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ASSESSMENT OF PROLONGED EFFECT OF REPEATED BOTULINUM TOXIN-A INJECTION FOR GUMMY SMILE CORRECTION

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ABSTRACT

Objective: The present study was conducted to evaluate the prolonged effect of repeated Botulinum toxin-A injection for correction of gummy smile.

Materials & methods: Sixteen subjects with a mean age of 23.5 years, showing excessive gingival display mainly due to hypermobile upper lip or mild vertical maxillary excess participated in this study. Standardized 2D frontal and profile both resting and maximum smile photographs were taken before and 14 days after each botulinum toxin -A injection and four months later. The study participants were randomly allocated into two groups where the first group received two injections that are four months apart while the second group received three injections that are four months apart as well.

Results: Both groups showed reduction in incisal-gingival display, upper lip mobility and upper lip length reduction fourteen days after injection, The first group relapsed almost back to baseline four months after the second injection, however the second group maintained a larger increment of the achieved corrections four months after the third injection.

Conclusion: From the results obtained from this study, it could be concluded that repeated injections of Botulinum toxin helped maintain a larger increment of the corrections achieved.

KEY WORDS: Gummy smile, Hypermobile upper lip, Botulinum toxin- A.

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INTRODUCTION

A smile is an essential element of face aesthetics. There is a considerable correlation between an individual's physical appearance and social attractiveness, which has been thoroughly proven in the literature. As a result, the most prevalent motivations for individuals seeking orthodontic treatment are to improve their smile and facial attractiveness. (1)

Smile aesthetics parameters may be divided into three categories: the lip framework (macro-esthetics), gingival tissues (mini-esthetics), and dentition (micro-esthetics). (2,3)

The framework for smiling is the center of the mini-esthetics investigation. The goal of orthodontic treatment is to create a social smile that is both aesthetically pleasing and functionally sound. No matter how the teeth appear when they are isolated, if they don't spatially match the rest of the facial structures, the overall impression will not be pleasing. As a result, the aesthetics of the smile framework is determined by characteristics such as the incisor and gingival display on the smile, smile symmetry, smile arc, vermillion display, and buccal corridors. (3,4)

Excessive gingival display during the smile has been an aesthetic issue for many patients, which can undoubtedly affect their psychosocial behavior, even though showing a small amount of gum (1-2 mm) during a normal smile is aesthetically acceptable and, in many cases, imparts a youthful appearance. (5)

The cause of the Gummy smile can be multifactorial and in order to provide the proper care, the etiology of the gummy smile must be precisely identified. Factors that contribute to Gummy smile include altered passive eruption, plaque-/drug-induced gingival enlargement, lip length, lip hypermobility, incisal wear/crown length, vertical maxillary excess, and gingival hyperplasia. (6)

Since Gummy smile is a multifactorial esthetic problem with different etiologies of which can only one be the cause or multiple causes can aggregate together to result in it and so it has multiple treatment options some of which are surgical including lip repositioning, gingivectomy and crown lengthening or even orthognathic surgery as well as the non-surgical methods including orthodontic intrusion, hyaluronic acid filler injection and botulinum toxin A injection .The current study was conducted to evaluate the durability of effects of repeated injections of Botulinum toxin A.(6)

MATERIAL AND METHODS

This study was approved by the ethical committee at the Faculty of Dentistry, Ain-Shams University*. All subjects were randomly selected from the outpatient clinic of the Orthodontic Department, Faculty of Dentistry, Ain-Shams University. All patients had been informed about the purpose of the study and possible complications; and signed an informed consent form.

All patients met the following inclusion criteria: Excessive gingival display more than 3 mm at the central incisors upon maximum smiling due to the any of the following etiologies (1) Hypermobile upper lip (2) Mild vertical maxillary excess. (3) Mild to excessive vertical maxillary excess in patients refusing orthognathic surgery. (4) Excessive vertical maxillary excess in patients expecting surgery as a temporary resolution.(5) Altered active or passive eruption requiring an adjunctive treatment. and (6) Females aging 18-30 years.

