Complications of BTX-A in Periocular Procedures

When used appropriately, treatment is generally safe and well tolerated by patients.\(^1\) Because the effects of botulinum toxin (BTX-A) generally begin to fade within 12 weeks, the duration of its side effects is also limited.\(^2\) Some of the undesired side effects of periocular applications of BTX-A include the following:\(^1\,\,\,^2\):

- Ecchymosis
- Rash
- Hematoma
- Headache
- Flu-like symptoms
- Nausea
- Dizziness
- Loss of facial expression
- Lower eyelid laxity
- Dermatochalasis
- Ectropion
- Epiphora
- Eyebrow and eyelid ptosis
- Lagophthalmos
- Keratoconjunctivitis sicca
- Diplopia

These side effects are rare.

In a systematic review investigating adverse effects related to the facial use of BTX-A, Zagui et al\(^8\) found that the most frequent adverse effect with the greatest risk was eyelid ptosis (3.39% of cases). Carruthers et al\(^9\) observed the condition in 5.4% of their cases. It is possible that the occurrence of eyelid ptosis was overvalued, as it was in the study published by Dutton,\(^10\) who reported a 13% occurrence rate in the cases evaluated. This result might be explained by the fact that this effect is easily diagnosed by examining the patient, whereas the diagnosis of other adverse effects depends on information provided by the patient. Therefore, nonspecific symptoms such as headache or infectious reactions might not be evidenced for being considered irrelevant. On the other side, the higher frequency of eyelid ptosis might have happened because it was diagnosed by an examiner.\(^8\,\,\,^11\)

It has been recommended to increase the concentration and reduce the volume of BTX-A injections to prevent unwanted diffusion to other muscles. Ptosis arises due to diffusion or accidental injection of the toxin into the orbital septum. In cases of ptosis severe enough to interfere with vision, the use of 0.5% apraclonidine ophthalmic drops to enhance Müller muscle function may be beneficial until the levator muscle function returns.\(^1\,\,\,^12\)

According to another meta-analysis of 1,003 patients, the most common complications besides eyelid ptosis (3.4%) were dry eye (2.3%), headache (1.6%), and eyebrow ptosis (0.6%).\(^13\) Eyelid ptosis often occurs due to impairment of the levator palpebrae superioris muscle after injections for the correction of glabellar lines invade the orbital septum. Ptosis emerges as early as 48 hours and can last from 2 to 12 weeks. To avoid eyelid ptosis due to intraorbital diffusion, a high-concentration, low-volume BTX injection is applied 1 cm from the edge of the orbital bone or more than 1.5 cm laterally from the lateral canthus.\(^14\)

Diplopia is a rare complication that usually occurs due to paralysis of the inferior oblique muscle. Dry eye and epiphora are other common complications of BTX administration. Blurred vision resulting from corneal exposure may occur due to disruption of the eye-closure reflex.\(^1\,\,\,^13\) There have been rare reports of acute angle closure glaucoma\(^15\,\,\,^16\) and retinal tearing due to globe penetration\(^17\) associated with BTX injection. To date, reported side effects include pain during injection, local edema, erythema, ecchymosis, alternate muscle weakness, and flu-like symptoms. Between 1989 and 2003, nearly all of the serious complications related to BTX injection reported to the US Food and Drug Administration (FDA) were a result of therapeutic applications using higher dosages (ratio of therapeutic:cosmetic purposes of 33:1). Of 253 cases with serious complications, 28 deaths were reported, none of which was related to the application of BTX for cosmetic purposes.\(^18\)
The proteins included in the preparations may cause antibody reaction against BTX injections. The BTX agent currently in use (since 1998) has a low protein load and therefore rarely induces an allergic reaction. However, an allergic reaction can occur due to the therapeutic use of high-dose BTX. Of 1,437 BTX-related adverse events reported to the FDA, nonserious allergic rash occurred in 17 cases of therapeutic use and 29 cases of cosmetic use, while serious allergic reaction/rash occurred in 11 therapeutic users and 2 cosmetic users. Decreasing the dose of BTX and increasing the interval between injections can reduce the risk of antibody production. In regards to malpractice, there have been reports to the FDA of side effects due to toxin spreading to surrounding tissues after BTX injection for cosmetic purposes, but no permanent serious side effects have been reported.

Side effects like bruising and hemorrhage can be minimized by discontinuing patients’ use of anticoagulants (aspirin, vitamin E, nonsteroidal anti-inflammatory drugs) 2 weeks prior to injection. In addition, the treated area should not be massaged for up to 2 hours after injection in order to accelerate the absorption of the injected BTX and reduce its spread to surrounding tissues.

Despite the side effects, BTX injections are safe and show a very good result. Side effects can be avoided by obeying manufacturer recommendations and remaining up-to-date with current information. When used as monotherapy or in combination with other treatment modalities, the use of BTX in a simple, minimally invasive procedure has turned back the clock for millions of patients.

References