Botulinum Toxin for the Treatment of Excessive Gingival Display: A Systematic Review

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Abstract

Background: To date, no standardized minimally invasive approach for the treatment of excessive gingival display exists.

Objectives: This systematic review aims to assess the evidence in the literature regarding the role of botulinum toxin injection in the management of gummy smile.

Methods: All publications through December 2014 and pertaining to the subject were electronically searched in PubMed, Embase, Scopus, and Web of Science, and the bibliographies of retrieved articles were manually screened.

Results: Out of 33 articles, 29 were discarded based on exclusion criteria. Although all 4 selected articles were in line with a role for botulinum toxin injection in the treatment of gummy smiles and the importance of targeting the levator labii superioris alaeque nasi muscle, studies differed in the type and the dose of toxin administered and the technique adopted.

Conclusions: Injection with botulinum toxin is a novel, safe, and cosmetically effective treatment for gummy smile when performed by experienced practitioners. However, further randomized controlled trials are warranted.

Level of Evidence: 4

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The smile, the cornerstone of all facial expressions, can indicate pleasure, favor, amusement, approval, or sometimes scorn. Not only does it reflect the inner feelings, but it is also an important aspect of socialization. There are 2 types of smiles: the social smile and the enjoyment smile.1 The former is voluntary, involving moderate muscle contraction, and the latter is involuntary, resulting from maximal contraction of the lip muscles.1,2 A cosmetic smile should be symmetric and displays less than 2 mm of the gum.2-4 Any exposure of the gum upon smiling beyond 2 mm is known as gummy smile (GS) or gingival smile and is often considered unattractive. A GS may result from delayed passive dental eruption, vertical maxillary excess, or hyperactivity of upper lip elevator muscles.3,5 In the presence of a high upper lip line, the diagnosis of long face syndrome should be suspected.5 If both physical examination and imaging confirm the diagnosis of vertical maxillary excess, a le Fort I osteotomy is then recommended.5,6 Other treatment modalities for GS include orthodontic treatment, bone resection, gingivoplasty, lip repositioning, and surgical...
manipulation of specific lip muscles. All of these procedures are complex, irreversible, and invasive. A simple new technique for the treatment of GS is botulinum toxin injection. First reported in a pilot study by Polo in 2005, botulinum toxin injection for GS treatment showed promising results. Though it did not gain United States (US) Food and Drug Administration (FDA) approval for this indication, botulinum toxin is currently often used to treat excessive gingival display as an off-label procedure in the US and other parts of the world. Six muscles have been targeted in the literature with various injection techniques, botulinum toxin types, and doses (Figure 1); the levator labii superioris alaeque nasi (LLSAN), the levator labii superioris (LLS), the zygomaticus minor (Zmi), the zygomaticus major (ZM), the depressor septi nasi (DSN), and the orbicularis oris (OO). Currently, there is no standardized approach for the treatment of excessive gingival exposure with botulinum toxin, and controversies still exist regarding this subject. This systematic review is an effort to summarize and compare available data guiding current practice and provide a road map for future research.

METHODS

This systematic review included all studies related to the treatment of gingival exposure with botulinum toxin injection through December 2014. On January 3, 2015, an online search of PubMed, Embase, Scopus, and Web of Science was conducted using the following search terms in combination: gingival-display OR gummy-smile OR asymmetric-smile OR gingival-exposure AND botox OR botulinum OR onabotulinumtoxinA OR abobotulinumtoxinA OR incobotulinumtoxinA. In addition, the bibliographies of retrieved studies were manually screened for articles pertinent to our review. Exclusion criteria were studies not specific to gummy smile treatment, studies without detailed description of the botulinum toxin injection technique, studies using another modality (surgery or laser), and case reports with fewer than 6 patients. For articles unavailable online, the corresponding authors were contacted by e-mail. The authors independently reviewed all articles and, based on the exclusion criteria, unanimously agreed on the final selection of articles for review.

