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The Effect of Botulinum Toxin Injection in Cleft Lip Repair

Evan Nuri Bapir*
Jalal Hamasalih Fattah**

Abstract

Background & Objectives: Cleft lip and palate are common congenital anomalies that require precise management with main component of repairing lip is the aesthetic outcome. Using botulinum toxin is new method to optimize the resultant scar. The aim of this study is to evaluate the effect of botulinum toxin type A following cleft lip repair on resultant quality of scar.

Methods: This is a comparative study conducted in Rizgary teaching hospital and private hospitals in Erbil – Kurdistan region/Iraq between July 2018 and April 2021. A total of 38 patients with cleft lip were included; bilateral and unilateral, complete and incomplete, isolated cleft lip and cleft lip and palate, 20 of them received botulinum toxin injection. Preoperative and postoperative photos were documented. Scars were analysed one year following repair.

Results: Among 38 patients, in comparison of outcome of using botulinum toxin (31.6%) following cleft lip repair to patients did not receive the injection (68.4%), the scar quality was better; linear scar in botox group 100%, non-botox group 80.8%, complications were less; early complications in botox group 8.3%, non-botox group 11.5% and late complications in botox group 0% non-botox 7.7% and satisfaction was better; parents of botox group were 100% highly satisfied while for those of non-botox group 84.6% highly satisfied, 7.7% satisfied and 7.7% unsatisfied. There was significant difference between the two groups but statistically not significant.

Conclusion: Botulinum toxin injections into the subjacent orbicularis oris muscle following cleft lip repair produced better appearing and narrower cheiloplasty scars.

Key words: Botulinum toxin ,Cleft lip, Cleft lip and palate, Cleft lip repair.

Introduction

Orofacial clefts are most common congenital anomalies in the head which occur either spontaneously or syndromic. The affected children and their families face a challenge that is exceptional which requires special care and many fields' intervention from birth to adulthood.[1] The problems of children with cleft lip and palate and their lengthy management period affects greatly on the children as well as their parents psychologically and socially.[2] In all parts of plastic and reconstructive surgery, art and science play an equal role in the management process but in cleft lip repair, art takes the most part.[3]For the last past 2000 years, cleft lip deformities had been repaired by surgeons. First try was executed in China. Several techniques and their modifications were introduced to obtain best accepted result in cleft lip repair like Le Mesurier 1949; Tennison 1952; Randall 1959; Pfeifer 1970; Millard 1976.[4] No procedure for the cleft lip repair can provide ideal results functionally and aesthetically in a constant manner.[4] The main component in the repair result is aesthetic outcome.[5]Repairing deformities of cleft lip

*M.B.Ch.B. Rizgary Teaching Hospital, Erbil, Kurdistan region-Iraq E-mail: esaqyevan@gmail.com.
**M.B.Ch.B. DGS, FIBMS (Plastic surg.), FEBOPRAS. ISAPS member, ASPS member
Assistant Prof. in plastic surgery. Head of Plastic surgery unit/ College of medicine/ Hawler Medical University, Erbil-Iraq.

necessitates careful attention in order to reconstruct the three dimensional characteristics of structures involved including lip and nose. This is achieved by re-establishing orbicularis muscle continuity. Many elements affect the final outcome of cleft lip repair, amount of tension on the wound during healing process has great influence.[6]Resultant scars of cleft lip repair are inevitably oriented in a manner that they lie perpendicular to relaxed skin tension lines which make them noticeable and mark the patient as born with cleft lip deformity for their entire life.[6] The facial expression muscles work by adjacent skin tension alteration as they are in superficial plane without bony attachments. Skin tension perpendicular to incision is more liable for unfavourable scarring because of distracting forces applied on the wound during healing process. Therefore, decrease in activity of the muscle which in turn reduces the tension on the skin during healing may improve the appearance of the resultant scar.[7]Temporary muscle relaxation by injection botulinum toxin might be beneficial in wound healing improvement.[8] Botulinum toxin which is a strong neurotoxin derived from Clostridium botulinum, its use had been approved to be safe and effective in treatment of many disorders.[9] Tollefson et al. was the first surgeon who published the use of botulinum toxin for orbicularis oris as chemodenervation prior to the primary cleft lip repair. Later, Galárraga published his findings of postoperative electromyography which confirms that botulinum toxin injection during cleft lip repair inhibited orbicularis oris muscle action.[6]The aim of this study is to evaluate the effect of botulinum toxin type A following cleft lip repair on resultant quality of scar. No previous similar research had been done in our locality

