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Botulinum Toxin for Facial Rejuvenation

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21.1 Introduction

Botulinum toxin has evolved over the last few years becoming both the patient and the plastic surgeon's best friend! Botox® Cosmetic is a household name, often referenced in movies, reality television shows, and the news, and lauded by many as a miracle antiaging drug. It is no wonder then, that Botox® Cosmetic is now interwoven into the fabric of our society. It works quickly with minimal downtime and is relatively painless in reducing facial wrinkles. The use of botulinum neurotoxin is the most common noninvasive cosmetic procedure in the USA with five million treatments performed in 2008. This figure represents a 537% increase in these procedures as compared to the year 2000 [1]. In addition, a new commercially available botulinum toxin, Dysport®, has been approved by the FDA for facial wrinkle treatment as an alternative to Botox® Cosmetic. Therefore, it is very important to have an understanding of the botulinum toxin's chemical properties, mechanism of action, commercial preparations, and clinical data regarding its administrations in order to avoid complications and to deliver maximal aesthetic results to one's patients.

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21.2 History

Classic botulism was first observed by Julius Kerner, a medical officer, who reported symptoms of skeletal and gut muscle paralysis, myadriasis, and maintenance of consciousness after the ingestion of improperly preserved foods in 1820 [2]. More than a century later, in 1973, Scott et al. described the first clinical application of botulinum toxin while investigating nonsurgical treatments of strabismus in a primate model [3, 4]. Subsequently, botulinum toxin type A was discovered to have widespread applications as a neuromuscular blocker in neurology, orthopedics, gastroenterology, and ophthalmology, eventually earning Food and Drug Administration (FDA) approval for disorders involving the facial nerve, adult strabismus, and blepharospasm in 1989 [2]. Cosmetic use of botulinum toxin type A is largely credited to Carruthers and Alistair in 1987, when they observed the aesthetic improvements and lessening of glabellar lines after injecting the neurotoxin into patients with blepharospasm [5]. This led to subsequent clinical trials and FDA approval of the use of Botox® Cosmetic to improve the appearance of glabellar lines in April 2002. Over the next few years, Botox® Cosmetic gained worldwide popularity as a safe and effective drug to treat facial wrinkles. Off-label usage for other facial muscles became widespread, and satisfaction was reportedly high and consistent. In April 2009, the FDA announced the approval of a new botulinum toxin type A formulation, Dysport®, for two separate indications: the treatment of cervical dystonia and the temporary improvement in the appearance of moderate to severe glabellar lines. The latter is currently being marketed by Medicis in the USA for its aesthetic indications. Dysport® has been used for cosmetic

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purposes in the UK since 1991 and has been approved in 27 other countries for aesthetic use with over two million single treatment cycles [6].

21.3 Chemical Overview

Botulinum neurotoxins are produced by the gram-positive anaerobic bacterium Clostridium botulinum (Fig. 21.1). Various strains of this bacterium exist, resulting in eight immunologically distinct serotypes: A, B, C1, C2, D, E, F, and G, seven of which are associated with paralysis [7, 8]. Botulinum neurotoxin types A and B have been extensively studied and are the only two to be used routinely for clinical purposes [9]. Currently, type A is the only serotype approved by the FDA for cosmetic purposes.

Botulinum toxin serotypes are synthesized as macromolecular complexes containing 150 kDa neurotoxin molecules as well as one or more nontoxin proteins [10]. The exact structure and molecular weight is determined by the clostridium strain that produced the neurotoxin and its particular serotype [10]. Furthermore, the percentage of active neurotoxin differs between the various serotypes [10]. Botulinum toxin type A forms a 500 kDa protein complex and 95% of its neurotoxin molecules are in the active form [10]. The 150 kDa neurotoxins can be converted into their active form by endogenous or exogenous proteases that nick the toxin into two polypeptide fragments, a 100 kDa heavy chain and 50 kDa light chain, that remain linked by a disulfide bond [10, 11]. The 100 kDa heavy chain portion of the active neurotoxin is responsible for binding of botulinum neurotoxin to membrane receptors at peripheral cholinergic nerve terminals [10, 12]. Once bound, the entire 150 kDa neurotoxin undergoes endocytosis and subsequent conformational change whereby the 50 kDa light chain moves out of the vesicular compartment and into the cytosol [10, 13]. Once in the cytosol, the light chain portion of the active neurotoxin acts as a zinc-dependent endopeptidase that inactivates one or more proteins of the SNARE complex, thereby inhibiting vesicular exocytosis [10, 14].

