

Does the Botulinum Toxin Affect the Philtral Length in Primary Repair of Unilateral Cleft Lip?

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ABSTRACT

Background: Repair of cleft lip deformities requires careful planning to create functional and aesthetically pleasing upper lip contour. Cleft lip scar has a serious impact on appearance. Many factors affect the formation of a scar, as continuous muscle contraction. The botulinum toxin has been used recently to minimize facial scarring by decreasing wound tension as it produce a localized muscle weakness. The injection of botulinum toxin into lip muscles reduces the continuous muscle contraction and skin tension and creates a good condition for wound healing and reduction of the formation of hypertrophic lip scar after lip repair. We suggest that preoperative botulinum toxin injection into the orbicularis oris muscle of wide cleft lip patients improves the outcome of cleft lip repair. **Methods:** In this study, 20 patients with complete unilateral cleft lip were divided into two groups, the first group was injected with botulinum toxin (10 patients) and the other group control (10 patients) was injected with saline. Injection was done with insulin syringe 7 days before primary lip repair using modified Millard cheiloplasty. The patient's scars were assessed using photography and scar length and width measurements after 3 and 6 months. **Results:** The difference between the two groups was statistically significant after 3 and 6 months. These results show that botulinum toxin had a better effect in decreasing the scar width and increasing the philtral length. **Conclusions:** Botulinum toxin injection into the orbicularis oris muscle in unilateral complete cleft lip preoperatively shows significant improvement in the cheiloplasty scar.

Key words: Botulinum toxin, Cleft lip repair, Philtral length

INTRODUCTION

Orofacial clefts primarily cleft lip and cleft palate are among the most common birth defects in population worldwide.^{1,2} According to the World Health Organization (WHO), one infant per 500-700 is born worldwide presenting with cleft lip and/or palate.³

The scar on baby's lip, following surgical repair of the cleft, marks him/her and affects both the child and the family socially and emotionally.

Tension applied to the wound edges during the healing process is considered one of the important factors that affect wound healing and the cosmetic outcome of skin scars⁴. Tension on the wound was also shown to prolong the inflammatory phase of wound healing resulting in scar hypertrophy.⁵

Hypertrophic scar following cleft lip repair is relatively common and may require surgical revision.⁶

The therapeutic value of botulinum toxin type-A is its ability to cause chemodenervation which is prolonged inhibition

of neurotransmitter release at peripheral cholinergic nerve terminals, and to produce local paralysis when injected into a muscle thus decreasing tension applied to the wound edges.⁷ The benefits anticipated from this intervention are minimizing the scar width and improvement of the nose and labial appearance.

PATIENTS AND METHODS

The study was conducted on twenty patients with complete unilateral cleft lip, selected from the outpatient clinic of Department of Plastic Pediatric Surgery, the Specialized Pediatric Hospital- Cairo University.

All patients were primary non syndromic complete unilateral cleft lip cases. They were 15 males and 5 females, age at presentation ranged from 3 to 6 months.

All patients were evaluated for:

- Family history, history of drug intake, associated congenital condition.

- General condition evaluated by pediatric physician.

For all patients, the following preoperative investigations were done:

- Complete blood picture.
- Bleeding profile (PT, PTT, and INR).
- Chest condition is assessed by pediatrician and anesthesiologist.
- Preoperative and postoperative photography 3 and 6 months frontal and basal views were taken.

All patients were informed about the procedure and the possible postoperative complications, and signed the consent.

The treatment plan for those patients consisted of the following stages:

- 1- Pre-operative injection of botulinum toxin.
- 2- Surgical stage

Pre-operative injection:

There are two groups, the first group was injected with botulinum toxin and the other group (control) was injected with saline.

Topical anesthesia was applied over the skin of lip on both sides of the cleft where the injection is done.

Injection was done with insulin syringe 7 days before primary lip repair by modified Millard cheiloplasty.

▪ **Group (1): (BTX-A group)**

The vial was reconstituted using 4 milliliter saline to obtain a 2.5 unit/0.1 milliliter solution as directed in the product inserts.

Botulinum toxin (1.5-2 U/kg) injected in the muscles of upper lip via 4 superficial injection sites. So, about 10 units are injected to each side.

▪ **Group (2): (control group)**

Use insulin syringe to aspirate 0.5 milliliter of saline solution.

There will be the same amount of normal saline injection, as BTX-A group in the muscles of upper lip via 4 superficial injection sites.

Injection sites:

On the cleft side:

First site of injection: 2mm laterally to the edge of the cleft and 1mm above the white roll of the lip.

