbital rim and to inject perpendicular to the belly of the muscle. Diffusion of the neurotoxin can cause paralysis of the levator palpebrae superioris, which can lead to upper eyelid ptosis [2, 13, 14, 16]. The abobotulinum-toxin A

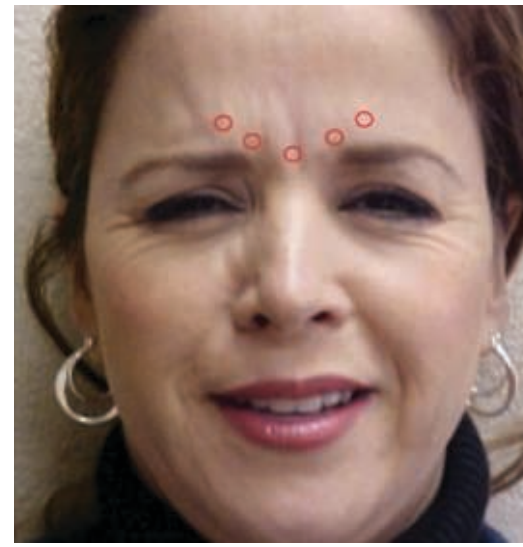

Fig. 12.1 Typical sites for five injection points to glabella

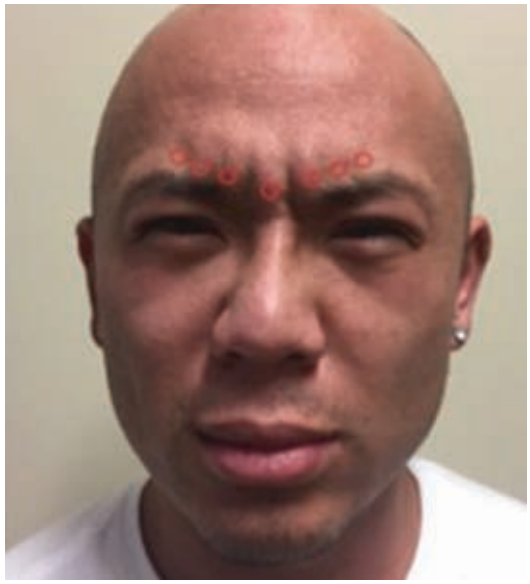

Fig. 12.2 Typical sites for seven injection points to glabella

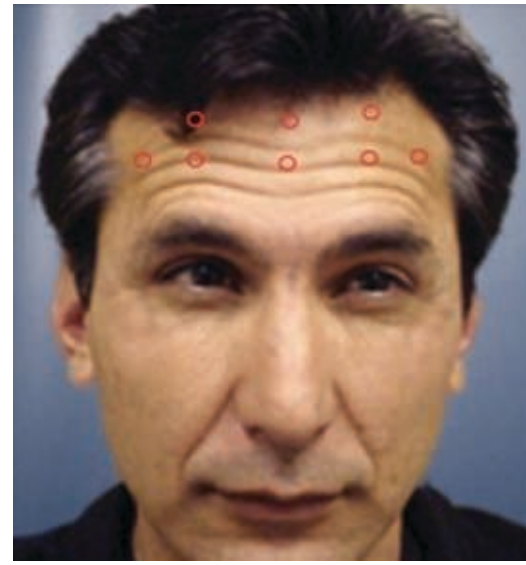

Fig. 12.3 Typical sites for injections to the frontalis muscle. Injections should be 2.5–3 cm above the orbital rim. A total of 10–25 units can be divided into 4–10 injection points based on the pattern of rhytids

(Dysport; Galderma Laboratories) has been shown to have a wider dispersion radius than the other BTX-A formulations. It is therefore this author's opinion that the clinician should be even more cautious with abobotulinum-toxin A in the lateral brow region especially in older individuals with existing brow ptosis and aging [17]. Ptosis can be managed with apraclonidine 0.5% eye drops (three times per day) until symptoms resolve [13, 14, 16]. Apraclonidine is an alpha-2-adrenergic agonist, which stimulates Mueller's muscle and can lead to a 2 mm elevation of the ptotic eyelid [1].