The exclusion criteria were: Excessive gingival display more than 3 mm at the central incisors upon maximum smiling due to the any of the following etiologies(1) Short upper lip.;(2) Patients on medications causative of gingival overgrowth.; (3) Altered passive eruption.;(4) Over erupted upper

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anterior teeth.; (5) Patients with previous history of allergy to botulinum toxin-A.; (6) Patients undergoing orthodontic treatment during which intrusion is planned. and (7) Pregnant/lactating women.

The power analysis of this study was based on the study by **Soris BAT et al (2021)** following up the effects of the use of botulinum toxin A in treatment of gummy smile over 7 months, the mean deviation was 2.067 and the standard deviation was 0.267.[7]

Two sample t-test at a conventional alpha level (p=0.05) with desired power of 80% was done. The calculations were performed using the G*power** software, which is based on the formulas of Cohen.

The test resulted in a total number of 8 patients in each group, so a total sample size of 16 participants were enrolled in the study.

The diagnostic procedure included history taking, clinical examination and radiographic examination.

Detailed history was taken, with special regard to medications that induce gingival enlargement and neuromuscular disorders that counteract usage of botox.

Extraoral examination included assessment of upper lip length measured as the distance between subnasale to upper lip stomion, incisal gingival display at rest and maximum smile measured as distance from incisal edge of maxillary central incisor edge to the upper lip stomion as well as lip mobility that is the difference between incisal display at rest and maximum smile and percentile lip mobility calculated according to the following formula (lip mobility/upper lip length at rest x 100).[8,9]

Profile examination was made to assess vertical facial proportions where long faces can be suggestive of vertical maxillary excess, also lip protrusion and incompetence can be associated with proclined incisors or protrusive maxilla that are both associated with GS, incisal gingival display at rest and smiling was also assessed from profile views.[8,9]

Intraoral examination included a special regard to oral hygiene, presence of signs of gingival inflammation or enlargement . Upper incisors inclination, presence of any chipping or attrition and any habits like nail biting or teeth grinding that can affect crown height/width ratio were also thoroughly investigated , chu gauge was used to assess crown width/height ratio and to calculate compensations needed .[9]

Also a graduated periodontal probe is used to measure sulcus depth to diagnose gingival enlargement as well as bone sounding to diagnose altered passive eruption.[9]

Lastly, radiographic examination, panoramic radiographs were taken for assessment of general periodontal health and lateral Cephalometric radiographs were taken where landmarks were identified, and cephalometric analysis was carried out to confirm the presence of VME. Several linear and angular measurements were used to confirm diagnosis including rickett's maxillary angle, mandibular plane angle, total and anterior facial heights .[9]

Standardized pre-treatment photographs (frontal, profile, close up frontal and profile resting and maximum smile) were taken in the Natural head position for every subject that was achieved by utilizing self-balance position which is achieved when the subject had her own feeling of natural head balance after head tilting exercises (moving their head back and forth) with little capacity while they stood looking into their eyes on a vertical mirror 1m away, and teeth occlusion was made in centric slightly.[10]

Standardization was also maintained by taking photographs where the camera was supported by a

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double spirited tripod that was placed at a fixed distance from the patient at every imaging instant.[11]

A graduated grey background was placed at a fixed distance behind the patients' head. The graduated scale is used as tool to facilitate accurate patient head orientation (The midsagittal plane parallel to grid lines and perpendicular to the floor) by matching the grid on the camera screen with the graduated scale lines as well as helping standardize magnification to aid accurate measurements while using photos on the chosen software.[10]

Patient face especially the site of injection was disinfected by ethyl alcohol 70% spray on sterile gauze. After allowing the disinfectant to dry, topical anesthetic cream (EMLA cream 25mg/g lidocaine -25mg/g prilocaine)* was applied at the injection site to minimize needle prick discomfort and to guarantee patient commitment to repeated injections.[12]

