Botulinum toxin versus mesotherapy on enhancement of facial scarring (A Controlled Randomized Clinical Trial)

Original Article

Noha Y. Dessoky [1] , Marwa G. Noureldin [2]

[1] Lecturer of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University. [2] Associate of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University.

ABSTRACT

Background: Most of the body's tissues can undergo wound repair following a disruption of tissue integrity. Upon healing, these wounds result in scar formation. The scars widen when the overlying musculature pulls apart suture lines. Botulinum Toxin A (BTA) is known to prevent fibroblast proliferation and it also induces temporary muscle paralysis. Also, mesotherapy is the non-invasive transdermal injection which can aid the skin to increase collagen and elastin production. Thus, both techniques are eligible for enhancement of facial scars.

Aim of this study The study was proposed to compare between the efficacy of early postoperative Botulinum Toxin type A (BTA) injection and mesotherapy growth factor AQ recovery serum on the scar appearance.

Materials and methods: Thirty-three patients requiring treatment of facial scars by primary closure were selected for this study and were randomly distributed into three groups. Group A(n=11) received BTA injection while group B (n=11): received mesotherapy growth factor serum with a derma pen injection. Both groups received the injections within a period of 5 days after primary closure. Group C (n=11) the control group where no further treatment was given after primary closure. Follow-up of the patients was at 1, 3 and 6 months postoperatively to evaluate the wound scar enhancement using Vancouver scar scale (VSS) Scores and wound width, in addition to clinical photographs.

Results: Results were statistically analysed and compared using the IBM Statistical Package for Social Science (SPSS) software version 22.0. The results of the Vancouver scar scale demonstrated no statistically significant difference between the 2 studied groups along all the periods of the follow up. However, both groups had a significant improvement on wound appearance in comparison to the control group. Regarding the wound width, the mesotherapy group showed a statistically significant decrease than the BTA group at 1 month postoperatively. However, later, the decrease in width between both groups was statistically insignificant.

Conclusion: It can be concluded from this research that both BTA injection and mesotherapy using the micro-needling technique, offered exquisite outcomes on facial scars by improving the scar appearance and decreasing the width with high patient satisfaction.

Key Words: Botulinum Toxin Type A, Mesotherapy, intradermal injection, facial scars

Received: 1 September 2024, **Accepted:** 13 September 2024.

Corresponding Author: Noha Youssry , Lecturer of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University. , **Mobile:** 01270060160, **E-mail:** dr_nohayoussry@hotmail.com, noha.taha@alexu.edu.eg

ISSN: 2090-097X, October 2024, Vol. 15, No. 4

INTRODUCTION:

People suffering from facial scars suffer drastically which may lead them to social withdrawal [1]. Opposing forces which pull any incision line which is made either surgically or through trauma will lead to widening of the scars by breaking the newly formed immature collagen. Muscle pull, elastic forces of adjacent skin and external pressure which are tensile forces cause mechanical influence on the resilient and immature collagen, which corelates to the relaxed skin tension lines (RSTL). These lines are perpendicular to the tension vector of the muscular contraction below. Scars which are against RSTL are subject to repetitive tension and result in scar hypertrophy [2].

Many solutions have been proposed to tackle this problem including corticosteroids injection [3], irradiation, ultrasound and silicone application [4,5] and many others, but they don't act on the underlying pathologic process, which is the distracting force of muscle pull.

Botulinum Toxin type A is a widely used medications for the treatment of wrinkle and facial contouring [6,7] and proven safe and reliable, with complications that can be reversed. Injecting Botulinum Toxin type A in nearby musculature around the traumatic or incisional wounds has been proposed by many studies [8,9]. However, Sound clinical evidence has been missing.

Another method to get around these restrictions is micro-needling therapy, also known as mesotherapy. It has shown a good clinical and histological response

 DOI:10.21608/omx.2024.317336.1262

to the skin. It includes a growth factor which support the skin's own healing mechanisms, that repair and regenerate skin by improving the circulation, antioxidant activity, and cellular regeneration [10].

The present study compared between the efficacy of early postoperative Botulinum Toxin type A (BTA) injection and mesotherapy growth factor AQ recovery serum on the scar appearance.

AIM OF THIS STUDY

The study was proposed to compare between the efficacy of early postoperative Botulinum Toxin type A (BTA) injection and mesotherapy growth factor AQ recovery serum on the scar appearance.

Patients

I. Study Design

The study is a randomized controlled clinical trial, following the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The Research Ethics Committee of Alexandria University, Faculty of Dentistry certified the approval of the research protocol (IRB No. 09262024/05- – IORG 0008839). This trial was registered on clinicaltrials.gov (ID: NCT06562023).

II. Study Sample

Sample size was estimated based on assuming 95% confidence level and 80% study power. The mean Vancouver Scar Scale after 6 months was 3.6 ±1.2 for the Botulinum Toxin type A (BTA) group, [11] 1.00 ±0.43 for the mesotherapy group, and 5.50 ±1.68 for the control group. [12] The highest sample size was calculated based on the mean difference between BTA and control group. A sample of 11 patients per group is required yielding an effect size of 1.301. Total sample size= number per group × number of groups=11 × 3= 33 patients.