12.4.2 Forehead

The frontalis muscle elevates the brow and leads to horizontal forehead rhytids. The frontalis is a large, vertically oriented muscle with significant variation between individuals. While it is usually depicted as two fan-shaped bands, there may be overlap of midline fibers. Those that have a central tendinous attachment may not need midline injections. The forehead shape varies in both the horizontal and vertical direction [1, 2]. The rhytid pattern also varies, with some patients having numerous fine lines whereas others have one or two deep lines. These anatomic variations, as well as the amount of movement the patient desires, affect the injection pattern and dose of neurotoxin used.

In general, the goal of treatment should be to soften the forehead lines while maintaining expressiveness and avoiding brow ptosis. Some recommend injecting above the midline of the forehead to avoid brow ptosis. Others site a safe zone 2.5–3 cm above the orbital rim. Typically the glabella is injected along with the forehead for a harmonious effect. Typical dosing for the forehead is between 10 and 25 units, which can be divided into 4–10 injection points depending on the rhytid pattern (Fig. 12.3) [1, 2, 6].

Patients may return complaining of asymmetry or peaking of the lateral brow after BTX-A injections to the forehead (Fig. 12.4). A thorough preoperative evaluation of eyebrow position and movement may help avoid asymmetries following neurotoxin use. Placing injection sites lateral and high enough on the forehead can minimize peaking of the lateral brow and at the same time avoid brow ptosis [1, 2]. These situations can be easily managed at the follow-up visit by injecting

Fig. 12.4 Peaked lateral brows can occur after neurotoxin injection to the frontalis. This woman presented with peaked lateral brows 2 weeks after injection of 15 units to the frontalis muscle

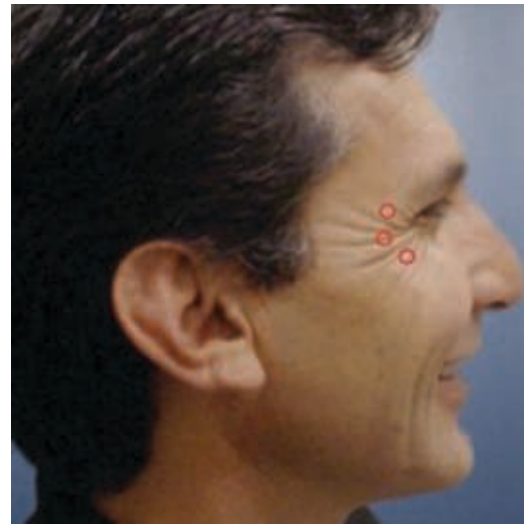

Fig. 12.5 Typical sites for injection to orbicularis oculi (crow's feet). A total dose of 10–30 units can be used, divided into 2–5 points per side. Injection points should remain 1–1.5 cm from the orbital rim and 1.5 cm from the lateral canthus

small amounts of neurotoxin in the area with too much movement. For lateral peaking, 2–3 units of BTX-A can be injected in the lateral forehead. It is advisable to wait 2 weeks after the initial injection before doing a touch-up, as there may be variation in how quickly muscles respond to the neurotoxin [2, 9]. It is important to document all touch-ups so that the following treatment can be tailored accordingly. It is a good idea to mention to patients prior to injecting them that small corrections may be needed at the follow-up visit.

12.4.3 Brow Elevation

The resting position of the brow is dependent upon the balance between the depressors of the brow and the elevator of the brow (the frontalis). Injection of neurotoxin in the glabellar complex can produce up to a 2 mm medial brow elevation. Injecting the superolateral orbicularis oculi immediately below the desired level of elevation can lead to lateral brow elevation. This injection should be superficial. Injecting too high in this area can lead to spread of neurotoxin to the frontalis which may lead to paradoxical brow ptosis. Injecting too close to the orbital rim may lead to unwanted spread of neurotoxin which can lead to upper eyelid ptosis [1, 2]. Typically women will prefer greater brow elevation than men [2].

12.4.4 Crow's Feet

Lateral orbital rhytids ("crow's feet") result from contraction of the orbicularis oculi as well as photoaging. The orbicularis oculi is a sphincter-like muscle, which encircles the eye. Smiling or squinting causes contraction of the muscle and over time, can lead to rhytids which extend radially from the lateral canthus. The injection technique in this region should match the pattern of wrinkles and should remain superficial, producing a characteristic wheal. A total dose of 10–30 units can be used, divided into 2–5 points per side (Fig. 12.5) [1, 2]. Typically men will tolerate more smile lines than women [2].