In comparing various preparations of botulinum toxin for medical use, it is important to consider the percentage of nicked versus unnicked neurotoxin, as the unnicked toxins may allosterically inhibit binding of nicked toxin to its intended receptor sites, thereby decreasing its potency [9]. Botulinum toxin type A is the most commonly used serotype for cosmetic practice because of its potency which is generated by endogenous proteases [10, 15]. Other serotypes, such as type B, may only be partially nicked and, therefore, not as potent when recovered from bacterial cultures [10, 16]. Clinical preparation of type B and other partially nicked or unnicked serotypes often require an additional "nicking step" where the unnicked toxin is exposed to exogenous proteases to increase the percentage of active neurotoxin [10] The active neurotoxin can be inactivated by heat, 85°C (185°F) or greater, for 5 min [17].

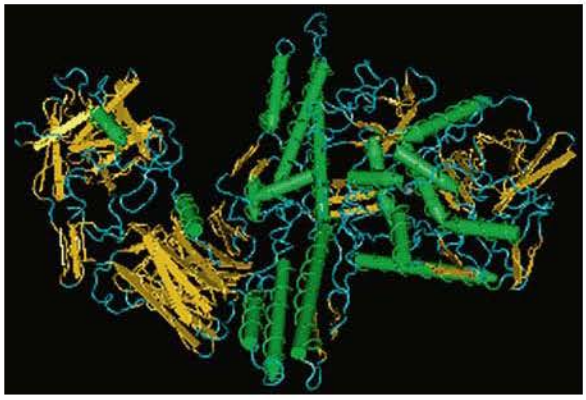

Fig. 21.1 Crystal structure of botulinum neurotoxin serotype A [6] (US National Library of Medicine Molecular Modeling Database http://www.ncbi.nlm.nih.gov/Structure/mmdb/mmdbsrv.cgi?uid=11100)

21.4 Specific Mechanism of Action

Botulinum neurotoxin causes temporary muscle paralysis by inhibiting acetylcholine release at peripheral cholinergic nerve terminals [17]. The various serotypes act via different intracellular molecules at presynaptic nerve endings. Botulinum toxin type A specifically cleaves SNAP-25 of the SNARE complex, preventing vesicles from anchoring and fusing with presynaptic membranes, thereby blocking acetylcholine release at the neuromuscular junction [4, 17]. The various neurotoxin serotypes cleave different intracellular SNARE proteins or the same protein at different sites [10]. Proper intramuscular injections of botulinum toxin type A at therapeutic doses cause partial

chemical denervation of muscle fibers resulting in localized reduction of muscle activity [17]. This is not a permanent effect, as new nerve endings form and recovery of acetylcholine transmission gradually occurs. As such, the effects of botulinum neurotoxin are temporary, and muscle activity should start returning within 4–6 months.

21.5 Onset and Duration of Paralysis

Although each botulinum neurotoxin has its unique onset of paralysis, period of clinical efficacy, and time of recovery, many generalities can be made in regards to the most commonly used serotype, type A [4]. Once facial muscles are injected with botulinum neurotoxin type A, clinical effects start becoming noticeable within 48–72 h, and paralytic effects peak during the following 7–14 days followed by approximately 90 days of steady results [4]. By the end of this period, new neuromuscular junctions and axonal sprouts will have replaced the nonfunctional junctions, so reinjection is generally recommended in 3–4 months [18]. The amount of time between injections will vary depending on which facial area is being treated. Stronger facial muscles, such as the corrugator supercilii and procerus muscles, may require more frequent treatments than the weaker orbicularis occuli, as an example. Furthermore, anatomical differences, genetics, age, gender, and skin quality may affect botulinum injection results. Questions still remain regarding the very long-term effects of botulinum toxin on muscle potency as more research needs to be conducted in this area.

21.6 Preparation of Botox® Cosmetic

Standard units of measurement for botulinum toxin are important to assess the potency of various serotypes. Units of biological activity (U) for botulinum toxin serotypes are determined according to a mouse lethality assay, where 1.0 U represents the amount of neurotoxin complex protein that is lethal in 50% of female mice following an intraperitoneal injection [7].

