Safety Profile of Combined Same-Day Treatment for Botulinum Toxin With Full Face Nonablative Fractionated Laser Resurfacing

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BACKGROUND Spread of botulinum toxin outside the treated muscle is a concern, when energy-based device treatment is performed on the same day as toxin injection.

OBJECTIVE We assessed the frequency of eyelid ptosis after the glabella/periorbital botulinum toxin injection and nonablative fractionated laser performed at the same session.

METHODS AND MATERIALS This single-center, retrospective study identified treatments consisting of glabella and/or periorbital botulinum toxin injection and nonablative fractionated laser treatment to full face from 2017 to 2019 and eyelid ptosis determined by documentation of the complication at a follow-up encounter, or prescription of apraclonidine.

RESULTS Six hundred sixteen treatments of glabella/periorbital botulinum toxin injection and full-face nonablative fractionated laser on the same day on 393 individuals were identified. Five hundred eighty treatments (94%) included botulinum toxin injected in the glabella, 541 (88%) in the periorbital areas, and 508 (82%) in the forehead. Nonablative fractionated lasers used to treat the cohort were a 1,927-nm thulium and a 1,550-nm er:glass laser. Eyelid ptosis complication was documented in one case (0.2%) following the combined laser and toxin treatment.

CONCLUSION The risk of spread of glabella/periorbital botulinum toxin to an unintended muscle was minimal in the setting of the concomitant full-face nonablative fractionated laser.

R. G. Geronemus: Medical advisory board for Allergan, Candela, Cearna, Cynosure, Cytrellis, Lutronics, Soliton; Investigator for Allergan, ArchiMedus, Avava, Candela, Cynosure, Cytrellis, Endo Pharmaaceuticals, Galderma, Kerastem, Lutronic, Merz, New York Stem Cell Foundation, Pulse Biosystem, Revance, Sciton, Sienna Labs; Stockholder for Cytrellis. The remaining authors have indicated no significant interest with commercial supporters.

Combining botulinum toxin with energy-based device treatment has demonstrated synergistic effect on rejuvenation of the face.[1–5] Combining treatments on the same day, rather than separating them through multiple visits, can be beneficial by producing greater improvement in a shorter amount of time and with less downtime.[6]

Upper eyelid ptosis is a possible complication with botulinum toxin injection to the upper face.[7] The frequency of eyelid/eyebrow ptosis is estimated 6.1% in a recent study of the US FDA Adverse Event Reporting System.[8] Ptosis of the upper eyelid is experienced because of migration of injected toxin to the levator palpebrae superioris, which is located in proximity to the commonly targeted procerus, corrugator supercilii, and orbicularis oculi muscles of the upper face.[9] There is a concern with potentially increased risk of spread of botulinum toxin to untreated areas due to tissue swelling and inflammation following energy-based device treatment.

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ISSN: 1076-0512 • Dermatol Surg 2020;00:1–5 • DOI: 10.1097/DSS.0000000000002851

Efficacy and safety of the same-day combination treatment with botulinum toxin has been studied with intense pulsed light (IPL), pulsed dye laser, diode laser, and radiofrequency device.[4,5,10,11] To our knowledge, there are no studies evaluating safety of same-day treatment with botulinum toxin and nonablative fractionated laser. We sought to evaluate the incidence of adverse events of eyelid ptosis, when botulinum toxin was administered in the upper face on the same day as nonablative fractionated laser treatment to the face.

Methods

Chart review of patients seen at a single private dermatology practice from January 1, 2017 to December 31, 2019 was performed. Patients 19 years or older at the time of a qualifying treatment were included. The qualifying treatment was defined as both full-face nonablative fractionated laser resurfacing and botulinum toxin injection in the glabella and/or periorbital areas performed on the same day. The periorbital areas included toxin injection to lateral brows and crow's feet. Low-energy low-density 1,927-nm fractional laser was excluded from the study.

Eyelid ptosis was identified by prescription of apraclonidine ophthalmic drops or clinic visit or telephone note within the first 4 weeks documenting the complication following the same-day combination.

The study protocol was approved by Asentral Institutional Review Board.