Injection points should remain 1–1.5 cm from the orbital rim and 1.5 cm from the lateral canthus to avoid unwanted spread of neurotoxin [1, 2, 18]. Spread into the orbit can weaken the lateral rectus or inferior rectus leading to diplopia

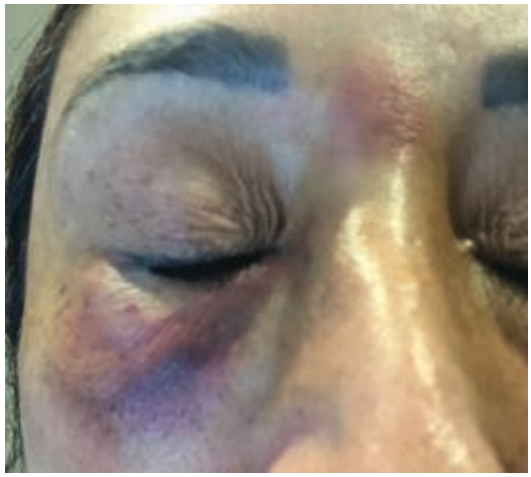

Fig. 12.6 Significant bruising after BTX-A injection to the crow's feet

[18]. Practitioners must be careful not to inject too far inferiorly. Inadvertent injection of the zygomaticus major muscle can affect upper lip tone and lead to lip asymmetry [13, 14, 16].

Lower-eyelid lid laxity should be evaluated with a snap test prior to injection. Those with laxity have increased risk of ectropion; therefore, injections should not be placed too medial or too inferior [2]. In general, injections should not be placed medial to the mid-pupillary line as there is increased risk of ectropion and epiphora [19]. There tends to be small, tortuous veins lateral to the eye, so bruising may occur with these injections (Fig. 12.6). A vein illuminator device may be helpful in avoiding veins. Ice before and after injections may also help to minimize bruising.

12.5 Bunny Lines

"Bunny lines" occur from animation of the periocular region and wrinkling of the nose. Contraction of the transverse portion of the nasalis muscle leads to wrinkling on the lateral nasal sidewall [1, 2]. The nasalis muscle originates from the maxilla and runs diagonally across the bridge of the nose [2]. It is important to differentiate bunny lines from transverse lines resulting from contraction of the procerus muscle as the injection technique is different [2].

Fig. 12.7 Typical appearance of bunny lines, caused by contraction of the nasalis. One to four units is injected superficially per side

A low dose (1–4 units) can be injected per side to target the transverse portion of the nasalis (Fig. 12.7). Injections should be superficial as this is a vascular area [2]. Care must be taken to palpate and avoid the angular artery, which tracks superiorly along the lateral nose [1]. Injection sites should avoid the levator labii alaeque nasi and levator labii superioris to prevent drooping of the upper lip. Injection sites should not be vigorously massaged in a downward direction as this may also cause unwanted spread of the neurotoxin [2].

12.6 Injection Technique for the Perioral Region

Sun damage, smoking, aging, and expression can lead to excessive vertical perioral rhytids. These unesthetic fine lines are best addressed with a combination of neurotoxin, fillers, and skin resurfacing [1–3]. The benefits and limita-

tions of each of these modalities should be thoroughly discussed with the patient. Neurotoxin use in the perioral region should be reserved for experienced practitioners as there is a complex interaction of muscles, specifically the orbicularis oris, depressor anguli oris, and mentalis [2].

12.6.1 Orbicularis Oris

The orbicularis oris is a sphincter-like muscle, which encircles the lips and contributes to the formation of perioral rhytids. Injection sites should be superficial and symmetric. Injection sites are typically along the upper and lower lip, with at least one site per quadrant of the mouth. The midline should be avoided as it may lead to flattening of the lip. The total dose for both lips is approximately 5–6 units with each injection point containing 0.5–2 units (Fig. 12.8). Injections can be placed just above the vermillion border or a few millimeters above the border. Injections that are too high can cause unwanted effects on the upper lip, such as eversion, inversion, or ptosis. Ice and/or topical numbing cream can be used for pain control [2].