Eye liner pen was used to mark the injection points, patients were instructed to smile as maximum as possible. In cases of anterior gummy smile "Yonsei point" is marked on both sides this point is 1cm lateral to the ala and 3 cm above the upper lip, while in cases of both anterior and posterior gummy smile a point one cm lateral to the bracketing of the nasolabial fold on both sides for targeting zygomaticus major as well as "Yonsei point". [13]

The Botulinum toxin -A used in the study was xeomin®** that was provided as freeze-dried powder, it was diluted by 4 ml of saline to draw a concentration of 2.5 units per 0.1 ml. After confirming adequate anesthesia, Insulin needle is inserted perpendicular and deep into the muscle (almost 2/3 needle length) where slow injection of the solution was done. Figure (1,2)

Fig. (1) Injection into Yonsei point

Fig. (2) Injection into bracket of nasolabialfold

Measurements:

For each patient enrolled in the study, post-injection 2D standardized photographs were taken in a similar standardization manner as the pretreatment photos.

Those photographs were taken at the following measurement times ,T0(before any treatment was made), T1(14 days after the first injection for both groups), T2(4 month after the first injection for both groups and time for second injection), T3(14 days after the second injection for both groups), T4(4 month after the second injection for both groups and time for third injection for the second group and end point of the study for first group),T5(14 days after

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the third injection for second group), T6(4 month after the third injection and end point of the study for second group)

Post-treatment photographs were also taken measure the following measurements:

1. Incisal-gingival display at maximum smiling: measured at incisal edge of the upper central incisors to the upper lip vermillion border. Figure (3)
2. Upper lip mobility: measured as the difference between incisal-gingival display at rest and maximum smile.
3. Upper lip length reduction: calculated according to the following formula (lip mobility/upper lip length at rest x 100).

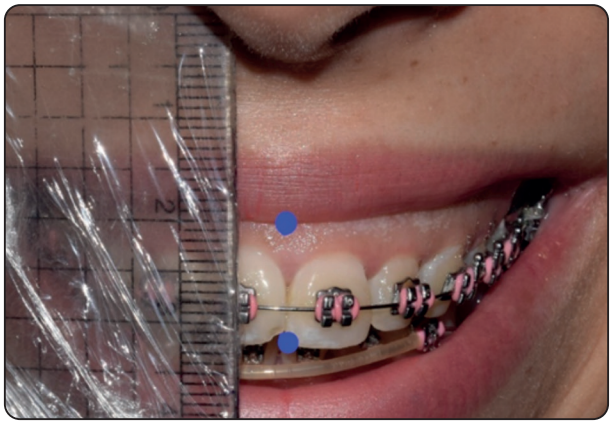

Fig. (3) Dentogingival display upon smiling.

RESULTS

Comparison between pretreatment & post treatment records as regarding incisal-gingival display between two groups was performed; by using ANOVA test, also it was similarly used to compare changes at different time periods within the same group.

As regarding incisal gingival display, At T0(pre-injection), T1(fourteen days after 1st injection), T2(four months after 1st), T3 (fourteen days after 2nd injection) as well as T4(four months after 2nd), there was no statistically significant difference between mean gingival display measurements in the two groups (P-value ≤ 0.05).

In Group I, Pair-wise comparisons between time periods revealed that there was a statistically significant decrease in gingival display from T0 to T1 followed by a statistically significant increase in gingival display from T1 to T2. There was a statistically significant decrease in gingival display from T2 to T3 followed by a statistically significant increase in gingival display from T3 to T4. There was no statistically significant difference between mean gingival display at T0, T2 and T4.

In Group II, there was a statistically significant change in gingival display by time (P-value ≤0.05). Pair-wise comparisons between time periods revealed that there was a statistically significant decrease in gingival display from T0 to T1 followed by a statistically significant increase in gingival display from T1 to T2.

