

Evaluating the Effects of Botulinum Toxins to Minimize Post Cleft Lip Hypertrophic Scar

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ABSTRACT

Background: Cleft lip deformity is one of the most common congenital anomalies. Repair of cleft lip may create too much tension especially when done in a wide cleft lip, and this may result in an unacceptable scar. **Aim:** To evaluate the efficacy of botulinum toxin in reducing or preventing post cheiloplasty hypertrophic scar. **Patients and methods:** Between the period from October 2019 to August 2021, 10 patients with cleft lip were subjected to primary cheiloplasty using the Millard rotation advancement flap technique followed by botulinum toxin injection into the site of repair. The follow-up period was 6 months post operation. **Results:** All our patients showed excellent results, which was evaluated using visual analogue scale assessment done by two independent surgeons. Our patients showed a barely visible scar 6 months post operation with no recorded hypertrophic scar. No side effects related to botulinum toxin injection were recorded. **Conclusions:** Botulinum toxin injection after primary cheiloplasty showed to be safe and effective in the prevention of development of an unacceptable hypertrophic scar.

Keywords: botulinum, cheiloplasty, cleft lip, hypertrophic scar

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INTRODUCTION

One of the most common congenital anomalies in humans is cleft lip and palate. The primary goal of any cleft lip and palate is to achieve a nearly normal appearance of the lip and nose, leaving minimal visible stigma. Most of the surgeons agreed that primary surgical repair is the most important determinant factor of both aesthetic and functional outcomes. There are a variety of cleft lip repair techniques with many modifications, which of course reflect the continuous evolution of the repair procedures. However, each type of surgical cleft lip repair is associated with a specific, consistent problem.¹⁻³

One of the unavoidable sequelae of any wound healing is scar formation. Scar formation can greatly impact the success of cleft lip repair. There are many factors that contribute to scar formation including the intrinsic wound healing capacity of the child, tissue tension, type of sutures, and duration of suture placement. Even if done by fully trained experienced cleft lip surgeons and under the best circumstances, unpredictable wound healing may occur, which may result in an obvious scar that would suggest a history of a previous repaired cleft lip. Also, this scar may lead to secondary lip and nose

deformities such as vermilion irregularities, distortion of the lip landmark, and asymmetry.^{4,5}

For unknown reasons, hypertrophic scar is unique to humans and thought to result from aberration in the physiological healing cascade following a wound. Hypertrophic scar usually occurs secondary to excessive tensile force across the wound. The incidence of a hypertrophic scar is high and can reach up to 40–70% after surgery. The incidence rate of hypertrophic scar after primary cleft lip repair can range from 8% to 47%. This high rate of hypertrophic scar following primary cleft lip repair is usually associated with high dissatisfaction among surgeons and patients and multiple revision procedures throughout childhood in order to correct this problem.^{6,7}

In this study, botulinum toxin was used in primary cheiloplasty and its effects were evaluated for reducing or preventing hypertrophic scar following primary cleft lip repair.

MATERIALS AND METHODS

A prospective study was conducted in the period from October 2019 to August 2021 at Al-Shaheed Ghazi Al-Hariri hospital in the medical city of Baghdad. Criteria included infants with unilateral cleft lip. All of the patients were subjected to primary cheiloplasty at approximately 3 months of age. The Millard rotation advancement flap technique was used in the operation. All the patients received a botulinum toxin A injection (Botox; Allergan, Inc., Iruin, Galif) at the end of the operation at the site of cleft lip repair.

Preoperative routine investigations were done for all the patients, including hemoglobin level, bleeding profile, and virology screen. Informed consents were obtained from patients' parents, explaining to them the procedure. Photographs in standard position of all the patients were taken preoperatively to compare them with the postoperative photographs.

Surgical Methods

All the operations were done under general anesthesia by the same surgical team. The standard Millard rotation advancement flap technique was used. After finishing skin closure, botulinum A toxin was prepared for injection. A botulinum toxin type A was used in a vial containing 100 units of toxin (Botox, Allergan, Inc., Iruin, Galif). Prior to injection, we reconstituted the vacuumized vial of Botox with 10 ml of unpreserved

normal saline, which was injected slowly into the Botox vial. Then the insulin syringe (30-gauge needle) was used to inject the botulinum toxin along the incision. Every 0.1 ml contained 1 unit of Botox. We performed 4 injections on both sides of the final incision line with each injection site about 5 mm from the surgical wound. The needle was inserted to the depth of the orbicularis Oris muscle. Then the wound was covered with Steri-Strip dressing.

Postoperative Care

The patients were kept in the hospital for one day after operation and then discharged the next day, keeping them on oral antibiotics for 7 days post operation. The parents were instructed to change the wound dressing twice daily and avoid bottle feeding for 21 days after operation. The cutaneous sutures were removed on the sixth day post operation. The patients were monitored through regular postoperative follow-up checkups for 6 months post operation.