Overtreatment of the perioral region can lead to serious dysfunction, such as difficulty with speech ("b" and "p" sounds), eating, drinking through a straw, pursing the lips, brushing the teeth, as well as decreased proprioception. Patient selection and education is paramount. Individuals who rely on their lips for their profession (i.e., musicians, singers, public speakers) are not good candidates for perioral neurotoxin injections. Treatment should be conservative and cautious [2].

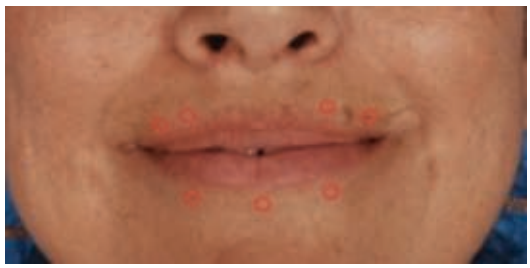

Fig. 12.8 Typical injection sites for the orbicularis oris. The total dose is approximately 5–6 units with each injection point containing 0.5–2 units

12.6.2 Depressor Anguli Oris

The depressor anguli oris (DAO) originates from the mandible and inserts into the angle of the mouth. The DAO pulls the corner of the mouth down and back, which contributes to a frowning appearance and the "marionette lines."

The DAO should be injected with low doses (2–5 units per side), typically with two injection sites per side (Fig. 12.9). If injection of the DAO is too close to the mouth, it can lead to unwanted spread of neurotoxin leading to oral incompetence, an asymmetric smile, and drooling (Fig. 12.10) [2].

12.6.3 Mentalis Muscle

The mentalis muscle is a paired muscle in the midline of the chin. It originates from the man-

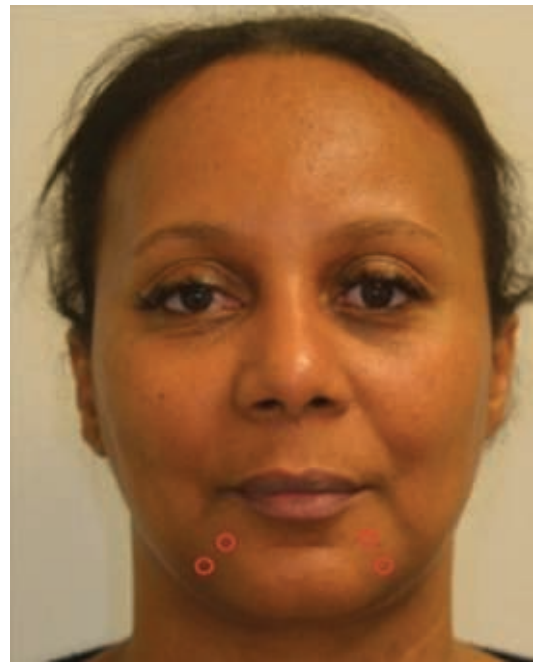

Fig. 12.9 Typical injection sites for the depressor anguli oris. A total of 2–5 units is injected per side

Fig. 12.10 An asymmetric smile is a potential complication that can occur if injections of the depressor anguli oris are too close to the mouth. This woman presented 2 weeks after 5 units were injected to mentalis and 2.5 units to each depressor anguli oris

dible, covers the chin, and inserts into the skin below the lower lip. Contraction of the mentalis raises the level of chin and everts the lower lip. Contraction of the muscle, along with loss of collagen and subcutaneous fat, causes the peau d'orange (dimpling) of the chin. While the mentalis is a paired muscle, only one central injection with neurotoxin is needed. The injection should be in the midline of the mentalis, angled upward. The muscle should be massaged laterally. The typical starting dose of BTX-A is 4–6 units but can be as much as 10–12 units [2].

Care should be taken to avoid injecting too high on the chin as this can affect the orbicularis oris, leading to lip incompetence and drooling. Avoid injecting the depressor labii as this can cause the lower lip to droop. Some patients with a dimpled chin may have a hypertrophic mentalis muscle in the setting of retrogenia and oral incompetence. These individuals should not be treated with neurotoxin as it may worsen the oral incompetence [2].

Some patients are unaware of chin dimpling, which typically appears during speech and with animation. This can be demonstrated with a hand mirror. Women are treated more often than men as their chins are more likely to develop dimpling. Treatment of this region can be beneficial in those undergoing a chin implant [2].

