Hyperhidrosis and Aesthetics

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Abstract

When one considers the avalanche of new indications and uses for botulinum toxins, it is truly surprising that this has all happened in such a short time. And the safety and dependability of these products are profound, when used appropriately. There is still much to be discovered about the potential of this agent when you contemplate the profound non-cosmetic benefits reported by clinicians and scientists from around the world. The mechanism of action has been studied in depth, and yet the benefits appreciated by people with chronic migraine or major depressive disorder, for instance, are unlikely to be explained by our current

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mechanistic understanding. Given that these toxins control acetylcholine at the motor end plates, and given that acetylcholine is central to practically every cell in the body, it will not be surprising to find that botulinum toxin researchers will be enjoying many decades of fruitful studies. The advent of the non-surgical aesthetic physician has helped push the clinical utilization of botulinum toxins well beyond its original adoption by oculoplastic surgeons in their patients with blepharospasm. We can expect that the next edition of this book to have a dozen or more new indications which will surprise us all.

Keywords
Brow ptosis · Crows feet · Facial expression · Glabellar lines · Hyperhidrosis · Platysmal bands · Prejuvenation · Rejuvenation · Sweating

1 Introduction

Botulinum toxin (BoNT) treatment is one of the most commonly performed noninvasive aesthetic procedures today. It has been shown to be safe, effective, and predictable. The origins date back to the 1980s, when patients were receiving BoNT-A for the treatment of strabismus, hemifacial spasm, and benign essential blepharospasm. However, it was Dr. Jean Carruthers, an ophthalmologist and oculoplastic surgeon, who discovered that one of her blepharospasm patients noted a marked reduction in the appearance of glabellar furrows. In partnership with her husband, Dr. Alastair Carruthers, a dermatologist and aesthetic medicine specialist, they began assessing the potential benefits on their staff and patients. In 1992, their landmark report on the efficacy of BoNT-A for the treatment of glabellar furrows was published (Carruthers and Carruthers 1992). Since then, the aesthetic benefits of BoNT have been the subject of intense investigation resulting in worldwide usage of this agent and in many new indications.

2 Indications

BoNT was granted its first approval by the US Food and Drug Administration (FDA) for cosmetic use in 2002 for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and procerus muscle activity. Its effects on wrinkles are mediated by directly acting on motor neurons to reduce muscle activity. In 2004, it was then approved for the treatment of primary axillary hyperhidrosis that is inadequately managed by topical agents. For this indication, it disrupts neurotransmitter release at autonomic endings and reduces the responsiveness of sweat glands to acetylcholine, which differs from known neuromuscular mechanisms (Shibasaki et al. 2009). The effective duration of impaired sweat secretion is also longer relative to impaired muscle contraction. BoNT was later approved in 2013 to temporarily improve the appearance of

moderate to severe lateral canthal lines ("crow's feet") associated with orbicularis oculi activity. Further, BoNT has been used off-label for many other indications, both medical and cosmetic.

Contraindications to BoNT include prior allergic reaction, injection into areas of infection, injection into areas of inflammation, breastfeeding, pregnancy (category C), and in those patients with neuromuscular diseases, such as myasthenia gravis and Lou Gehrig's disease. Caution should be given if patients are on certain medications, such as cholinesterase inhibitors and calcium channel antagonists, which can alter its metabolism.

3 Hyperhidrosis

In response to increased body temperature or stress, sweating is a normal physiologic response. It is controlled by the sympathetic nervous system. When initiated, muscarinic receptors on eccrine glands are activated by acetylcholine from postganglionic neurons to release sweat. Sites of high eccrine gland density include the palms, soles, forehead, and axillae. In hyperhidrosis, patients experience excess sweating beyond what is considered to be physiologically normal in response to stimuli. This can vary between individuals. The most common sites of hyperhidrosis include the axillae, palms, and soles in decreasing order (Lear et al. 2007). Hyperhidrosis can be significantly debilitating to routine activities of daily living for some patients, and it can greatly affect patient quality of life (Hamm et al. 2006). This is particularly the case when other treatments, such as topical aluminum chloride, have failed, since BoNT can offer a very effective treatment strategy, if only temporary.