RESULTS

The initial search on PubMed, Embase, Scopus, and Web of Science yielded 33 articles. Of these, 29 were discarded based on exclusion criteria: 16 studies were not specific to gummy smile treatment, 8 did not describe the technique of botulinum toxin injection or used another modality of treatment, and 5 were case reports with fewer than 6 patients. The manual bibliographical search of articles did not find any additional pertinent publications. Therefore, 4 articles were included (Figure 2) in our review. No randomized controlled trials (RCT) were identified in our search, and all included articles were prospective studies. The total number of patients in the 4 selected studies was 112. The number of patients in each study ranged from 14 to 52. Injection points used per side ranged from 1 to 3, and only 1 study differentiated between
anterior, posterior, mixed, and asymmetric GS. Muscles targeted by the injections were the LLSAN, the LLS, the ZM, and the Zmi. Three of the studies used onabotulinumtoxinA (Botox, Allergan, Irvine, California) with concentrations ranging from 2 IU/0.1 mL to 3.1 IU/0.1 mL. The remaining study used abobotulinumtoxinA (Dysport, Ipsen Biopharm Limited, Wrexham, United Kingdom) with a concentration of 25 IU/0.1 mL. The total dose of botulinum toxin injected per side ranged from 1.95 IU to 6 IU and from 2.5 IU to 7.5 IU for onabotulinumtoxinA and abobotulinumtoxinA, respectively (Figure 3). Pre- and postinjection gingival exposure measurements were reported in only 3 studies. Improvement of gingival display ranged from 71.93% to 98%. Detailed injection techniques, product preparation, amount of botulinum toxin used per treated side, gingival exposure measurements, improvement percentages, short-term adverse events, and gingival exposure measurements, improvement percentages, short-term adverse events, and treatment longevity are reported in Table 1. All described short-term adverse events were present solely in the first weeks following initial treatment. Facial asymmetries and other smile deformities were easily corrected with additional botulinum toxin injections. There were no reported long-term adverse events in any of the studies.

**DISCUSSION**

The etiology of excessive gingival display upon smiling has been thoroughly documented by Ezquerra et al. Three distinct components have been described: the bone in case of excess vertical maxilla, the gum in delayed passive dental eruption, and the muscles in hyperfunctioning upper lip elevators. A le Fort I surgery with impaction is the standard approach for correction of vertical bone excess.15-18 Short, square teeth, indicating a delayed passive eruption, have been traditionally treated by dentists using crown lengthening surgery involving gingivectomy, gingivoplasty, or apically positioned flaps with or without bone resection.19-22 The upper lip muscles hyperactivity has been managed with various techniques, including vestibular mucosa resection,23,24 myectomy with partial resection of levator muscles,25 and subperiosteal dissection of lip-elevating musculature.5,26 These irreversible and invasive interventions all aim at lowering the gingival display upon smiling to less than 2 mm. A novel and less invasive approach to treating hyperfunctional lip muscles is treatment with neurotoxins, which are safe, reliable, and reproducible. Since it is reversible, botulinum toxin injection constitutes an option for temporary correction of GS for patients willing to undertake more invasive and definitive procedures at a later date. Furthermore, with increasing age, the lip lengthens and makes this temporary and less invasive procedure more appealing to both patients and practitioners. In summary, botulinum toxin injections for treatment of excessive gingival display is indicated when the patient presents with gingival display upon smiling that...
Table 1. Summary of Botulinum Toxin Injection Techniques and Outcomes in the Treatment of Excessive Gingival Display

| Study, Year       | Study Design | Injection Technique (Muscle)                                                                                                                                                                                                 | Number of Patients | Product and Preparation                                                                 | Units per Side (UI) | Pre-injection Gingival Exposure (mm) | Post-injection Gingival Exposure (mm) | Improvement Percentage (%) | Short Term Adverse Events (Number of Patients) | Treatment Longevity (Weeks) |
|-------------------|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------|---------------------|-------------------------------------|-------------------------------------|---------------------------------|-----------------------------------------------|-----------------------------|
| Polo, 2008        | Prospective  | 2 injection points: overlapping points of LLSAN and LLS and the LLS and Zmi (LLSAN, LLS, Zmi)                                                                                                                               | 30                 | Botox (onabotulinumtoxinA) reconstituted to 2.5 UI/0.1 mL                               | 5                   | 5.2                                 | 0.09 at 2 weeks                     | 98 at 2 weeks                    | Pain at injection site (8), twitching at injection site (4), headache (1), dizziness (1) | > 24                        |
| Mazzuco and Hexsel, 2010 | Prospective  | Anterior GS: 1 injection point on the nasolabial fold, 1 cm lateral and below the nasal ala (LLSAN)                                                                                                                   | 3                  | Botox (onabotulinumtoxinA) reconstituted to 2.5 UI/0.1 mL                               | 2.5 or 5            | NS                                 | NS                                 | 96 at 20-30 days                  | None                                                          | 12-20                       |
|                   |              | Posterior GS: 2 injection points: (1) nasolabial fold, at the point of greatest lateral contraction during the smile (2) 2 cm lateral to the first point, at the level of the tragus (ZM, Zmi) | 7                  | Botox (onabotulinumtoxinA) reconstituted to 2.5 UI/0.1 mL                               | 5                   | NS                                 | NS                                 | 61.06 at 20-30 days              | Slightly asymmetric smile (1), “sad smile” due to hyperactivity of the depressor anguli oris muscles (1) | 12-20                       |
|                   |              | Mixed anterior and posterior GS: both anterior and posterior points of injection (LLSAN, ZM, Zmi)                                                                                                                     | 3                  | Botox (onabotulinumtoxinA) reconstituted to 2.5 UI/0.1 mL                               | 6.25 or 7.5         | NS                                 | NS                                 | 90.1 at 20-30 days              | None                                                          | 12-20                       |
|                   |              | Asymmetric GS: posterior points of injection on the side of greater gum exposure and only the lowest point on the contralateral side (ZM, Zmi)                                                                            | 3                  | Botox (onabotulinumtoxinA) reconstituted to 2.5 UI/0.1 mL                               | 5 on one side and 2.5 on the other | NS                                 | NS                                 | 71.93 at 20-30 days              | None                                                          | 12-20                       |
| Sucupira and Abramovitz, 2012 | Prospective  | 1 injection point 3 to 5 mm lateral to the nostril (LLSAN)                                                                                                                                                              | 52                 | Botox (onabotulinumtoxinA) reconstituted to 3.1 UI/0.1 mL                              | 2                   | 3.62                                | 0.58 at 2 weeks                     | 84 at 2 weeks                    | None                                                          | > 12                        |
| Suber et al., 2014 | Prospective  | 3 injection points: (1) 2 mm lateral to the alar-facial groove (2) 2 mm lateral to the first injection (3) 2 mm inferior and between the first 2 sites (LLSAN, LLS)                                                                 | 14                 | Botox (onabotulinumtoxinA) reconstituted to 2 UI/0.1 mL                                | 4-6                 | 4.89                                | 0.75 at 2 weeks                     | 85 at 2 weeks                    | None                                                          | 12                          |