The most frequently used formulation of botulinum neurotoxin type A includes the 900 kDa formulation (Botox® Cosmetic; Allergan; Irvine, California). Botox® Cosmetic is packaged in a vial containing 100 U of vacuum-dried neurotoxin complex (approximately 4.9 ng of protein), 0.5 mg of human albumin, and 0.9 mg of sodium chloride for a composite pH of 7.0 [17]. Botox® Cosmetic requires reconstitution with non-preserved sterile 0.9% sodium chloride before clinical use [17]. Reconstituted Botox® Cosmetic should be "clear, colorless and free of particulate matter" [17]. Members of the Botox® Cosmetic consensus panel noted that most clinicians use a dilution of 2.5–3.0 ml of 0.9% non-preserved saline per vial to obtain a reconstituted solution at a concentration of 4.0 Units/0.1 ml [18]. They also noted that a number of dilutions are acceptable and depends on practitioner preference as well as the total number of units to be injected [18]. The authors dilute 100 U of Botox® Cosmetic in 4.0 ml of non-preserved sterile 0.9% saline to simplify the process of loading syringes and injecting with consistency. In this case, 1.0 ml will contain 25 U of Botox® Cosmetic which will simplify calculations of how much Botox® Cosmetic is injected in each area. The dosage can be adjusted based on each individual patient's anatomy and, ultimately, their results.

Unopened 100 U vials of Botox® Cosmetic are stable for up to 24 months when refrigerated at 2–8°C [17]. Since botulinum toxin type A solution does not contain a preservative, it should be administered within 4 h after reconstitution [17]. The manufacturer recommends use of the entire reconstituted product within 4 h when stored at 2–8°C for maximum efficacy [17]. Clinically, we have noted that Botox® Cosmetic stays effective even when administered after the recommended 4 h have elapsed. One study demonstrated that reconstituted botulinum toxin type A maintains its efficacy and potency in treatment of glabellar frown lines for up to 6 weeks with proper storage at 4°C [19].

21.7 Preparation of Dysport®

Dysport®, a 500–900 kDa formulation (Dysport®; Medicis; Scottsdale, Arizona) [4] of botulinum toxin type A, was originally launched in 1991 and was approved by the US FDA in April 2009. Similar to Botox® Cosmetic, Dysport® has shown a good safety profile and low incidence of treatment failures. Although both Dysport® and Botox® Cosmetic contain botulinum toxin type A, they differ in their process of manufacture and potency determination, method of

purification, and formulation. Consequently, Dysport® and Botox® Cosmetic should be regarded as individual botulinum toxin type A products with their own individual unit dosing requirements rather than generic equivalents [20].

Dysport® is formulated by fermentation of the bacterium Clostridium botulinum. The neurotoxin is recovered through a series of steps including chromatography, precipitation, dialysis, and filtration [20]. The recovered complex is then dissolved in an aqueous solution of lactose and human serum albumin which is then filtered and freeze-dried [20]. Unlike Botox® Cosmetic, the lactose in Dysport® acts as a bulking agent [20]. Therefore, the product seen in the vial resembles a small cake of white powder facilitating its reconstitution with saline prior to clinical use [19]. Dysport® is packaged as a freeze-dried powder in a single-use vial in which 5.0 U contains 12.5 ng of protein, 2.5 mg of lactose, and 125 μg of albumin [21]. Each 300 U vial of Dysport® is to be reconstituted with 2.5 ml of 0.9% sterile, preservative-free saline before injection [21]. Reconstituted Dysport® should be a clear and colorless solution [21]. Dysport® is stable for 1 year when refrigerated at 2–8°C [21]. Once reconstituted, Dysport® should be stored in the original container at 2–8°C and used within 4 h of reconstitution [21].

21.8 Comparing Botox® Cosmetic and Dysport®

Botox® Cosmetic and Dysport® differ in terms of their preparation and formulation, including the method of extraction, diluents and stabilizers used, and recommended volume of injection [22]. One of the main differences in their formulations is the protein concentration. Dysport® contains 12.5 mg of protein per 500 U whereas Botox® Cosmetic contains approximately 5.0 mg more protein per 100 U [17, 21]. This is significant since botulinum toxin proteins can cause an immune response at high doses. An immune response can lead to the development of neutralizing antibodies that prevent the effects of the neurotoxin [23]. Therefore, protein load and potential for antibody formation are two factors that physicians must bear in mind when choosing a formulation for botulinum toxin therapy. Additional research is needed to determine the clinical significance of lower protein load of Dysport® as compared to Botox® Cosmetic.