Second site of injection: just below the alar base.

On the non-cleft side:

First site of injection: 3mm laterally to the edge of the cleft and 1mm above the white roll of the lip

Second site of injection: just below the nasal sill

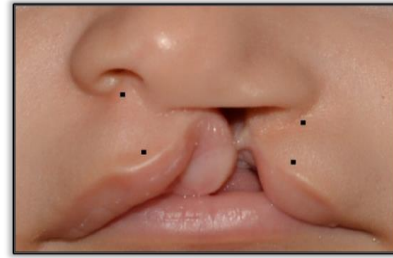


Fig. (1): Sites of injections

Surgical technique

All procedures were done under general anesthesia, with central oral endotracheal tube and I.V. line. Lip repair was done using modified Millard technique.

Incisions sites are then marked.

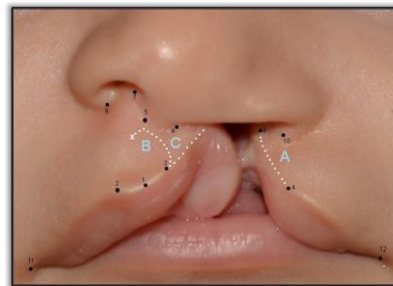


Fig. (2): Landmarks and cutting design for modified rotation-advancement technique: (A) advancement flap, (B) rotational flap, (C) C-flap

Before incision, it is important to measure the distance from the peak of Cupid's bow to the columellar base on each side. This will give an assessment of how much the cleft has shortened the lip.

Incisions

After meticulous and careful marking, the lip is injected with approximately 3 ml of 1% lidocaine with 1:200000 epinephrine into the lip and alar base for hemostasis governed by heart rate of the patient.

Full thickness incision is done.



Fig.(3): All incisions are made

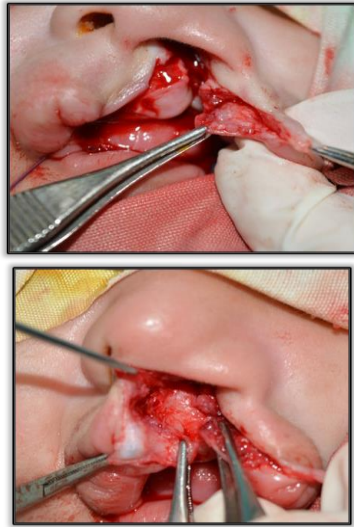


Fig. (4): Muscle incisions on the lateral and medial flaps.

Closure

Closure begins with 4-0 vicryl sutures placed in simple interrupted manner with the buried knots, to reconstruct the orbicularis oris muscular sphincter.

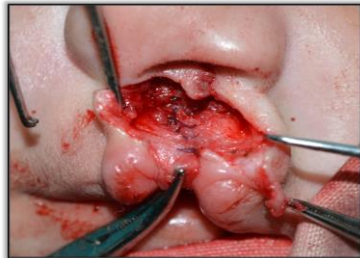


Fig. (5): The orbicularis oris muscle fibers and nasal floor are closed with sutures.

Finally, 5-0 vicryl sutures are placed in the vermillion and the mucosa of the lip completing the closure.



Fig. (6): Final closure of the cleft lip repair with modified rotation-advancement technique.

1- Post-operative care

- Immediate Postoperative instructions:

- Soft arm restrains are used for 2 weeks to prevent any trauma.
- Feeding is performed using a syringe with a soft tipped catheter for 5-7 days.
- No nipples or pacifiers are used for 1 week.
- Postoperative massage of the scar starts 2 weeks after the operation and is continued for 8 weeks, twice daily to soften the scar.
- The sutures are removed 7 days postoperatively.

- Follow-up visits:

- 1st visit: 1 week postoperative to remove stitches and to assess any lip dehiscence or scar infection and the patients were photographed.
- 2nd visit: 3 months postoperative photography to evaluate the scar width and length of philtral ridge.
- 3rd visit: 6 months postoperative photography to evaluate the scar width and length of philtral ridge.

- Assessment parameters:

- Length of philtral ridge (in cleft and non-cleft side)
- Scar width

Photographic measurements

Standard photographs were taken; objective measurements were obtained from the photographs using the ruler as a control reference.

One standard surgical ruler was placed over the lower lip and a frontally orientated photograph of the patient was taken after 3 and 6 months to evaluate the scar width and length of philtral ridge using the ImageJ program (National Institutes of Health, Bethesda, MD).

