



Complications of botulinum toxin and fillers: A narrative review

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Abstract

Background: Cosmetic surgery and esthetic procedures have become a billion dollar industry owing to the ever-growing demand of the population to stay young. The injectable treatments including fillers and botulinum toxin have become highly popular because of their quick, predictable and lasting results in the management of facial wrinkles and rejuvenation. Although these treatment modalities are relatively safe, they are associated with certain side effects.

Aims: In this review, we will focus on the complications of fillers and botulinum toxin.

Patients/Methods: The literature research considered published journal articles (clinical trials or scientific reviews). Studies were identified by searching electronic databases (MEDLINE and PubMed) and reference lists of respective articles. Only articles available in English were considered for this review.

Results: Brow ptosis and asymmetry are common adverse effects of botulinum toxin while the most common adverse effects associated with fillers are the local injection related effects manifesting as erythema, edema, pain, and ecchymosis.

Conclusion: It is important that the treating physician is well verse with the various fillers and botulinum toxin complications and their management as some of the complications can be severely debilitating.

KEYWORDS

botulinum toxin, cosmetic surgery, filler, side effects

1 | COMPLICATIONS OF BOTULINUM TOXIN

Botulinum toxin acts by inhibiting the release of acetylcholine at the motor end plate leading to muscle paralysis. The selective paralysis of certain muscles is the basis of botulinum toxin treatment but paralysis of adjacent or other muscles can lead to the complications.

1.1 | Brow ptosis

It is a common complication arising in the treatment of the frontalis muscle for addressing horizontal forehead lines with botulinum toxin. This complication can be avoided by staying at least 2-3 cm above the supraorbital margin or 1.5-2 cm above the eyebrow while injecting into the frontalis. This technique spares the function of the inferior frontalis muscle fibers in the area thereby preventing ptosis.^{1,2} In patients where horizontal forehead lines are present along with glabellar frown lines, it is important that the glabellar area is treated along with the forehead; otherwise, unopposed depressor action of the glabellar muscles will lead to brow ptosis.^{2,3} Ptosis of the upper eyelid is also seen when injecting the toxin in and around the glabella due to migration of injected toxin through the orbital septum leading to weakening the levator palpebrae superioris. It is commonly seen when botulinum toxin is injected close to the bony supraorbital margin at the midpupillary line and when large volumes of diluted toxin are injected in the area.^{3,4} Lid ptosis can also be seen in elderly who have dermatochalasis of the skin of the eyelids and who unconsciously use the lower fibers of their frontalis to lift the brow and the eyelids. With the weakening of this compensatory action of the frontalis by botulinum toxin, a secondary blepharoptosis can appear.⁴⁻⁶

Ectropion, diplopia, xerophthalmia, and lagophthalmos. Injection of high doses of botulinum toxin into the area of lateral canthus can cause complications such as ectropion, diplopia, xerophthalmia, and lagophthalmos.^{1,2} Ectropion occurs due to the inadvertent weakening of the muscular sling of the lateral orbicularis due to diffusion of the toxin. Diplopia can occur due to the diffusion of the toxin through the orbital septum leading to weakening of the lateral rectus and other extraocular muscles. Xerophthalmia can occur if the toxin is injected too deeply in the upper lateral aspect of the periocular area thereby affecting the secretion of the lacrimal glands. Lagophthalmos is another rare complication resulting due to the loss of the normal sphincteric function of the orbicularis oculi, and the improper closure of the eyelids. Loss of the sphincteric functions of the orbicularis oculi and eyelid weakness can occur when the toxin diffuses into the palpebral portion of the orbicularis oculi leading to lagophthalmos. These complications can be reduced by injecting the toxin subdermally and lateral to an imaginary vertical line that passes through the lateral canthus.^{1,2,6}

1.2 | Lip ptosis and asymmetry

It is a rare complication seen when the toxin is injected below the superior margin of the zygomatic arch or too low along the nasal side-walls thereby diffusing into the upper lip elevators, that is, levator labii superioris alaeque nasi and levator labii superioris leading to asymmetry and ptosis of the upper lip and even difficulties in speaking and eating.⁷⁻⁹ Overdosing of the toxin over the upper lip can cause many different adverse functional changes, which can include the inability to form certain letters, to articulate different sounds, and to pronounce various words. There can be inability to approximate the lips tightly, which can lead to fluid or even food incontinence and drooling.

1.3 | Dysphagia, hoarseness, and neck weakness

Botulinum toxin treatment of horizontal rhytides and vertical bands in the neck is very safe, but complications can occur due to improper technique. As the underlying muscles of deglutition, phonation, and neck flexion are also cholinergic, higher doses of botulinum toxin or deeper injection can result in xerostomia, dysphagia, dysarthria, and neck weakness.^{10,11} A small number of patients may complain of either a difficulty or rarely an inability to lift the head and to keep it still and erect.