Due to manufacturing differences, a single unit of Botox® Cosmetic differs in potency from a single unit of Dysport®. This results in a marked difference in dosing between these two products. Since Botox® Cosmetic has been the most widely used botulinum toxin type A preparation, the clinical efficacy of Dysport® is described in reference to it. Clinical studies have described doses of Dysport® that can be 2.5–6 times higher compared to doses of Botox® Cosmetic when treating the same condition [24, 25].

The difference between the potency units of Botox® Cosmetic and Dysport® remains a controversial issue despite 15 years of clinical studies. The manufacturer of Botox® Cosmetic supports higher conversion ratios, 4–5:1 (Dysport®: Botox® Cosmetic), which is the current consensus among medical faculty. On the other hand, the manufacturers of Dysport® argue that a lower conversion factor of 3–2.5:1 (Dysport®: Botox® Cosmetic) is just as efficacious [26].

It has also been suggested from clinical studies that Dysport® is likely to diffuse further from the injection site than Botox® Cosmetic and that the Botox® Cosmetic formulation provides a longer dose ratio of 2.5:1 (Dysport®: Botox® Cosmetic) [10, 27]. However, these data are heavily contested and more research is needed regarding this topic. Since its use in 1991, Dysport® has been shown to be effective and safe in treating the upper face, but long-term safety data regarding diffusion and other effects in aesthetic indications are much more limited than for Botox® Cosmetic.

21.9 Botulinum Toxin Type A Injection and Follow-Up Care

In order to minimize common local reactions to botulinum toxin therapy (i.e., bruising), it is recommended that patients refrain from taking medications that inhibit clotting such as vitamin E, aspirin, and nonsteroidal anti-inflammatory drugs 10–14 days before treatment. Pain is commonly reported by patients as a result of botulinum toxin type A injections and can be markedly reduced by pretreating the area with ice for 5 min prior to injection or applying a local anesthetic cream such as betacaine, or both. Pre- and posttreatment application

of ice is a safe, cost-free, and effective skin analgesic that has been shown to significantly decrease pain perception, swelling, and bruising as well as the duration required to complete a series of injections [28]. Patients should be instructed not to massage the injection sites to avoid unintentional diffusion of the botulinum toxin [4]. Mode of injection may vary between physicians. The authors recommend injecting with a 1.0 ml syringe and a 30 gauge needle for ease of injection, consistency, and minimal pain to the patient.

More research is needed regarding the effects of exercise on botulinum toxin injections. According to the American Society of Plastic Surgeons (ASPS), 28% of its members from one particular study permit their patients to exercise immediately after treatment [9]. An additional 50% allow exercise later the same day of treatment, and the remaining 22% recommend waiting until the following day [9].

21.10 Locations of Treatment

In the upper face, botulinum toxin type A is indicated for treatment of wrinkles caused by the hyperdynamic muscular action of the corrugator supercilii and procerus muscles (glabellar wrinkles), the orbicularis oculi muscles (lateral canthal fold wrinkles or crow's feet), and the frontalis muscle (forehead wrinkles). In the lower face, botulinum toxin type A is used to treat the wrinkles formed by the orbicularis oris, the mentalis, and the platysma with its corresponding transverse neck lines. When treating each area, it is important to track injection location, number of injection points, and total units of botulinum toxin used. This section discusses recommended doses of Botox® Cosmetic for different locations of treatment based on the results of consensus recommendations from a study conducted by the ASPS [9].

21.10.1 Upper Face

The three principal areas of Botox® Cosmetic treatment in the upper face are the frontalis muscle, which contributes to formation of transverse forehead lines, the corrugator supercilii and procerus muscles, which contribute to formation of glabellar lines (Figs. 21.2 and 21.3), and the orbicularis oculi muscles, which contribute to formation of crow's feet (Fig. 21.4). Consensus recommendations on number of Botox® Cosmetic units for treating the upper face has decreased overall; however, the range of injection points remains unchanged. For transverse forehead lines, the recommended range of Botox® Cosmetic units is 6–15 U for women and 6–15 U or greater for men [9]. This is a marked decrease from older recommendations which suggested using 10–20 U for women and 20–30 U for men. The recommended range in number of injection points for transverse forehead lines remains 4–8.