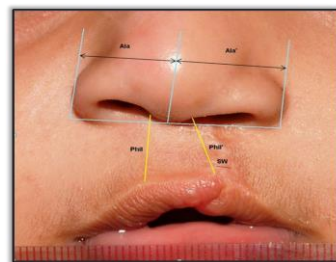


Fig. (7): Points and distances taken into consideration in the evaluation of cleft lip 6 months post-operative, scar width (SW), philtral ridge length (Phil).

Statistical analysis

All statistical analyses were conducted using SPSS software (version 17.0; IBM Corporation, NY, USA). VSS score, scar width, length of philtral ridge and width of alar base were compared.

The independent t-test was used to compare groups. Statistical significance was defined if $P \leq 0.05$. Data are presented as mean \pm standard deviation.

RESULTS

Twenty patients were included in the study, 20 patients completed follow up and photos were taken at 3 & 6 months. All patients had unilateral complete cleft lip divided into 2 equal groups:

- **Group (1): (BTX-A group):**

Botulinum toxin injection (1.5-2 U/kg) in the muscles of upper lip via 4 superficial injection

site, 7 days before primary lip repair by modified Millard cheiloplasty.

This group involved 10 patients, 7 males and 3 females, their age ranged from 98-137 days with a mean of 115 days and average weight of 5.25kg. 6 patients had left complete cleft lip, and the other 4 cases had right complete cleft lip

- **Group (2): (control group):**

The same amount as group (1) of normal saline was injected 7 days before primary lip repair at the same sites.

This group involved 10 patients, 7 males and 3 females, with an age range from 99-144 days with a mean of 114 days and average weight of 5.3kg. 7 patients had left complete cleft lip, and the other 3 cases had right complete cleft lip.

- ☒ **Length of philtral ridge**

The length of philtral ridge value on non-cleft side and cleft side on BTX-A group and control group are presented in table (1)

Table (1): Mean \pm SD values of the length of philtral ridge changes after treatment on non-cleft side and cleft side on BTX-A group and control group.

Period	BTX-A		Control	
	non-cleft*	Cleft*	non-cleft*	Cleft*
1 week	9.94 \pm 1.94	8.33 \pm 1.61	9.40 \pm 1.38	7.26 \pm 1.19
3 months	11.01 \pm 2.15	9.29 \pm 1.95	11 \pm 1.55	8.10 \pm 1.52
6 months	10.51 \pm 2.17	9.35 \pm 1.51	12.32 \pm 1.35	9.37 \pm 1.19

* Mean \pm SD

Table (2): Mean \pm SD values of the difference between the philtrum length in cleft and non-cleft side on BTX-A group and control group.

Period	BTX-A		Control		P Value
	Mean	SD	Mean	SD`	
1 week	1.61	0.74	2.13	1.14	0.235
3 months	1.72	0.938	2.90	1.37	0.037
6 months	1.50	1.05	2.95	1.21	0.011

*Insignificant difference ($P > 0.05$)

- The difference between the philtrum length in cleft and non-cleft side (noncleft – cleft) was statistically insignificant in 1 week but it was statistically significant at 3 and 6 months between BTX-A and control groups. So, the botox decrease the difference in philtral length between cleft and non-cleft side.

- ☒ **Scar width**

The width of scars in the BTX-A group were significantly better than in the control group as P value was 0.011 at 3 months and 0.000 at 6 months as listed in table (3) & figure (8).

Table (3): Mean and standard deviation values of Scar width.

Scar width	BTX-A		Control		P Value
	Mean	SD	Mean	SD	
3 months	1.96	0.54	2.66	0.56	0.011**
6 months	1.84	0.57	3.29	0.49	0.000**

**significant difference ($P < 0.05$)

- Control group after 3 months (2.66 ± 0.56) show higher difference mean value (score) than BTX-A group (1.96 ± 0.54). The difference between groups was statistically non significant as indicated by independent t test.
- Control group after 6 months (3.29 ± 0.49) show higher difference mean value (score) than BTX-A group (1.84 ± 0.57). The difference between groups was statistically non significant as indicated by independent t test.
- The difference between two groups was statistically significant in all months. These results show that the botox had a better effect in decreasing the scar width.
- In both groups no complications (i.e., infection, bleeding, wound dehiscence, oral incontinence, or feeding dysfunction) were encountered.

Group (1): (BTX-A group):

Case 1



a- Preoperative



b- After 3 months



c- After 6 months

Case 2



a- Preoperative



b- After 3 months



c- After 6 months

DISCUSSION

The tension applied on the healing wound edges increases the risk of hypertrophic or widened scar, especially if the wound is orientated perpendicular to the direction of the underlying muscle fibers.^{4,5} Consequently,

reducing tension around a wound is important for improving scar quality and reducing the incidence of hypertrophic scars.