Results

393 patients underwent a total of 616 combination treatments of botulinum toxin and full-face nonablative fractionated laser on the same day at the authors' practice in the 3-year study period. Among these 393 patients, 363 (83%) were women. The mean age at the time of combination treatment was 58.9 years, ranging from 25 to 91 years. Two hundred seventy-three (69%) patients received 1 combination treatment during the study period, 73 (19%) received 2 treatments, 24 (6.1%) received 3 treatments, and 23 (5.9%) received 4 or more treatments.

The 616 combination treatments were performed by 10 board-certified dermatologists. Two physicians performed most treatments, totaling 514 (83%). Five hundred eighty treatments (94%) included botulinum toxin injected in the glabella, 541 (88%) in the periorbital areas, and 508 (82%) in the forehead. In the glabella and periorbital areas, onabotulinumtoxin A alone was used in 518 cases (84%), onabotulinumtoxin and abobotulinumtoxin in 94 (15%), whereas abobotulinumtoxin alone was used in 4 (1%). One hundred twenty-four cases had documented units of botulinum toxin injected per anatomic area. Onabotulinumtoxin was exclusively used in the glabella treatment at average of 14.1 units (range 2–40). For the periorbital treatment, onabotulinumtoxin (mean 12.4 units) or abobotulinumtoxin (mean 56 units) were used.

Nonablative fractional 1,927-nm thulium laser therapy was most commonly administered in our cohort. Five hundred fifty-one combination treatments (89%) involved full-face resurfacing with 1,927-nm fractional laser alone. Fifty-three treatments (8.6%) were performed by both 1,550- and 1,927-nm nonablative fractional lasers to the face. In these cases, 1,550-nm erbium glass laser treated focal areas of the face (e.g., periorbital, perioral) with 1,927 nm to the areas of the face not treated by 1,550 nm, or both 1,550 and 1,927 nm to the full-face. Nine were treated with 1,550 nm alone. Two had a combination of 1,927- and 10,600-nm ablative fractional CO_2 laser together, where CO_2 laser was used solely for the perioral area. In both cases, botulinum toxin was injected to the upper face.

Of the 616 treatments, 1 had documented eyelid ptosis. This was a 56-year-old woman with Fitzpatrick skin type I who had 1,927-nm thulium laser treatment to the face (energy: 10 mJ, density: 65%, 8 passes) and 40 units total of onabotulinumtoxin A injected to the glabella, crow's feet, forehead, and platysma. Her eyelid ptosis was recorded at the follow-up visit 13 days after the treatment. Her medical history was notable for hypothyroidism, for which she took levothyroxine 75 μg daily.

Discussion

Little is known about the incidence of upper eyelid ptosis when upper face botulinum toxin is administered on the same day as full-face non-ablative fractional laser resurfacing. Adverse events related to botulinum toxin for aesthetic treatment of the upper face were reported in multiple randomized or open-label clinical studies and postapproval studies.[12] Common adverse events include injection site pain, edema, bruising, headache, blepharoptosis, and eyebrow ptosis.[12,13] An adverse event of our interest in the setting of the same-day treatment with nonablative fractional laser is blepharoptosis.

Eyelid ptosis, caused by diffusion of toxin to the levator palpebrae superioris muscle, can be a functionally and cosmetically disturbing complication. It can happen with toxin injection in the glabella and crow's feet.[13,14] Although it is not a permanent complication, its persistence can last for up to 13 months.[15] Apraclonidine topical ophthalmic solution improves eyelid ptosis, but complete resolution of ptosis with apraclonidine may take 4 to 6 weeks.[16]

Extent of botulinum toxin migration in tissue was investigated using animal models. Botulinum toxin has been demonstrated to spread through muscle fascia to neighboring muscles.[17] In a rabbit experiment, 10 units of botulinum toxin diffused up to 45 mm from the injection site.[18] The higher the dose, the larger the area affected.[18]

Migration of botulinum toxin is a concern, even when it is used as a single therapy. Its risk for migration may increase because of tissue manipulation and edema from the same-day light or energy-based therapy. In clinical studies with ablative laser, botulinum toxin was administered 1 week before or 1 month after laser resurfacing to show more improvement in rhytides than laser therapy alone. These studies found that botulinum toxin injection separated by one to a few weeks from ablative resurfacing was safe without ptosis.[1–3,19] Some authors recommended separating treatments for botulinum toxin injection and energy-based therapy.[1,6,20]