To treat the corrugator and procerus muscles of the glabellar complex, 10–30 U of Botox® Cosmetic is recommended for women versus 20–40 U for men [9]. The recommended range of injection points for the glabellar lines remains 5–7, although men may require more sites. It is important to inject the whole length of the corrugator muscle extending to the area above the pupil, otherwise the wrinkle correction may be incomplete. When there are furrows in the glabellar region, supplementing botulinum toxin injections with filler, such as a hyaluronic acid, may improve the results by addressing the dermal component of the wrinkle, whereas the botulinum toxin addresses the muscle component. The two injectables may be done simultaneously or on separate visits.

The current recommended dosage for treating crow's feet is 10–30 U of Botox® Cosmetic for women and 20–30 U of Botox® Cosmetic for men [9]. The crow's feet are the only facial muscles where recommended doses are relatively unchanged for women and increased for men. The recommended range of injection points for crow's feet remains 2–5 per side. The pattern of wrinkles varies tremendously in this area. One must be able to differentiate wrinkles caused by sun damage versus wrinkles caused by hyperdynamic muscle activity. Botulinum toxin is very effective for treating the latter; however, skin wrinkles may need to be addressed by fillers, surgery, laser treatments, or other modalities.

At our institute, the amount of Botox® Cosmetic injected is usually based on each individual's anatomy and prior clinical experience with Botox® Cosmetic, when applicable; however, we have tended to see better results when injecting the forehead in the 20–25 U range for both men and women. This observation holds true for all three areas of the upper face.