Materials and methods

A comparative study conducted between July 2018 and April 2021, 38 consecutive patients with cleft lip were included. All the operations were performed at Rizgary teaching hospital, PAR private hospital and CMC private hospital in Erbil city – Kurdistan region of Iraq. The history was taken from parents and babies were examined thoroughly. The cleft type and severity were documented. Preoperative photos were taken in operation theatre. The operations were performed under general anaesthesia. The cleft lip defects were repaired; unilateral by Mohler rotation advancement flap (Figure. 1) and bilateral with Millard technique (Figure. 2). Following completion of the operation, injection of the bolutinum toxin (10 units) was made at four points (2.5 unit in each point), each 5 mm away from the wound edge (Figure 3). Single dose intravenous antibiotic was given intraoperatively. Oral antibiotic was prescribed postoperatively for one week. Parents were taught to make wound dressing with topical ointment twice daily. There was no need to stitch removal as the skin was sutured with 6/0 vicryl. Parents were instructed to place tapes across upper lip wound and both cheeks (Figure 4). Silicone gel was prescribed to use following second week of surgery for three months. Patients were followed up at 1 week, 2 weeks, 1 month, 3 months, 6 months and 1 year following the surgery. Postoperative photos were taken during these periods.Inclusion criteria were babies born with isolated cleft lip; unilateral and bilateral, complete and incomplete; and cleft lip and palate. Exclusion criteria were syndromic cleft and revision cleft lip.The study protocol was approved by ethical committee of Kurdistan board of Medical Specialties. Informed consent obtained from all of parents of the babies. Data were analysed using statistical package of social science SPSS V. 26. Chi square test of associates was used to compare between proportions.

Fisher exact test was used when the expected count of more than 20% of cells of the table was less than 5. A p-value of less or equal to 0.05 was considered statistically significant.

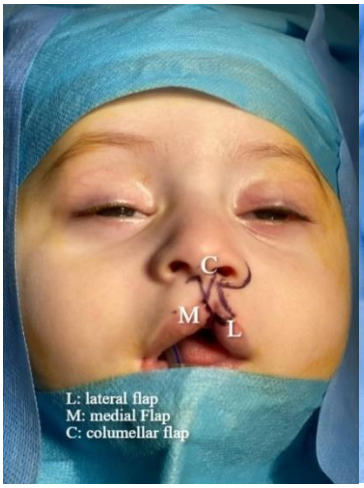

Fig (1): Mohler rotation advancement marking for unilateral cleft lip repair

Fig (2): Millard technique marking for bilateral cleft lip repair.

Fig 3: marking sites of botox injection, 2.5 U in each. 5 mm away from wound edge.

Fig 4: postoperative tapes placed on lip and cheeks.

Results

Total cases of 38 babies with cleft lip were included, male 25 (65.8%) and female 13 (34.2%). Their age ranged from 3 to 18 months, mean age ± SD was 5.39 ± 3.19 months. Isolated cleft lip was in 13 (34.2 %) and combined cleft lip and palate in 25 patients (65.8 %). The cleft type was unilateral in 34; right side 21 (55.3%) and left side 13 (34.2 %), and bilateral in 4 patients (10.5%). The cleft severity was complete in 14 (36.8 %) and incomplete in 24 patients (63.2 %). The babies received botox injection were 12 (31.6%) and the remaining 26 (68.4%) did not receive the injection (Table 1).

Table (1): Demographics of patients.