1.4 | Asymmetry

Asymmetry is a common complication and is usually due to injector placement or patient's anatomic variation. "Spock" eyebrow is a common asymmetry presenting as curvature of the lateral brow occurring due to imbalance arising from the deactivation of the central frontalis and the activity of the lateral frontalis which lifts the brow tail which can be corrected by placing some additional toxin at the active area of the muscle.^{2,4}

1.5 | Injection site complications

They include local edema, erythema, bruising, and pain at the injection and adjacent sites. Using a small gauge needle and paying close attention to the superficial vessels can limit bruising especially around the lateral canthus region. Icing can minimize pain and also cause vasoconstriction to minimize bruising. Some patients can present with a dull and transient headache with general body malaise after the injection. Serious reactions like anaphylaxis, urticaria, soft tissue edema, and dyspnea are rare.

2 | COMPLICATIONS OF FILLERS

As the use of dermal fillers is increasing, the complications associated with them have also increased, which vary from mild injection

site reactions to severe hypersensitivity reactions and granulomas, vascular occlusion, and blindness.

2.1 | Injection site complications

The most common adverse effects associated with fillers are the local injection related effects manifesting as erythema, edema, pain, and ecchymosis. These adverse effects are usually mild and transient and last <1 week.¹² The injection associated pain can be minimized by the use of small gauge needle or blunt cannulas and the application of local anesthetic and ice prior to the injection. The erythema and ecchymosis can be minimized by stopping the intake of any blood-thinning medications like aspirin or NSAIDs at least 1 week prior to the injection.

2.2 | Inappropriate injection technique related complications

Inappropriate injection technique can lead to adverse effects such as palpable nodules, visible implants, and over- or under correction. Filler injections that are too superficial can lead to a bluish discoloration due to Tyndall phenomenon or hemosiderin deposition as a result of intradermal bleeding during the injection. Superficial injection can also lead to small nodular collections of the filler material, which can be treated with aspiration, drainage, or hyaluronidase injection.¹³ Superficial injection of calcium hydroxylapatite can lead to small whitish nodules on the surface of the skin. Superficial silicone injections can cause fibrosis and lead to formation of foreign body granulomas called siliconomas resulting in nodules.¹⁴

2.3 | Allergy and hypersensitivity reactions

Fillers can cause hypersensitivity reactions and foreign body granulomas, which can manifest as erythema, induration, and nodular swelling at the site of injection manifesting within a few days or even after years of injection. Bovine collagen can cause a localized hypersensitivity reaction within a few days or a systemic hypersensitivity reaction manifesting as fever and urticaria, which may require a short course of oral corticosteroids. Foreign body granulomatous reactions to fillers can occur after a long time, manifesting as indurated nodular swellings at the site of injection, which may require intralesional corticosteroid injections. The pathogenesis of these hypersensitivity responses may be attributed to the presence of small amounts of protein contaminants in the fillers, which can cause hypersensitivity reactions and granuloma formations.¹⁵

2.4 | Vascular adverse effects

Filler induced skin necrosis due to inadvertent intravascular injection of filler is a rare but serious complication. It is commonly seen over

the glabellar region due to injection into the supratrochlear artery. Retinal embolism due to the intravascular injection into the supratrochlear artery, supraorbital, angular, and dorsal nasal arteries is also a rare complication. Cerebral ischemic events due to the retrograde flow of filler emboli in the internal carotid artery are another rare but a life-threatening complication.¹⁶ This complication can be mitigated by aspirating the needle before injecting, keeping the needle moving while injecting, using a less dense filler and by injecting low volumes over two or three sessions rather than injecting a high volume in a single session.¹⁷⁻¹⁹ If any features of tissue necrosis appear, injection must be stopped immediately, and an immediate injection of hyaluronidase enzyme is important to minimize the tissue necrosis. Topical oxygen therapy, low molecular weight heparin, systemic steroids, sildenafil, filler removal through puncture, and intravenous prostaglandin are reported to be useful in cases where hyaluronidase is not effective.¹⁸

2.5 | Infections

Injectable fillers are associated with the risk of infections, which may result due to a breach in the skin's surface. Wide varieties of bacterial, viral, and fungal infections have been reported with the use of fillers. Reactivation of herpes simplex infection is commonly seen after lip augmentation, which can be prevented by avoiding the procedure in patients with active infection or by initiation of antiviral therapy before the procedure in patients with recurrent infection. Bacterial infections like cellulitis and abscesses are also seen due to staphylococcal and streptococcal infections, which may require broad-spectrum oral antibiotic therapy. Mycobacterium abscesses and mycobacterium chelonae infection have also been reported after the use of contaminated fillers.^{20,21} Biofilm formation over the dermal fillers has also been reported which can cause a variety of complications including cellulitis, abscesses, nodules, or granulomatous inflammation, which can manifest even years after dermal filler injections. Empiric antibiotic therapies with two or three classes of antibiotics are recommended in cases of suspected biofilms while awaiting pcr results.²² The risk of infections with filler injections can be minimized by using proper aseptic injection technique reducing the number of piercings while injecting, using the smallest gauge needles possible, avoiding injecting into inflamed or infected skin, and avoiding injecting through previous layers of filler.²³