The skin of the upper lip is at risk of hypertrophic scars because of the repetitive movements of the underlying orbicularis oris muscle during speech, eating and drinking, and

facial expression that transmits tension forces distracting and widening the healing wound. Primary cheiloplasty scars are more conspicuous because they do not align with the relaxed skin tension lines of the face. A patient's cheiloplasty scar is a lifelong marker and affects both the child and the family socially and emotionally.⁸

Gassner et al⁹ treated lower facial wounds with Botox. The toxin was injected into the orbicularis oris, buccinator, and zygomaticus muscles to reduce the tension over the wound edges. The resulting scars had excellent appearance and patients accepted the minor temporary functional limitations of the mouth. The repair of the cleft lip deformity represents a special situation because the upper lip pressure is increased after the repair. In wide clefts, the high tension may lead to wound dehiscence. The use of Botox helps in reducing this complication in wide clefts.¹⁰

In this study, we included twenty patients with non-syndromic unilateral complete cleft lip; they were randomly divided into two equal groups. The first group was injected by botulinum toxin one week preoperatively at a dose of 1.5-2 units/kg on unilateral complete cleft lip to improve the appearance of the resulting scar postoperatively, while the control group was injected with saline prior to surgical procedure by one week and both groups were repaired by modified Millard cheiloplasty

Tollefson et al (2006)¹¹ reported injection of 1-2 units/kg of botulinum toxin injection in infants with bilateral cleft lip one week before surgery.

Injection of BTX-A prior to surgery on the skin will reduce the cycles of micro-trauma in the early phases of wound healing^{12, 13} and inhibit the secretion of nor-epinephrine from the sympathetics, thus increasing the circulatory perfusion with subsequent improvement of the wound healing process.¹⁴

Following application of botulinum toxin type-A, the clinical effect occurs within approximately 3-7 days, followed by 1-2 weeks of maximum effect, which then levels off to a moderate plateau until full nerve recovery within 3-6 months.¹⁵

Thus in the present study we chose to inject the botulinum toxin a week before the operation so that at time of surgical repair of the cleft lip the clinical effect of the botulinum toxin starts to appear. On the other hand, Galárraga¹⁶ in 2009

reported the use of Botox (a total of 10 Units) during surgery of unilateral cleft lip repair and Chang et al⁸ in 2014 reported the use of intra-operative injection of BTX-A (1 Unit/kg) in the orbicularis oris muscle immediately after wound closure.

Galárraga¹⁶ considered the intraoperative administration of botox is appropriate instead of injecting it preoperatively, because the children frequently suffered from upper respiratory tract infection that often delays the surgery. But preoperative injection can overcome this problem as botulinum toxin action starts within a week from administration and continues up to 6 months, so respiratory tract infection of children will not be a problem in postponing the patient surgery as surgical repair can be done at any time within 6 months of the toxin injection.

None of our patients showed any complications as infection, bleeding, wound dehiscence, or feeding dysfunction. Similar results with this study were observed in the previous studies,⁸ and the hypertrophic scar was less in BTX-A group.

To our knowledge, this current study represents the first objective evaluation of philtrum length following botulinum toxin injection into the upper lip before cheiloplasty. There was a significant improvement in philtrum length in BTX-A group at 3 and 6 months postoperatively. Also, there was a statistically significant in scar width which was measured 1 mm above the white roll with ImageJ program (National Institutes of Health, Bethesda, MD) using the ruler as a control reference.

Chang et. al. also stated that the width of scars in the experimental group were significantly better than in the control. They measured the scar width in two points first point was 1 mm above the white roll and the second point was 1 mm below the C-flap suture line.⁸

Other methods are used to improve the quality of scar after lip repair surgery, as laser therapy, massage therapy, topical application of many material as silicone material, onion ointment, and vitamin E, or even by surgical scar revision.

Postoperatively usually the patients use cosmetic creams for a long time to improve quality of the scar but at the same time this will be expensive for the patients who cannot afford. Although botox is expensive it is used once in small amount where a few patients can share one

vial of botox. The long lasting effect of botox postoperatively will decrease the incidence of second operations for scar revision.

CONCLUSION

From the results of this study it can be concluded that:

Injection of Botulinum toxin type A (Botox) in muscles of upper lip one week before cleft lip repair is a safe and effective option for minimizing wound tension and scarring in children with wide cleft lip deformities, as it shows significant statistical difference of philtrum length and scar width between cleft and non-cleft side and significantly improve the quality of scarring.

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