When patients present with a primary focal hyperhidrosis, a thorough history should be elicited by the practitioner. To make the diagnosis, the patient must have excessive focal sweating for at least 6 months without apparent secondary cause for this. Secondary causes can include medications or systemic health problems, and they are usually associated with generalized hyperhidrosis. Relevant workup is indicated if there is any concern about potential causative conditions, such as endocrine or metabolic conditions, neurologic disorders, and neoplastic disease. There should also be at least two of the following characteristics: age of onset less than 25 years old, positive family history, cessation during sleep, frequency at least once a week, bilateral and relatively symmetric, and all sufficient to impair daily activities (Hornberger et al. 2004). It is important for the clinician to obtain information pertaining to the extent that activities are affected, since this condition can be quite debilitating for patients. Oftentimes, patients will have already failed topical medications, such as aluminum chloride, and may want to avoid systemic medications, such as glycopyrrolate.

Focal sites of hyperhidrosis are typically injected superficially with BoNT. Each injection is placed about 1–2 cm apart to allow for diffusion into surrounding tissue. Deeper injections should be avoided in order to prevent denervation to deeper structures, such as local nerves and muscles, which will cause temporary weakness. Pain is minimal when injecting the axillae, but quite an ordeal on the hands and feet.

However, the procedure is usually well tolerated. Different techniques can be utilized to minimize pain, such as icing the area to be treated or the application of a pre-procedural topical anesthetic. A variety of dilutions have been used, but dilute concentrations to allow for diffusion are generally preferred. In one study with 320 patients, 94% of those who received 50 units of BoNT-A into each axilla experienced a 50% or greater reduction in sweat at 4 weeks compared to 36% in the placebo group (Naumann and Lowe 2001). By 16 weeks, these rates became 82% for the treatment arm and 21% for the placebo arm. For palmar hyperhidrosis, doses of either 50 or 100 units into each hand decreased sweating for at least 2 months and for 6 months in most patients (Saadia et al. 2001). Another study demonstrated 80–90% improvement with effects lasting for up to 12 months (Grunfeld et al. 2009). Temporary hand weakness lasting several days or weeks can be experienced. Hyperhidrosis of the soles is more difficult to manage even with higher doses of BoNT. Although some studies have shown similar results between varying dosages of BoNT, 50 units of BoNT-A per single site is considered to be the standard starting dose. If necessary, this dose can be increased to 100 units for each side. While responses have been demonstrated to be durable for several months, this can vary between patients.

4 Glabella

One of the most popular uses of BoNT has been for the treatment of glabellar lines. It has long been used clinically as a safe and effective option even years before it was officially approved by the FDA for cosmetic use. Multiple studies have demonstrated the efficacy and predictable outcomes for patients treated with BoNT for glabellar lines. In 2002, Carruthers et al. demonstrated a significant reduction in glabellar line severity at maximum frown and rest in a multicenter, double-blind, randomized, placebo-controlled study, and effects were maintained by many patients through 120 days (Carruthers et al. 2002). More recently, Carruthers et al. also showed that repeated and regular treatments over time were associated with progressive improvement in glabellar lines at rest (Carruthers et al. 2016).

The glabellar complex consists of two corrugator supercilii muscles laterally and the vertical procerus muscle medially, which serve to pull the brows inferiorly and medially. The corrugator supercilii muscles lie somewhat parallel to the medial eyebrows and insert deeply into the bone medially and laterally extend to about the mid-pupillary line where they insert into the deep dermis. However, no two patients are absolutely identical, and it is best to visualize these muscles during maximum contraction with frowning to optimize the injection points. For treatment of the glabellar complex, a standard approach involves five injection points consisting of one site centrally for the procerus, two sites for the medial portion of the corrugators, and two points for the lateral portion of the corrugators. The medial head is injected more deeply, and the lateral component should be injected intradermally. Traditionally, it has been taught that injections for the corrugators should be performed at least 1 cm above the orbital rim in order to prevent unwanted downward diffusion. However, the intradermal technique for the lateral corrugator

component seems to avoid the eyelid ptosis problem. Dosing depends on the strength of the glabellar complex, size of the muscles, and desired outcomes. For most patients, 18–24 units of BoNT-A is sufficient. An additional 10–30 units may often be necessary for patients with stronger glabellar complexes, especially in males. Carruthers and Carruthers demonstrated that males with glabellar rhytides may benefit from starting doses of at least 40 units of BoNT-A (Carruthers and Carruthers 2005).