There was a statistically significant decrease in gingival display from T2 to T3 followed by a statistically significant increase in gingival display from T3 to T4. From T4 to T5(fourteen days after 3rd injection), there was a statistically significant decrease in gingival display followed by non-statistically significant change in gingival display from T5 to T6(four months after 3rd). The mean gingival display at T6 showed statistically significantly lower value compared to gingival display at T0. (Table 1) (Figure 4,5,6)

Similar changes were also recorded as regarding upper lip mobility as well as upper lip length reduction either while comparing the same group at different time periods or comparing the two groups. (Table 2,3)

TABLE (1) Descriptive statistics and results of repeated measures ANOVA test for comparison between gingival display at different time periods within each group

Time	Group I (n = 8)		Group II (n = 8)	
	Mean	SD	Mean	SD
T0	14.61 ^{A}	1.46	16.02 ^{A}	1.53
T1	11.44 ^{B}	1.43	13.2 ^{C}	2.35
T2	14.29 ^{A}	1.36	15.69 ^{AB}	1.62
T3	11.5 ^{B}	1.38	13.34 ^{C}	2.26
T4	14.37 ^{A}	1.44	15.34 ^{B}	1.72
T5	-	-	13.2 ^{C}	2.28
T6	-	-	13.83 ^{C}	0.92
P-value	<0.001*		<0.001*	
Effect size (Partial Eta squared)	0.927		0.894	

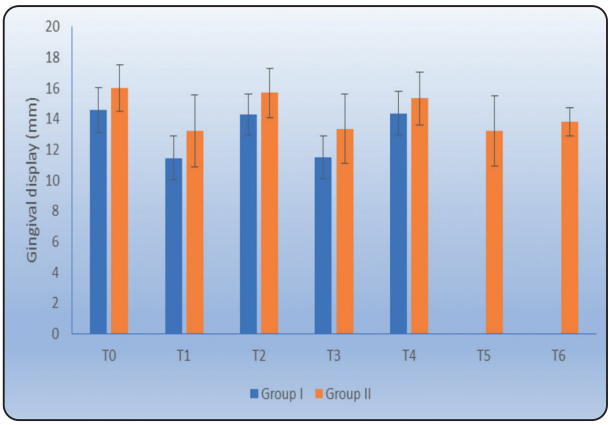

Fig. (4) Bar chart representing mean and standard deviation values for gingival display measurements in the two groups

Fig. (5) Changes in incisal gingival display for group 1 case

Fig. (6) Changes in incisal gingival display for group 2 case

TABLE (2) Descriptive statistics and results of repeated measures ANOVA test for comparison between upper lip mobility at different time periods within each group

Time	Group I (n = 8)		Group II (n = 8)	
	Mean	SD	Mean	SD
T0	13.21 ^{A}	0.91	13.6 ^{A}	1.77
T1	10.04 ^{C}	0.67	10.82 ^{C}	2.4
T2	12.9 ^{B}	0.73	13.27 ^{B}	1.83
T3	10.1 ^{C}	0.64	11.04 ^{C}	2.25
T4	12.97 ^{B}	0.87	12.92 ^{B}	1.95
T5	-	-	10.78 ^{C}	2.44
T6	-	-	11.98 ^{C}	2.14
P-value	<0.001*		<0.001*	
Effect size (Partial Eta squared)	0.955		0.881	

: Significant at P ≤ 0.05, Different superscripts in the same column indicate statistically significant change by time

TABLE (3) Descriptive statistics and results of repeated measures ANOVA test for comparison between upper lip length reduction in the two groups

Time	Group I (n = 8)		Group II (n = 8)		P-value	Effect size (Partial Eta squared)
	Mean	SD	Mean	SD		
T0	56.9	4.9	58	11.4	0.810	0.004
T1	44.1	3.2	46	11.4	0.646	0.016
T2	55.6	3.9	56.6	11.2	0.816	0.004
T3	43.5	2.5	47	11.3	0.397	0.052
T4	55.9	4.5	55.1	11.5	0.862	0.002
T5	-	-	45.9	11.7	-	-
T6	-	-	51	11.2	-	-