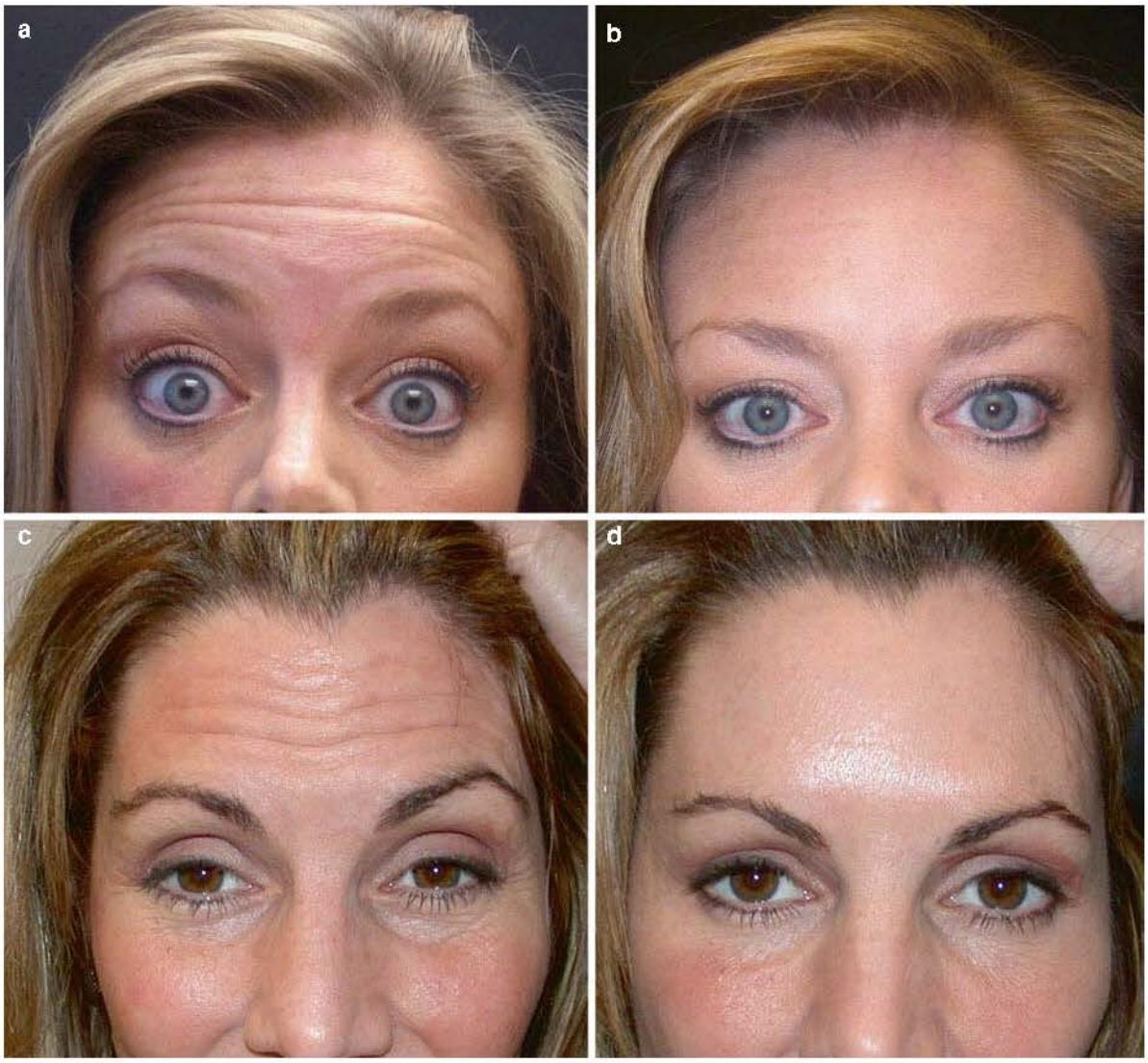

Fig. 21.2 Frontalis muscle (forehead wrinkles) treatment with Botox® Cosmetic. (**a**, **c**) Pretreatment. (**b**, **d**) Posttreatment

21.10.2 Midface

The current consensus for treating the midface is that volume restoration via fillers produces a more aesthetically pleasing result over rhytid reduction using botulinum toxin. In treating areas of the midface, such as malar smile lines and nasolabial folds, the majority of medical faculty from the ASPS study advised against the use of botulinum toxin alone to avoid causing a frozen look or an inability to smile [9]. The exception is malar wrinkles as an extension of crow's feet, where the injection of botulinum toxin can be done more medially when injecting the crow's feet.

21.10.3 Lower Face

Treating the lower face with botulinum toxin is not as readily accepted by plastic surgeons as treating the upper face because of alternative methods of treatment, lack of consistently great results, or a combination of these reasons. Botox® Cosmetic is currently recommended

Fig. 21.3 Corrugator and procerus muscles (glabellar wrinkles) treatment with Botox® Cosmetic. (**a**, **c**) Pretreatment. (**b**, **d**) Posttreatment

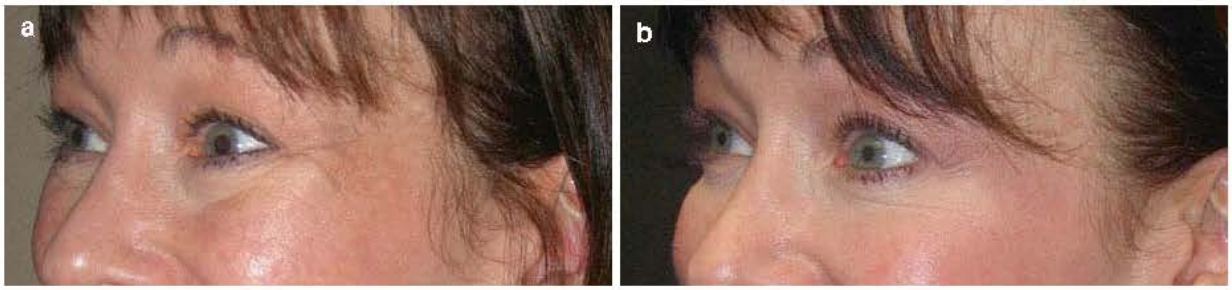

Fig. 21.4 Orbicularis oculi (crow's feet wrinkles) treatment with Botox® Cosmetic. (**a**) Pretreatment. (**b**) Posttreatment

for treating three targeted muscles of the lower face. These include the orbicularis oris, which contributes to the development of perioral wrinkles with aging, the mentalis, which leads to formation of an irregular chin contour due to muscle hyperactivity (Fig. 21.5), and the platysma bands, which become more prominent with aging. For perioral wrinkles, the consensus recommendation is 4–5 U of Botox® Cosmetic for both

men and women, and two to six injection points total for both lips [9]. In treating the mentalis area, 4–10 U of Botox® Cosmetic is recommended for both men and women, and one to two injection points [9]. To treat the platysma bands and corresponding horizontal neck lines, the recommended dosage is 40–60 U of Botox® Cosmetic total per neck (about 10 U per band on average) [9]. The recommended number of injection points for this area is 2–12 per band for women and 3–12 per band for men. At our institute, we tend to favor fillers and surgical correction for the lower face over the use of botulinum toxin.