For patients who desire lateral brow lifting, 4–6 units of BoNT-A can typically be injected into the lateral tail of the brows. Depending on the dosing and technique, brow elevations of 1–4 mm have been achieved (Huang et al. 2000; Ahn et al. 2000). However, even without this lateral brow injection, lifting of the brows can be seen with treatment of the glabellar complex due to outward diffusion of BoNT (Carruthers and Carruthers 2007). It is important to note that this technique may be more appropriate for female patients as opposed to males, who often desire straighter and less arched brows.

5 Frontalis

Treatment of the frontalis, which induces the horizontal forehead lines, represents another popular use of BoNT in facial aesthetics. The frontalis is generally a thin and broad muscle that covers 60–80% of the forehead. It serves to raise the eyebrows and upper eyelids. Horizontal forehead lines are a normal part of aging, which is due to repeated contraction of the frontalis over time. BoNT therapy has long been used safely to help reduce the appearance of these lines and, if used early enough in life, can prevent these from forming in the first place.

Over time, several different injection techniques have been described, consisting of varying patterns and dosing strategies. It is important to note that any one pattern may not be perfect for all patients and that each patient requires personalization in the treatment approach. Remember that some patients have two somewhat obliquely placed frontalis muscles with a central divarication over the mid forehead, while others might have a continuous sheet of muscle across much of the forehead. Thus, each patient needs to be assessed and treated accordingly. The injection points should generally be at least 1–2 cm above the orbital rim in order to decrease the risk of subsequent brow ptosis (Carruthers et al. 2004). Significant relaxation of part of the forehead might appear to induce some "new" horizontal lines by the hairline. The typical number of injection points can vary between 6 and 12 sites, and the total dose might range from 10 to 20 units of BoNT-A. It may be best to start with lower doses and slowly increase as needed. Men may also require higher starting doses due to increased musculature strength. The total dose is divided by the number of injection points, while each point is typically injected with 1–2 units each. A multicenter, randomized trial demonstrated that BoNT-A treatment of forehead lines was tolerable, effective, and sustained (Solish et al. 2016). Treatment of forehead lines has also been associated with increased patient satisfaction and significant improvements in appearance-related emotional and psychological issues (Ogilvie et al. 2019).

6 Crow's Feet

Patients often desire periocular rejuvenation for prominent lateral canthal lines, or so-called crow's feet. These represent a prominent and easily identifiable sign of aging and result from degenerative changes in the bone and soft tissues, increased skin laxity, photodamage, and smoking. Crow's feet originate from the lateral canthus and often fan outward. Four common lateral canthal rhytid patterns have been described and include full fan pattern in 47% of patients, lower lid and upper cheek area alone in 25% of patients, upper eyelid skin down to the lateral canthus in 18% of patients, and only the skin immediately surrounding the lateral canthus in 10% of patients (Kane 2003). Lateral canthal lines are clinically at their maximum when patients are instructed to squint or smile. Hyperkinetic movements by the lateral orbital portion of the orbicularis oculi muscle encircling the orbital rim play a large role. Therefore, it's to be expected that BoNT therapy is useful in helping to ameliorate the appearance of crow's feet.