: Significant at P ≤ 0.05, Different superscripts in the same column indicate statistically significant change by time

DISCUSSION

Of these various treatment approaches of gummy smile, Botulinum toxin-A injection is a relatively simple, noninvasive, less adverse-effective, and of a debating belief of being reversible treatment approach that is drawing a lot of attention.[14]

According to **Jankovic J** the therapeutic value of this Botulinum toxin-A derives from its ability to inhibit the release of acetylcholine from the presynaptic nerve terminal, causing local chemo denervation thus reducing muscle contractility.[15]

Despite **Felber ES (2006)** stated that**,** the effect of paralysis occurs within 3–7 days after intramuscular administration, while the maximum effect is seen after 1–2 weeks, then tapers down to a moderate plateau until full nerve recovery within 3–6 months.[16] On the contrary, studies by **Polo M(2005)** and **Mazzuco R & Hexsel D(2010)** have stated that repeating injections can lead to sustained results owing to muscle memory and reduction of muscle activity.[17,18]

In terms of incisal gingival display changes, closely similar results to those of our study were reported in the study by **Hexsel D et al. (2021)**, the mean anterior gingival exposure, at baseline, was 3.5±1.2 mm for the patients treated with 2.5 U and 4.0±1.0 mm for those treated with 5 U. It reduced significantly 4 and 12 weeks after treatment with both doses, the results of his study showed the average reduction of gingival exposure with 5 U per side was was significantly larger than that obtained with 2.5 U.[19]

Also, the study by **Soris BAT et al. (2021)** showed a high degree of agreement with results of the current study**,** the mean value of gingival display on maximum smile prior to injection was 7.07±1.280 mm, while On day 7 and 15 postinjection the mean value was 5.07±0.961 mm, this significant reduction lasted no more than the fourth month provided that the study involve a single injection of each participant.[7]

As compared to the study of **Polo M (2008)** in his study made on 30 patients, the Preinjection gingival display averaged 5.2 mm (±1.4 mm) in the 30 subjects. At 2 weeks post injection, mean gingival display had declined to 0.09 mm (±1.06mm). [20]

The difference in results compared to our study can be attributed to the difference in the product used in the study where in the study of polo the used botulinum Toxin-A was Botox (Onabotulinum toxin A) that is supposed to be of slightly higher potency and longevity compared to incobotulinum used in the study , also the method of recording the patient maximum smile and the effort done to record such a smile is essential to ensure that the amount of gingival display before and after correction represents the actual changes.

As regarding upper lip mobility represented as difference between incisal gingival display between rest and smile or as the difference in lip length between repose and smile . Slightly higher changes in the upper lip mobility were reported in the study by **Polo M (2005)** where the mean pre-injection upper lip length during maximum smiling was 10±1.87mm, while the mean post injection upper lip length during maximum smiling was 14±1.58mm, this can similarly be attributed to the difference in the product used, the method of measurement applied that was just a ruler placed to patient face in the study and the recording of the maximum smile.[17]

Similarly, in the study by **Cengiz A, Goymen M and Akcali C (2020)**, the mean upper lip length during maximum smiling before injection for group 1 was (15.84±3.2)mm, that increased to (18.98± 3.26)mm 15 days after injection, but reduced again to (16.48±2.85)mm after six months assessment, for group 2 the mean upper lip length during maximum smiling before injection was (16.22±2.31)mm that increased to (17.13±1.80)mm 15 days after injection but decreased again to (16.58±2.19)mm six months after injection.[21]

And finally assessment of changes in upper lip length reduction (Effective or Percentile lip length) showed similar results to the study by **Polo M (2005)** where the effective increase in upper lip length upon smiling was 131%,120%, 124%, 117%, and 129% (mean, 124.2%) for patients 1 through 5, respectively. [17]

CONCLUSIONS

Repeated injections of Botulinum toxin-A for cases of gummy smile due to upper lip hypermobility and mild VME helps maintain a larger increment of the corrections achieved.