3 | CONCLUSION

Botulinum toxin and fillers injections are types of aesthetic procedures that are gaining popularity due to their relatively fast effects with lower procedure and recovery time in comparison with surgery. Although the overall side effects profile of such procedures is low, in depth knowledge of anatomy, the patient's medical history, possible complications related to the specific product and location and close follow-up are pivotal to safe and effective treatments and results.

DISCLAIMER

We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work.

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REFERENCES

- Carruthers A, Carruthers J. Clinical indications and injection technique for the cosmetic use of botulinum A exotoxin. *Dermatol Surg*. 1998;24:1189-1194.
- Klein AW. Complications and adverse reactions with the use of botulinum toxin. *Dis Mon*. 2002;48:336-356.
- Klein AW. Dilution and storage of botulinum toxin. *Dermatol Surg*. 1998;24:1179-1180.
- Carruthers A, Carruthers J. Botulinum toxin type A: history and current cosmetic use in the upper face. *Semin Cutan Med Surg*. 2001;20:71-84.
- Carruthers A, Carruthers J. The treatment of glabellar furrow with botulinum A exotoxin. *J Dermatol Surg Oncol*. 1990;16:83.
- Carruthers JD, Carruthers JA. Treatment of glabellar frown lines with C. botulinum-A exotoxin. *J Dermatol Surg Oncol*. 1992;18:17-21.
- Matarasso A. Discussion: new indications for botulinum toxin type A in cosmetics: mouth and neck. *Plast Reconstr Surg*. 2003;110:86S-87S.
- Goldwyn R, Rohrich R. Consensus recommendations on the use of botulinum toxin type A in facial aesthetics. *Supplement to Plast Reconstr Surg*. 2004;114:1S-22S.
- Matarasso SL, Matarasso A. Treatment guidelines for botulinum toxin type A for the periocular region and a report on partial upper lip ptosis following injections to the lateral canthal rhytides. *Plast Reconstr Surg*. 2001;108:208-214.
- Klein AW. Complications and adverse reactions with the use of botulinum toxin. *Seminars Cut Med Surg*. 2001;20:109-120.
- Blitzer A, Binder WJ, Aviv JE. The management of hyperfunctional facial lines with botulinum toxin: a collaborative study of 210 injection sites in 162 patients. *Arch Otolaryngol Head Neck Surg*. 1997;123:389-392.
- Lafaille P, Benedetto A. Fillers: contraindications, side effects and precautions. *J Cutaneous Aesthet Surg*. 2010;3:16-19.
- Bergeret-Galley C, Latouche X, Illouz YG. The value of a new filler material in corrective and cosmetic surgery: DermaLive and DermaDeep. *Aesthetic Plast Surg*. 2001;25:249-255.
- Bigatà X, Ribera M, Bielsa I, Ferrándiz C. Adverse granulomatous reaction after cosmetic dermal silicone injection. *Dermatol Surg*. 2001;27:198-200.
- Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg*. 2008;34:S92-S99.
- Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Invest Dermatol*. 2013;6:295-316.
- McCleve DE, Goldstein JC. Blindness secondary to injections in the nose, mouth, and face: cause and prevention. *Ear Nose Throat J*. 1995;74:182-188.
- Lemperle G, Rullan PP, Gauthier-Hazan N. Avoiding and treating dermal filler complications. *Plast Reconstr Surg*. 2006;118:S92-107.
- Kassir R, Kolluru A, Kassir M. Extensive necrosis after injection of hyaluronic acid filler: case report and review of the literature. *J Cosmet Dermatol*. 2011;10(3):224-231.
- Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg*. 2013;15:226-231.
- Rodriguez JM, Xie YL, Winthrop KL, et al. *Mycobacterium chelonae* facial infections following injection of dermal filler. *Aesthet Surg J*. 2013;33:265-269.
- Cassuto D, Sundaram H. A problem-oriented approach to nodular complications from hyaluronic acid and calcium hydroxylapatite fillers: classification and recommendations for treatment. *Plast Reconstr Surg*. 2013;132:48S-58S.
- Bailey SH, Cohen JL, Kenkel JM. Etiology, prevention, and treatment of dermal filler complications. *Aesthet Surg J*. 2011;31:110-121.

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