GS, gummy smile; LLS, levator labii superioris; LLSAN, levator labii superioris alaeque nasi; NS, not specified; ZM, zygomaticus major; Zmi, zygomaticus minor.

exceeds 2 mm and at least one of the following: (1) the main cause of GS is muscle hyperactivity, (2) the patient opts for the least invasive treatment, (3) the patient requests a temporary treatment while awaiting definitive surgery, or (4) treatment is a complement to surgical treatment.

This systematic review aimed at summarizing the different injection techniques used for GS treatment. In the 4 included studies, the LLSAN was the lip elevator muscle consistently injected. The LLSAN originates from the frontal process of the maxilla, runs obliquely, and divides along the
deep surface of the skin into two fascicles (medial and lateral) that insert into the nasal ala and upper lip. Injecting the LLSAN can be performed along its course, either a few millimeters lateral to the nostril, 1 cm lateral and below the nasal ala, or in the nasolabial fold at its intersection with the LLS. In their intent to individualize the treatment approach, Mazzuco and Hexsel classified GS according to the area of gingival exposure (anterior, posterior, mixed, and asymmetric types) and injected the respective muscles accordingly. However, in the case of posterior and asymmetric GS, when the anterior muscle group, including the LLSAN, was not injected, a lower average improvement was noted: 61.06% and 71.93% in posterior and asymmetric groups, respectively compared with 96% and 90.1% in anterior and mixed groups, respectively. This further obviates the LLSAN as a crucial muscle in the treatment of GS. Hwang et al, in this regard, used measurements done on cadavers to identify the “Yonsei point,” the point that would target 3 muscles, including the LLSAN, in a single injection. This landmark was identified as the center of a triangle formed by the convergence of the LLSAN, the LLS, and the Zmi muscles and is located 1 cm lateral to the ala horizontally and 3 cm above the lip line vertically in both men and women.

Increasing the number of injection points per side does not seem to lead to an improved aesthetic outcome. Though Sucupira and Abramovitz used only one injection point lateral to the nostril targeting the LLSAN, the average improvement of 84% obtained with a unique injection point is comparable to the average improvement of 85% obtained with 3 injection points in the Suber et al study and the average improvement of 98% obtained with 2 injection points in the Polo study. However, this equivalent outcome might also be the result of a heterogeneous baseline patient population as the average preinjection gingival display of 3.62 mm measured in the Sucupira and Abramovitz study is lower than the one measured in the other 2 studies. In a recent publication, Polo advised that the dose and injection sites of botulinum toxin should be tailored to the severity of gingival display: 1 injection site when the gum exposure is inferior to 7 mm and 2 injection sites when it exceeds 7 mm.