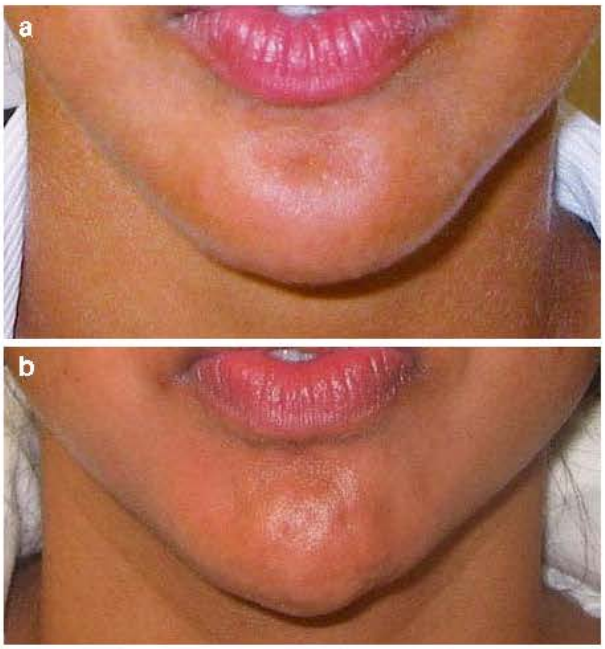

Fig. 21.5 Mentalis (dimpled chin) treatment with Botox® Cosmetic. (**a**) Pretreatment. (**b**) Posttreatment

21.11 New Frontiers for Botulinum Toxin in Facial Rejuvenation

Now that botulinum toxin has become a staple of the plastic surgery world, it is not all that surprising that it is being used in cosmetic treatments outside of its conventional use in reducing facial wrinkles. One example is the use of botulinum toxin in treating excessive gingival display or "gummy smile" (Fig. 21.6) as an alternative to surgery. The elevator muscles of the upper lip include the levator labii superioris, levator labii superioris alaeque nasi, levator anguli oris, zygomaticus major and minor, and depressor septi nasi [9]. At our institute, we inject about 25 U total of Botox® Cosmetic to the levator labii superioris and orbicularis oris muscles to resolve a "gummy smile."

Another emerging trend is the use of botulinum toxin for masseter reduction in treating facial widening [9]. According to the ASPS, clinicians who treat this area use anywhere from 10–50 U of Botox® Cosmetic per side; however, 25–30 U per side is generally recommended [8]. In treating facial widening with botulinum toxin, the underlying cause should be the masseter muscles and not mandibular bony prominence [9].

Fig. 21.6 Excessive gingival display (gummy smile) treatment with Botox® Cosmetic. (**a**) Pretreatment. (**b**) Posttreatment

21.12 Contraindications

Botulinum toxin is contraindicated for patients with known hypersensitivity to any ingredient in the formulation, including albumin [17]. It should not be used in treating special patient populations with known neuromuscular disorders and peripheral motor neuropathies such as multiple sclerosis, Eaton–Lambert syndrome, and myasthenia gravis since further muscle paralysis may exacerbate muscle weakness [4, 17].

Since Botox® Cosmetic is considered a category C drug, it should be avoided in women who are pregnant or breastfeeding. Also, the physician should be cautious when using Botox® Cosmetic in patients who have had surgery in the target area since muscles may have been repositioned or weakened, and also in patients who have any inflammatory skin conditions at the injection site [29]. Furthermore, people who have had an allergic reaction to tetanus immunization should refrain from having Botox® Cosmetic injections in case of an allergic reaction.

Dysport® is contraindicated for patients with any of the above stated hypersensitivities to botulinum toxin preparations. Dysport® is also contraindicated in patients known to have allergies to cow's milk protein since Dysport® may contain trace amounts of these proteins [21].

21.13 Avoidance of Potential Pitfalls

General complications associated with botulinum toxin treatment include mild erythema at the site of injection that may last a few hours due to needle sticks. Ecchymosis may last a few days and most commonly occurs when injecting crow's feet, where the skin is thin and the veins are more superficial. Ecchymosis can be reduced by advising patients to avoid taking any aspirin or other anticoagulants prior to treatment as well as applying local anesthetic cream and/or ice packs to the injection site before and after treatment. Asymmetry may occur and may have a prolonged effect, but will self-correct when the botulinum toxin wears off.