Due to different patterns of crow's feet and varying levels of severity, individualized treatment approaches utilizing BoNT are always recommended. Standard injection techniques can only offer a helpful starting point for practitioners. Any baseline asymmetry should be noted, photographed, and discussed with the patient prior to procedure. If this is not pointed out, the patient is going to think that the asymmetry was caused by the procedure when they scrutinize their face following the procedure. Injections are placed superficially into the subcutaneous space immediately under the dermis in order to minimize the risk of diffusion to deeper muscles and to avoid bruising. Various injection patterns have been described. Standard technique involves injections that are placed about 1–1.5 cm from the lateral canthus using three or four injection points spaced about 1 cm apart in an arcuate pattern. Typical dosing regimens range from using 4–8 units of BoNT-A per side. A multicenter, double-blind, placebo-controlled study by Carruthers et al. demonstrated effective and well-tolerated treatment with 12 units of BoNT-A to each side for moderate to severe crow's feet lines (Carruthers et al. 2014). Response duration for the treatment of crow's feet was proven to be greater than 4 months using data from trials that included 833 patients receiving BoNT-A (Baumann et al. 2016). Compared to placebo, BoNT-A treatment of crow's feet lines was associated with patients experiencing significant improvements in perceived appearance, attractiveness, age, tiredness, and satisfaction (Dayan et al. 2015).

7 Orbicularis Oris and Depressor Anguli Oris

While BoNT was originally promoted for the upper face, it has since grown in popularity for treatment of the lower face, especially around the mouth. Perioral lip lines, downward turning of the angles of the mouth, and lengthening, thinning, and inversion of the upper lip are all common concerns. Perioral lines can be exaggerated not only from photodamage but also from repetitive pursing of the lips, which can be associated with habitual smoking and drinking through straws. The perioral region

comprises an interdigitating complex of muscles capable of creating profoundly subtle yet recognizable facial expressions, such as fear, anger, disgust, sadness, and literally hundreds of others. Two of the most significant muscles include orbicularis oris and depressor anguli oris (DAO). The orbicularis oris surrounds the opening of the mouth and serves to aid with speech, mastication, expression, sucking, and puckering. The DAO is a triangular-shaped muscle that extends from the inferior mandible to the angle of the mouth, and its main function is to depress the angle of the mouth.

For patients with clinically significant perioral lines and exaggerated downward turn of the oral commissures, BoNT therapy can prove to be an effective treatment option. While full relaxation of some muscles of the upper face may often be desired and implemented, such a request for the lower face would be incompatible with normal social activities where use of these muscles is important for vital activities, such as mastication, drinking, and phonation. Practitioners should be conservative with placement and dosage. For the orbicularis oris, typical treatment consists of four symmetrical superficial injections of 1–2 units of BoNT-A to the upper lip and two injections to the lower lip along the cutaneous aspect of the vermillion border. The midline and corners of the lips should be avoided to prevent flattening of Cupid's bow and weakness in muscles used for elevating the lips (Kaplan et al. 2007). Treatment with BoNT not only can smooth vertical lines but can also enhance lip fullness and lip eversion (Semchyshyn and Sengelmann 2003). For treatment of the DAO, injections should be in the mid to lower third of the muscle. The oral commissure can be traced inferiorly to just above the mandible, where the injection should be located about 1 cm posteriorly from this point in order to avoid treatment of the depressor labii inferioris (DLI), which sits more medially. Effects on the DLI can cause lower lip dysfunction and flattening of its contour. A dose of 4–6 units of BoNT-A per side is typical. Best results are observed in young patients who have greater muscle strength without significant laxity or adjacent lipodystrophy (Goldman and Wollina 2010). Whenever treating the perioral region, be aware that this may impact the patient's livelihood for those who depend on precise movement of their lips while singing, whistling, or playing a wind instrument.