REFERENCES

1. Al Fawzan A. Reasons for seeking orthodontic treatment in Qassim region: a Pilot Study. 2012;1.
2. Sharma PK, Sharma P. Dental Smile Esthetics: The Assessment and Creation of the Ideal Smile. Semin Orthod. 2012;18(3):193-201.
3. Tauheed S, Islam U, Behroz Khan C E, Hassan S, Raza HA. Macro, Mini and Micro-Esthetics: An Evaluation of Orthodontically Treated Patients.
4. Aravind Krishnan R, Nivedita Sahoo. Role of Macro, Mini and Micro Esthetics in Orthodontics. LAP Lambert Academic Publishing; 2020.
5. Jacobs PJ, Jacobs BP. Lip repositioning with reversible trial for the management of excessive gingival display: a case series. Int J Periodontics Restorative Dent. 2013;33(2):169-175.
6. Nir Silberberg, Moshe Goldstein, Ami Smidt. Excessive gingival display— Etiology, diagnosis, and treatment modalities. Quintessence Int (Berl). 2009;40(10):809-818.
7. Soris BAT, Shenoy KV, Ramadorai A, Kumar CSCS and Marimuthu L. Botulinum Toxin-A in the Treatment of Excessive Gingival Display: A Clinical Study. J Maxillofac Oral Surg. 2022;21(1):51-57
8. Roe P, Rungcharassaeng K, Kan JYK, Patel RD, Campagni W Vand Brudvik JS. The Influence of Upper Lip Length and Lip Mobility on Maxillary Incisal Exposure. Am J Esthet Dent.2012;2(2);116-125
9. El-Bokle D and Ghany AHA. A systematic diagnostic scheme for excessive gingival display "gummy smile." AJO-DO Clinical Companion. 2022;2(4):335-343.

10. R Mahmoud. Analysis of smile characteristics among the Egyptian population. “Master thesis”, Cairo, Egypt, Ain Shams University. 2010.

11. Sharara HA. Miniscrew-aided Fixed Orthodontic Appliance versus Miniscrew-aided Thermoplastic Splint for Treatment of Gummy Smile and Vertical Maxillary Excess A Randomized Clinical Trial “PhD thesis”, Cairo, Egypt , Ain Shams University.2023

12. Eppley BL. Easing Botox Administration With EMLA Cream. Aesthet Surg J. 2004;24(1):79-81.

13. Al Wayli H. Versatility of botulinum toxin at the Yonsei point for the treatment of gummy smile. Int J Esthet Dent. 2019;14:86-95.

14. Azam A, Manchanda S, Thotapalli S and Kotha SB. Botox Therapy in Dentistry: A Review. J Int Oral Health. 2015;7(Suppl 2):103-105.

15. Jankovic J. Botulinum toxin in clinical practice. J Neurol Neurosurg Psychiatry. 2004;75(7):951-957.

16. Felber ES. Botulinum toxin in primary care medicine. J Am Osteopath Assoc. 2006;106(10):609-614.

17. Polo M. Botulinum toxin type a in the treatment of excessive gingival display. American Journal of Orthodontics and Dentofacial Orthopedics. 2005;127(2):214-218.

18. Mazzuco R and Hexsel D. Gummy smile and botulinum toxin: A new approach based on the gingival exposure area. J Am Acad Dermatol. 2010;63(6):1042-1051

19. Hexsel D, Dal’Forno T, Camozzato F et al. Effects of different doses of abobotulinumtoxinA for the treatment of anterior gingival smile. Arch Dermatol Res. 2021; 313(5):347-355.

20. Polo M. Botulinum toxin type A (Botox) for the neuromuscular correction of excessive gingival display on smiling (gummy smile). Am J Orthod Dentofacial Orthop. 2008;133(2):195-203.

21. Cengiz AF, Goymen M and Akcali C. Efficacy of botulinum toxin for treating a gummy smile. American Journal of Orthodontics and Dentofacial Orthopedics. 2020;158(1):50-58.