In the upper face, a significant concern when injecting botulinum toxin is the migration and diffusion of the toxin from the target muscle to unintended muscle groups. One of the most common complications in the upper face is brow ptosis, which can be caused by the following reasons. The first possible reason is excessive diffusion of the toxin in the frontalis muscle. This complication may be avoided if injection is given no closer than 1 cm above the bony orbital rim in the mid-pupillary line and avoiding overtreatment of the frontalis by using low doses of botulinum toxin [9]. Brow ptosis may also occur if the patient has upper eyelids with weak muscles and redundant skin which cause dependence on forehead muscles to elevate the upper eyelids. In this situation, complication can be avoided by abstaining from botulinum toxin treatment altogether or performing an upper blepharoplasty prior to treatment with botulinum toxin.

Another reported complication is eyelid ptosis and diplopia, resulting when botulinum toxin diffuses to the levator palpebrae superioris [30]. In more severe cases, dry eye and eye pain can result when the toxin affects the innervation of the lacrimal gland via the petrosus major nerve [29]. Such complications have been shown to occur more commonly during therapeutic uses of botulinum toxin type A, such as in the treatment of blepharospasm, where higher doses of the botulinum toxin are injected as compared to cosmetic treatments [31]. Therefore, using lower doses and more dilute concentrations of a botulinum toxin A formulation may reduce complications [32]. If a patient develops ptotic or droopy eyelid, one treatment used by plastic surgeons is Iopidine® (apraclonidine 0.5%) eye drops. Iopidine® is an α2-adrenergic agonist that is indicated for glaucoma patients needing intraocular pressure reduction. It is also effective as a short-term treatment for eyelid ptosis by contracting Müller's muscle, which helps elevate the upper eyelid. At our institute, we recommend applying one or two drops to the affected eye three times daily until ptosis resolves.

In the lower face, one particular complication is partial lip ptosis, after administration of botulinum toxin to the periocular region for treatment of crow's feet, caused by weakening of the zygomaticus major muscle [30]. Complications of botulinum toxin treatment in the lower face may result in an asymmetric smile, mouth incompetence, drooling, flaccid cheek, reduced proprioception, and difficulties in speech if the perioral muscles are overly paralyzed [33]. It is recommended that patients who depend on full function of the perioral muscles (i.e., musicians) not be treated with botulinum toxin in the lower face [33]. Potential complications of platysma band injection are dysphagia and neck weakness [34]; however, these complications require further

investigation. Due to the variety of potential complications that exist, botulinum toxin injections demand a full understanding of each individual patient's face by the physician administering the treatment.

21.14 Long-Term Safety of Botulinum Toxin Type A

Botox® Cosmetic is one of the most widely studied drugs in history and has proven to have an excellent safety profile. Patients should be informed about the potential complications of botulinum toxin type A. However, they should also be made aware of the low probability of these effects and reminded that most adverse effects are slight and temporary. One study demonstrated long-term safety of botulinum toxin type A based on a retrospective analysis of 50 patients who had Botox® Cosmetic treatments for facial wrinkles for up to 9 years [35]. Less than 1% of the total 853 sessions in this 9 year period resulted in a treatment-related unfavorable outcome [34]. Of these events, five were determined to be treatment-related [35]. Therefore, a substantial amount of research and clinical experience supports the safety and effectiveness of Botox® Cosmetic as a noninvasive cosmetic procedure. Dysport® has also demonstrated to be an efficacious and safe treatment for the upper face, but there is less data on Dysport® as it has just recently been approved by the FDA.

21.15 Conclusions

Botox® Cosmetic has been hailed a miracle drug due to its good safety profile, low incidence of treatment failures, and remarkable age-defying results. As the most common, minimally invasive cosmetic procedure in the year 2008, the Botox® Cosmetic treatments have been very popular. With a new competitor on the scene, Dysport®, the demand for these two products will continue to rise. Thus, it will be critical for the plastic surgeon to have a good understanding of facial anatomy and the wrinkles caused by various facial muscles in order to provide reasonable surgical and nonsurgical treatment options. Furthermore, it will become increasingly necessary for the plastic surgeon to be equipped with a thorough knowledge of botulinum toxin's basic science, new formulations, and the most recent literature concerning its administration in order to be at the frontline of competing botulinum toxin treatments as well as avoid complications and deliver maximal aesthetic results to patients.

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