RESULTS

In this study, 10 patients with unilateral cleft lip were subjected to surgical repair using the Millard rotation advancement flap technique and postoperative botulinum toxin A injection at the site of the repair. The mean age of the patients was 3.2 months. Of the patients, males were 7 while females were 3. The site of unilateral cleft lip was 8 cases on the left side and 2 cases on the right side. Seven out of ten patients had a complete unilateral cleft lip. In all of our cases, we reported no complications due to the injection of botulinum toxin A such as oral muscle weakening, which leads to feeding difficulties or surgical complications such as wound dehiscence. Postoperative final assessment of the appearance of scar was done 6 months after operation. The subjective assessment of the scar was done by two independent surgeons in which they were asked to assess the scar width, elevation, and the color match with reference to the adjacent skin. Both independent surgeons rated their assessment on the visual analogue scale, which ranged from zero to 10, where zero meant poor result, 1–3 fair result, 4–6 good result, and 7–10 excellent result. The mean visual analogue scale for all our patients was 8, which meant an excellent result with a barely visible scar and color mismatch with adjacent normal skins (Fig. 1–3).



Figure 1: Before and after 6 months.



Figure 2: Before and after 6 months.



Figure 3: Before and after 6 months.

DISCUSSION

One of the major concerns of the patients is the post-surgical scar, which is especially relevant in today's culture as this is largely driven by advances in social media where there's major emphasis on facial appearance. Hypertrophic scar that follows cleft lip repair can lead to functional and aesthetic complications and in turn needs a frequent secondary revision, which increases the stress of parents and patients in addition to

increased aesthetic and surgical risk. Asian patients were the most susceptible group for post cleft repair hypertrophic scar 36.3%.^{8,9}

The first report of use of botulinum toxin A for treatment of facial scarring was reported by Shern et al.¹⁰

Using botulinum A toxin in lacerated facial wound leads to muscle denervation and thus eliminates tension across the wound and subsequently prevents scar hypertrophy during wound healing; this is based on the facts that the most important risk factor for hypertrophic scar formation is tension across the wound. Later on, Tollefson et al. in 2006 used botulinum toxin A injection to immobilize the orbicularis oris muscle prior to primary cheiloplasty in three infants with cleft lip.¹¹ In this study, we evaluated the effect of botulinum toxin A after primary cheiloplasty to prevent or reduce incidence of hypertrophic scar after cleft lip repair. Our results showed a satisfactory outcome in terms of a nearly visible scar at 6 months of age with no side effects related to botulinum toxin A injection such as oral sphincter incompetence or wound dehiscence. The site of injection was done on either side of repair, and it was directed to orbicularis oris muscle. Of course, adequate and proper repair of the orbicularis muscle repair is the mainstay step in cleft lip repair since it bears the majority of the tension that occurs along the wound.

Chang et al. had done double randomized vehicles controlled prospective study, in which 60 patients with unilateral cleft lip had undergone primary repair, and they were divided into two groups: group (A) that received botulinum toxin A injection into the orbicularis oris muscle and group (B) that received vehicle injection into orbicularis oris muscle. Both groups received the injection immediately after wound closure. Their results showed that there was significantly better visual analogue scale scores and narrow scar width in those patients who received botulinum toxin A injection. However, Vancouver scar scale assessment showed no difference between the two groups. They concluded that botulinum toxin A injection in the orbicularis muscle after cleft lip repair gives a narrow scar with a better appearance.¹²

Orbicularis oris muscle denervation through use of botulinum toxin A injection was proved by Galarvaga¹³, when he subjected five children with cleft lip to injection of 10 units of botulinum toxin A into the upper lip during

surgery. Before surgery, an electromyographic study was done for all patients, and its finding was compared with postoperative electromyographic findings. His result showed a significant change: $P < 0.039$.

In electromyographic tracing obtained after injection of botulinum toxin especially at rest, a decrease in orbicularis muscle action after cheiloplasty is not important for reducing the incidence of post cleft lip repair hypertrophic scar, but it may play a role in reducing the outcome of the excessive lifting of soft tissue during primary cleft lip repair, which has a considerable effect on the inhibition of the sagittal development of the mid-face region after primary cheiloplasty.¹⁴ In addition to muscle relaxation, there's emerging evidence that indicates that botulinum toxin A may directly modulate the action of fibroblast with reduction of the transforming growth factor $\beta 1$ (TGF- $\beta 1$). By blocking TGF- $\beta 1$, this minimizes the fibroproliferative response. These findings were approved by Zhibo Xiao et al. in their experimental study.¹⁵

Both Pascual-Pascual and Pascual-Castroviejo have demonstrated the safety of botulinum toxin A injection in infants less than 2 years old, where their average starting dose was 6.55 unit/kg, which was used for correction of obstetrics brachial plexus palsy and cerebral palsy; this dose was much higher than the dose used in primary cheiloplasty.¹⁶

CONCLUSIONS

The use of botulinum toxin A injection after primary cheiloplasty has showed promising results with regards to regarding reducing or preventing post cleft lip hypertrophic scar.

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