A few studies on the same-day use of botulinum toxin and energy-based device therapy were conducted previously. The most studied combination is with IPL. Fifteen subjects received IPL treatment to the entire face followed by botulinum toxin injections in one cheek and saline injections in the other cheek.[5] The injections were performed intradermally in a grid-like pattern after IPL. No facial muscles, including lip elevators, were affected by botulinum toxin. In a larger study, 30 subjects received IPL to the face and then botulinum toxin to crow's feet.[1] The study reported mild erythema and bruising for adverse events with no ptosis. A retrospective review of 19 patients found that several devices, including IPL, pulsed dye laser, diode laser, monopolar radiofrequency, and Nd:YAG laser, may be combined with botulinum toxin on the same day without decreased efficacy or weakening of muscles not targeted.[11]

Nonablative fractional lasers are frequently used for facial rejuvenation by addressing signs of photoaging, including wrinkles, uneven texture, and hyperpigmentation. Adding botulinum toxin injection on the day of resurfacing improves facial wrinkles more noticeably than laser alone and would therefore increase patient satisfaction. Our retrospective study found that blepharoptosis is a rare complication of 0.2% (1 out of 616) in the same-day combination treatment of periorbital botulinum toxin and full-face nonablative fractional laser. The complication rate may have been under-reported in our study because of its retrospective design, where blepharoptosis incidence was extracted from clinic visit and telephone notes and apraclonidine prescription. However, we believe that our patients with noticeable eyelid ptosis would be more likely to report the complication to us than to ignore the symptom or to look for a treatment elsewhere. Although our study is not designed to compare the incidence of blepharoptosis of the same-day combination treatment to that of toxin treatment alone, the complication rate of 0.2% is in the lower end of the reported range of 0% to 5.4% in clinical trials with botulinum toxin alone.[21–34]

The low risk of blepharoptosis with same-day treatment may be because of the fact that 1,927-nm wavelength causes more superficial damage than other nonablative fractional lasers. Because eyelid ptosis from same-day combination therapy was rare, it is difficult to identify predisposing factors. The patient

who developed eyelid ptosis was a healthy Caucasian woman in her fifties, other than hypothyroidism. Her treatment dosing and settings of botulinum toxin and 1,927-nm laser treatment was not unusual compared with those of other patients who did not develop eyelid ptosis.

The physicians in our practice usually perform resurfacing first and avoid botulinum toxin injection before laser procedures. Our result of a low risk of blepharoptosis in the same-day combined therapy represents the outcome when toxin is injected on the same day after laser, so we recommend caution if injection is administered before laser.

Botulinum toxin dosing per treatment session was recorded in the patients' charts throughout, whereas dosing per anatomic site was recorded in the one fifth of our cohort. In these cases, with recorded doses per anatomic site, 2 to 40 units of onabotulinumtoxin to the glabella and 2 to 40 units of onabotulinumtoxin or 40 to 80 units of abobotulinumtoxin to the periorbital areas appeared to be safe. Capturing botulinum toxin dosing per anatomic site for all patients, which could not be achieved in our retrospective study, would have provided valuable information, because diffusion to a larger area is expected with a higher dose of botulinum toxin.

Onabotulinumtoxin A was almost exclusively used for glabella and orbicularis oculi injection in this study, and it may limit generalization of the result to the other types of botulinum toxin. There is a paucity of data regarding distinctive diffusion characteristics of onabotulinumtoxin, abobotulinunmtoxin, and incobotulinumtoxin. In a mouse model, the 3 types of botulinum toxin exhibited a similar degree of diffusion.[35] But clinical studies showed that abobotulinumtoxin may spread to a larger area than onabotulinumtoxin.[36–38]

Blepharoptosis rarely occurred in our study of numerous same-day combined treatments of botulinum toxin injection in the glabella/orbicularis oculi and full-face nonablative fractional resurfacing. We conclude that nonablative fractional laser does not increase migration risk of botulinum toxin when the treatments were performed concomitantly.

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