8 Platysma

During the aging process, platysmal hypertrophy and separation can be pronounced, especially due to the dermal and subcutaneous atrophy. This can be accentuated with speech and movement, which becomes clinically evident as prominent platysmal bands and perpendicular horizontal lines. The presence of platysmal bands at rest is the result of increased muscular resting tone. This is a cosmetic rather than a medical problem and can be ameliorated with BoNT. Total dosage can be based upon how many bands are present in addition to their length and severity. Modest dosing levels are considered to be 30–50 units of BoNT-A. Higher doses from 60 to 250 units were previously associated with adverse effects (Chen and Cohen 2015). Modest dosing can typically offer noticeable cosmetic improvement without increased risk for

complications. During the injection procedure, the patient should be asked to contract their platysmal bands by grimacing. The non-dominant hand can be used to pinch the platysmal band, which not only assures precise injection into the muscle but also helps to distance it from deeper underlying structures. Intramuscular deposition of 2–5 units of BoNT-A can be spaced about 1–2 cm apart along the length of the platysmal band. Relaxation of the vertical platysmal bands, improvement of the horizontal neck lines, and enhancement of the mandibular line can all be expected after 1–2 weeks (Trévidic et al. 2015). Duration of BoNT can vary depending on injection technique, dosage, and patient, but typically ranges between 3 and 4 months. A recent systematic review has demonstrated BoNT to be relatively safe and effective for the treatment of mild to moderate platysmal bands (Sugrue et al. 2019). However, practitioners must be cautious not to inject too deeply or to use high dosages in order to avoid diffusion to deeper neck muscles, which may affect neck movement and create problems with phonation and glutition.

9 Masseter

One out of five people have bruxism, which is a nighttime grinding of the teeth that is often associated with sleepless nights for them (and their partners). This can leave them with an aching pain in their jaws and temporomandibular joints, headaches, and significant masseter hypertrophy. BoNT therapy has been found to be of great benefit by relaxing these muscles of mastication after which the patients sleep better, wake up more refreshed, and have fewer bruxism symptoms. More recently, BoNT has been used to improve the aesthetic appearance of those with a heavy-set lower face related to masseter hypertrophy unassociated with bruxism. This has become an especially popular treatment for patients of Asian descent, where many would like a more oval-shaped face.

Prior to injection, the patient is instructed to clench the jaw so that the borders of the masseter can be best palpated. Various techniques have been described to help map the rough outline of where the masseter resides. However, more pronounced masseters can be typically palpated with relative ease. About two to three injection points are typically performed in the area of maximal bulge. Injections should be placed intramuscularly. Caution should be advised to avoid injecting too cephalically as the facial nerves might be negatively impacted. Dosing depends on the muscle bulk, but it typically ranges from 10 to 30 units of BoNT-A per side. Repeat injections are often necessary at intervals of 3–4 months in order to reach the desired outcome and facial shape. In a study of 50 patients treated with repeat injections, patients experienced durable responses that were maintained at 4-year follow-up (Shome et al. 2019). When performed appropriately, procedures have been shown to offer adequate results and safety profiles (Yeh et al. 2018). Most complications appeared within 2–4 weeks and disappeared within 12 weeks. The so-called Popeye sign, where the relaxed masseter muscle following BoNT treatment is projected outwards with contraction, might last for about 1 week until the rest of the masseter

is impacted equally. Practitioners should familiarize themselves with regional anatomy for safe injections.

10 Conclusion

BoNT has surprised many by how effective this agent has been, both on- and off-label, in medical and aesthetic conditions while providing efficacious and safe outcomes. And now that millions of people have received BoNT, a second wave of interest exists in conditions, such as chronic depression, which are quite separate from the aesthetic area. There seems no end to the discovery of benefit. It is so rewarding to be able to treat people, some of whom feel past their best, with such a safe and relatively simple treatment. For those who are averse to surgery, and even in conjunction with surgery, fillers and neurotoxins used in combination seem to have no end in popularity. Safety is of prime importance with any treatment, and so it is true also in aesthetic medicine. Practitioners must know their injection anatomy and understand the pharmacology of BoNT in order to appreciate how best to help their patients and how to both prevent and treat complications. In the end, the field might well look at the youth of this country to determine when best to start treatment with these agents. Prejuvenation, which is "treatment to prevent the appearance of aging," is taking hold. The earlier that patients start, the more effective these treatments will be (Spanogle et al. 2014). The shifting of goals to prevent the appearance of fine lines and wrinkles may offer improved cosmetic outcomes in the long term than simply working to ameliorate deep wrinkles after the fact.

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