Variable	Patients with Botox (n= 12)		Patients Without Botox (n= 26)	
	No.	%	No.	%
Age				
1 – 5	10	83.4	13	50
6 – 18	2	16.6	13	50
Gender				
Male	9	75	16	61.5
Female	3	25	10	38.5
Cleft type				
Isolated cleft lip	8	66.6	5	19.2
Cleft lip and palate	4	33.4	21	80.8
Cleft side				
Right	4	33.3	17	65.4
Left	6	50	7	26.9
bilateral	2	16.7	2	7.7
Cleft severity				
Complete	3	25	11	42.3
Incomplete	9	75	15	57.7
Type of repair				
Mohler	10	83.3	24	92.3
Millard	2	16.4	2	7.7

The complications were lower in patients who received botox than those who did not, but statistically there was no significant difference (Table 2). Two of the patients among 26 who did not get injected with botox needed surgical revision while none of the patients with botox injection required revision.

Table (2): Complications postoperatively.

	Patients with botox		Patients without botox		p-value
	no	%	no	%	
Early complications					
Nil	11	91.7	23	88.5	0.620
Infection	1	8.3	2	7.7	
Dehiscence	0	0	1	3.8	
Late complications					
Nil	12	100	24	92.3	1.000
Whistle deformity	0	0	2	7.7	

Parents' satisfaction was 100% highly satisfied among patients who received botox injection while for those who did not receive the injection; 84.6% highly satisfied, 7.7% satisfied and 7.7% unsatisfied.The quality of scar outcome which was assessed with photographic measurements using adobe Photoshop version 21.1, was compared between patients received botox and those did not. There was clinically difference between two groups in terms of scar appearance but statistically not significant Table (3).

Table (3): Scar appearance in comparison between the injected and non-injected botox of cleft lip following repair.

Scar appearance	Patients with botox (n=12)		Patients without botox (n=26)		p-value
	No	%	No	%	

Linear scar	12	100%	21	80.8%	0.127
Hypertrophic scar	0	0%	3	11.5%	
Wide scar	0	0%	2	7.7%	

Figures 5, 6, 7 and 8 showing appearance of scars following cleft lip repair, first three cases received botulinum toxin injection following repair and the last did not.

Figure (5): three months old baby with unilateral incomplete cleft lip, received botox injection following repair; A – preoperative, B – one month postoperative, scar is red, C – after sixth months, scar is visible, D – one year following repair, scar is barely noticeable.

Figure (6): four months old baby with unilateral complete cleft lip, received botox injection after repair; A – preoperative, B – one year postoperative, scar is almost invisible.

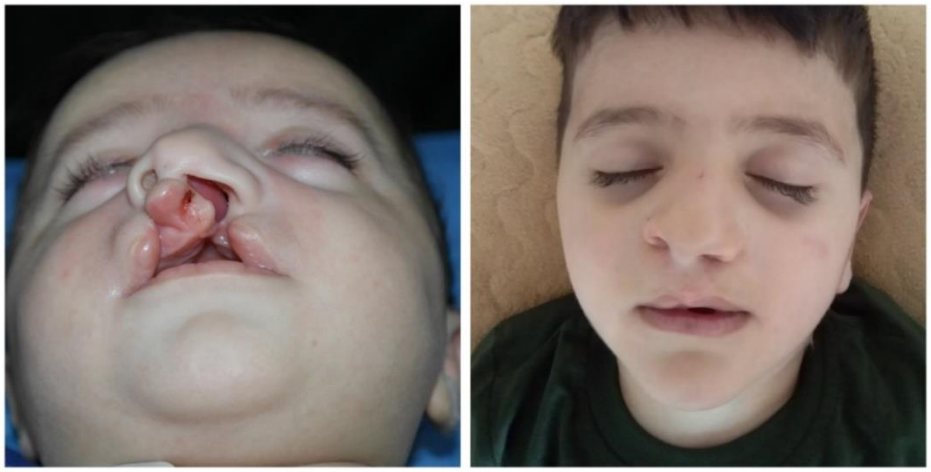

Figure (7): four months old baby with bilateral cleft lip, received botox injection following repair; A – preoperative, B – one year postoperative, scar is linear on both sides.