12.7 Injection Technique for the Neck

12.7.1 Platysma Bands

Platsyma bands in the neck may become prominent with age or after rhytidectomy. BTX-A can be a useful way to soften the bands in patients with adequate skin elasticity and minimal submental fat. The platysma depresses the mandible, everts the lower lip, and pulls the corners of the mouth down and back. Injection sites are placed approximately 1 cm apart along the band, with 3–5 sites per band (Fig. 12.11). The total dose ranges from 20 to 30 units depending on how many bands are treated and the number of injection sites per band. The patient should be asked to contract and the practitioner should grasp the band with the nondominant hand while injecting neurotoxin directly into the belly of the muscle. This technique avoids unwanted diffusion of neurotoxin into strap muscles which

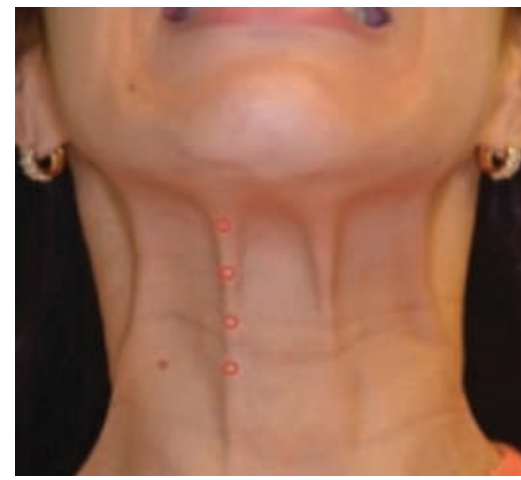

Fig. 12.11 Typical sites for injections to platysma bands. Injection sites are placed approximately 1 cm apart along the band, with 3–5 sites per band, for a total of 20–30 units

can lead to neck weakness, dysphagia, and dysphonia [2, 19].

Patient selection is important as this works best in younger patients with good skin elasticity. Patient's expectations should be reasonable as platysma band injection is not a substitute for surgery and will not improve skin elasticity. Platysma band injection can be useful approximately 2 weeks before liposuction of the submental region or before skin resurfacing. Platysma band injection can be combined with injection of the DAO and fillers to restore volume in the perioral region [2, 19].

Conclusion

While not true complications, there are unwanted sequelae of neurotoxin use, such as swelling, injection site pain, needle marks, mild erythema, bruising, and rarely hematoma [1, 9–11, 13, 18]. Earlier onset of action in one anatomic site occurs commonly and is not a true complication [1]. This may manifest as an asymmetry in brow movement and patients should be warned that this might happen. It is best to wait 2 weeks for neurotoxin to take full effect before considering a touch-up, as minor discrepancies may correct themselves as the neurotoxin takes effect [9, 10].

Pain at injection sites can be minimized by using smaller-gauged needles. Ice or topical numbing cream can be used. Bleeding and bruising can be minimized by holding anticoagulation 7–10 days prior to the procedure, icing immediately before injection, avoiding vessels, and injecting superficially. Bleeding can be managed by holding pressure and applying ice.

The most disconcerting complications are unwanted spread of neurotoxin and neuromuscular blockade of unintended muscles. For example, injection too low on the forehead may lead to brow ptosis. Injection of the glabella, which is too close to the orbital rim, may lead to upper eyelid ptosis. Injection of the crow's feet, which is too close to the eye, may result in diplopia. Injection of the crow's feet too low on the cheek can lead to upper lip asymmetry. Injection in the perioral region can lead to oral incompetence, difficulty with speech and eating, lip asymmetry, and drooling. Injection of the platysma bands can lead to dysphonia, dysphagia, and neck weakness [1, 2, 13, 14, 16, 19]. In general, such complications are rare and can be avoided by respecting the anatomy of the face and neck and injecting with care.

The use of botulinum toxin type A in cosmetics has expanded greatly since its approval by the Food and Drug Administration (FDA) for reduction of glabellar rhytids. Botox is also approved for lateral canthal lines [9]. Experienced clinicians have been using BTX-A in other areas off-label to improve the appearance of rhytids and facial harmony.

The recommendations and diagrams presented in this article should serve only as general guidelines. Treatment planning must be tailored to individual variation. Thorough preoperative evaluation of the muscles of facial expression and rhytid pattern as well as careful injection technique can avoid most complications associated with neurotoxin use. Understanding the patient's goals of treatment and pointing out any limitations will improve outcomes and patient satisfaction.

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