Both onabotulinumtoxinA and abobotulinumtoxin A were successfully employed in our selected studies. There is no universally agreed upon conversion rate for these available toxins; nevertheless, based on the standard conversion rate adopted in the literature between abobotulinumtoxinA and onabotulinumtoxinA of 2.5:1 IU, the amount of abobotulinumtoxinA used by Mazzuco and Hexsel (2.5 to 7.5 IU) appears comparable to the amount of onabotulinumtoxinA used in the other studies (1.95 IU to 6 IU). Thus, it seems that at equivalent doses, abobotulinumtoxinA and onabotulinumtoxinA yield similar results.

When comparing the onabotulinumtoxinA cumulative doses injected per side and ranging between 1.95 IU and 6 IU, it seems that both low and high doses could be used effectively in the treatment of GS. In this regard, Garcia and Fulton showed that low-dose injection of botulinum toxin per muscle (2-5 IU) was as effective as higher doses. Though prior studies have demonstrated a correlation between higher doses of botulinum toxin and intensity and duration of muscle paralyses, no conclusion can be drawn regarding duration and intensity of doses used in the 4 included studies. A safe approach advocated by some authors consists of starting with low toxin doses initially, with retouching at a later stage if required.

Polo noted that the average gingival show had still not returned to baseline values at 24 weeks postinjection. Similarly, Mazzuco and Hexsel demonstrated that there is a prolonged reduction of gingival exposure following several injections of botulinum toxin. One explanation for this process is that prolonged muscle paralysis occurring after several injections can ultimately lead to partial muscle atrophy and permanent decrease in contraction capacity, even after disappearance of the toxin effect.

Several undesirable effects of the treatment of GS with botulinum toxin have been reported: asymmetric smile easily corrected with additional injections, collapse of the oral commissure resulting in a “sad appearance,” lengthening of the upper lip, “joker smile,” inferior lip protrusion, drooling, and difficulty smiling, speaking, or eating. Though most of these adverse events are easily corrected with retouching at the follow-up visit, some can cause substantial dysfunction lasting several months. These complications are most often due to poor injection techniques or inappropriate amounts of botulinum toxin resulting from limited experience. In fact, several authors agreed that these injections should be reserved to highly experienced practitioners.

There are several limitations to this review. Though prospective, the 4 included studies harbor different confounding factors and biases. In addition, the lack of a randomized controlled trial prevented us from performing a traditional meta-analysis and limited our systematic review to a form of pooled analysis. The large amount of variability between studies, especially in the measurement methods of pre- and postinjection gingival display, restricted the inter-study comparison. All retrieved studies had a small sample size, which might be due to the fact that this treatment modality is relatively new. Other limitations were inter-practitioner disparities, individual anatomic variations of the patients included in the studies and publication bias, as only published articles were evaluated.

CONCLUSIONS

Botulinum toxin injection is a new, effective, and reversible method for GS treatment. Depending on the individual component of the GS, botulinum toxin injection can be used as an independent treatment, as an adjunct to other invasive
techniques, or as a temporary measure while waiting for a permanent solution. Based on data available in the literature, the LLSAN muscle should be considered as the key component in GS treatment. Other potential targets to take into consideration are the LLS, the ZM, and the Zmi muscles. The injection of botulinum toxin in the mid and lower face must be carefully performed and only by experienced practitioners. Table 2 summarizes the main findings and recommendations attained in this review. Faced with the paucity of data, future adequately designed, randomized controlled trials are warranted to compare the efficacy of described techniques and assess the impact of infiltrated muscles, amount of toxin used and injection of onabotulinumtoxinA versus abobotulinumtoxinA on clinically relevant outcomes.

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Table 2. Key Points

- Treatment of GS with botulinum toxin is indicated when the patient presents with gingival display superior to 2 mm and at least one of the following:
  - The causative mechanism of GS is muscle hyperactivity.
  - The least invasive treatment is preferred.
  - As a temporary treatment while awaiting surgery.
  - As an adjunct to surgical treatment.
- LLSAN muscle is the key component in gummy smile treatment. Other potential targets are the LLS, the ZM and the Zmi muscles.
- At equivalent doses based on a conversion rate of 2.5:1 IU, abobotulinumtoxinA and onabotulinumtoxinA yield comparable results.
- Both low and high doses could be used effectively in the treatment of GS but higher doses may lead to increased adverse events.
- A safe approach consists of administering low toxin doses initially with retouching at a later stage when required.
- The treatment of GS with botulinum toxin lasts for at least 12 weeks.
- Following several injections with botulinum toxin, there is prolonged reduction of gingival exposure.
- Treatment of GS with botulinum toxin should only be performed by experienced practitioners.

GS, gummy smile; LLS, levator labii superioris; LLSAN, levator labii superioris alaeque nasi; ZM, zygomaticus major; Zmi, zygomaticus minor.
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