Figure (8): three months old baby with right sided incomplete cleft lip, did not receive botox injection; A- preoperative, B – postoperative, the scar is wide.

Discussion

Cleft lip is common congenital anomaly in the craniofacial area. The deformity disturbs function and appearance of the babies born with the defect. Their treatment is difficult and their outcome is not satisfactory as it is hard to attain great results from complex deformity. Multidisciplinary approach is the essential approach to deal with these patients to achieve the efficient therapy[4]. To obtain the required long lasting effective final outcome aesthetically and functionally of patients with cleft lip deformity, every step of treatment has significant role that affects patients their whole life[2]. Every effort is made to restore normality of all tissues in the cleft defect especially the underlying muscle, rather than restricting to overlying skin[10]. Cleft lip scar is a permanent marker to the babies born with the anomaly. The location of the scar is hard to conceal and its visibility imposes psychological impact on their bearers[2]. The facial muscles that are responsible of facial expressions are located in superficial plane, which their action apply tension on skin and subcutaneous tissue. This muscular tension effects on edges of the

wound and makes the scar prone to unwanted results like hypertrophy and wide scar. Thus, decreasing this tension on the scar through the muscles is essential way to improve the quality of scar and reduce the chance of obtaining undesirable scar. Scars of cleft lip are located perpendicular to line of pull of subjacent orbicularis oris muscle, which is in continuous use throughout life. Those repetitive attacks of tension forces cause micro trauma to the wound during healing process which in turn leads to elongation of inflammatory process and subsequently more fibrosis[7]. Clinically, this will apparent as widening and/or hypertrophy of scar[11]. In principles of wound healing, basic therapy is immobilization. Paralysis of the muscle underlying the wound temporarily is a new method to reduce the tension on wound edges through the healing process[12]. Botulinum toxin had been investigated for its ability to reduce movement and consequent tension on treated site wound edges[13]. Botulinum toxin affects the scar in many ways. It delays fibroblast growth by inhibiting cell cycle. It decreases expression of connective tissue growth factor as well as inhibits growth of fibroblasts. It also reduces transforming growth factor- β1 in fibroblasts. Additionally, it reduces inflammatory cells infiltration during healing time. The paralysis of the muscle made by botulinum toxin decreases the tension of the wound throughout wound healing process. Lastly, it inhibits collagen production and restricts hypertrophy by inhibiting cell cycle[14]. The botulinum toxin is used for variety of diseases in patients and its safety in children is approved by researches, however it is not commonly used particularly in facial region[15]. Tollefson et al. was the first one to publish his use of the botulinum toxin for upper lip in cleft lip repair surgery in young infants of 3 to 6 months. Pascual-Pascual and Pascual-Castroviejo had studied the botulinum toxin safety in children younger than two years[6]. Our study observed that intraoperative injection of the botulinum toxin following cleft lip repair affects scar quality to a degree of getting better appearance cosmetically. Although there was no significant difference statistically between patients received botox and patients did not receive botox injection in terms of scar appearance, but all patients with the injection had linear scar while five of patients without botox injection had hypertrophic and wide scar. In relation to complications, none of patients developed drooling due to effect of botox. Only one patient had infection among injected group and two of patients among non-injected ones. Late complications were nil in injected group and two of non-injected cases had whistle deformity. In general, parents and surgeon satisfaction was higher in botox group patients.Many studies had been conducted to assess the effect of botulinum toxin injection on the scar outcome, but only one study which had been accomplished at Taiwan used the injection for cheiloplasty. They observed same results of better appearing and narrower scars. Our limitation was number of patients in this pandemic era. We recommend a study with larger number of patients included to assess the difference more precisely.

Conclusion

Inducing temporary paralysis of orbicularis oris muscle during cleft lip repair surgery is a new approach to decrease the tension on healing wound edges effectively through inhibition of action of the muscle by botulinum toxin thus optimizing outcome of scar appearance. Further studies with larger number of patients are recommended.

Conflicts of interest

There were no conflicts of interest.

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