Software

Sample size was based on Rosner's method (13) calculated by G*Power 3.0.10. (14)

III. Study Setting and Location

Participants were selected from the Emergency Ward of Alexandria University Teaching Hospital and will be operated under the authority of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University.

IV. Criteria for patient selection

Inclusion criteria

1- Patient aged range from 20-40 years old
2- Patient suffering from vertical or oblique forehead lacerations caused by trauma. (12)
3- Recent and fresh wounds.
4- Atrophic scar (linear scar).

Exclusion criteria

1- Infected wound. (12)
2- Patient on chemotherapy treatment and history of malignancy.
3- Patients suffering from burns on the forehead or complicated lacerations.
4- Allergy to drugs used in this study.

V. Randomization

The enrolled patients (n=33) were randomly assigned into three equal groups using a computerized random number generator software, (15) The numbers were hidden in sealed envelopes with an allocation ratio of 1:1:1.

VI. Grouping of the patients

Group A: (n=11): Patients received BTA injection within a period of 5 days after primary closure.
Group B: (n=11): Patients received mesotherapy growth factor serum with a derma pen within a period of 5 days after primary closure.
Group C: (n=11): Control group where patients received no further treatment after primary wound closure.

Materials

• AboBotulinumToxin A (BTA) Dysport (500 SU) (Ipsen Biopharm Ltd., Wrexham, LL13 9UF, UK U.S.)
• Mesotherapy growth factor AQ recovery serum (AQ Skin Solutions, Irvine, California, USA). It is cosmetic therapy (16) consisting of Active Ingredients including: Human Fibroblast Conditioned Media Contains Growth Factors: Transforming Growth Factors (TGF -Beta), Granulocyte Monocyte Colony Stimulating Factors (GM -CSF), Platelet Derived Growth Factor (PDGF), cytokines, Interleukins (IL), Tetrahexyldecyl Ascorbate, a form of vitamin C, Tocopheryl Acetate, a form of Vit E., Menthyl Lactate & Lactic acid, Sodium Hyaluronate and an anti-microbial agent.
• Derma pen (Derma pen Dr. Pen, China). The instrument consists of a rechargeable hand piece with disposable needles at one end, which uses a motor to drive the movement of the needles on the forehead.
• Needle cartridge tips (Needle cartridge tips, China).
• Digital vernier calliper (150 mm, 6 -inch, electronic, stainless steel vernier calliper).

METHODS

Preoperative assessment

1- History

Full detailed personal data, past medical history, dental history and the chief complaint were registered including cause, time, place and type of assault.

2- General examination

Performing extra-oral and intraoral examination were performed for all patients through inspection and palpation. Also, vital signs and general state of health of each patient were monitored and observed.

II. Operative phase

a) Preoperative patient preparation

On the day of arrangement with the emergency department, a surgeon blinded to the following clinical approach performed primary repairs for all patients under local anaesthesia. The suturing procedure were performed in a layered manner with 4-0 vicryl (Ethicon Co., Delhi, India) and 6-0 prolene (Ethicon Co., Delhi, India). The sutures were then removed on the 7th day postoperatively.

b) Operative procedure

1- For group A and B, the patients received the injections within a period of 5 days after primary closure.
2- The patients were operated under an aseptic technique.
3- The patient's forehead skin was cleaned with ethyl alcohol then by ether
for complete removal of oils on the skin.
4- For pain control, topical anesthetics as Lidocaine 2.5% and prilocaine 2.5% topical cream (EMLA cream; Astra Zeneca, Sodertalje, Sweden) and cold iced packs were applied on the scar area.

Group A (BTA injection group)
1- The BTA injections were operated by the same surgeon.
2- The whole forehead including the repaired wound area were injected using insulin syringe in the intradermal and intramuscular layers.
3- The supraorbital rim was spared to avoid lid ptosis.
4- AboBotulinumToxin A Dysport (500 SU), was prepared by mixing 2 mL of 9 mg/mL (0.9%) saline with 500 U of BTA (250 U/mL). Finally, an amount of 75 U of BTA was prepared.
5- Along the sutured site and within a distance of 0.5 cm, the BTA was injected into various regions. (Figure 1)

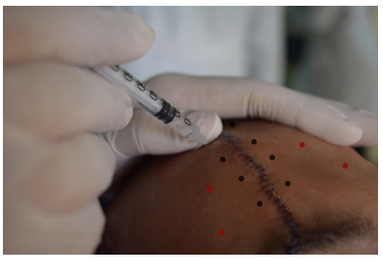


Figure 1:BTA injection along the suture line

6-The 12.5 SU/cm amount was injected into multiple sites on both sides of the wound along the length of the scar.
7-A supplementary 25-50 U was injected within 5 days of the initial injections in cases where incomplete muscle paralysis is detected.

Group B (mesotherapy growth factor group)

1- Injection was performed by derma pen in the intradermal layer on the forehead skin of the repaired wound.
2- The micro-needling injection was executed by a single surgeon.
3- Topical application of anaesthetic cream covered for 30 minutes on the forehead area.
4- A first layer of AQ recovery serum (0.1 ml) was applied topically to the scar area.
5- A Derma pen with a needle length of 1.5-2.1 mm was used on the scar line for micro-needling the AQ recovery serum at a depth of 0.5-1mm. (Figure 2)

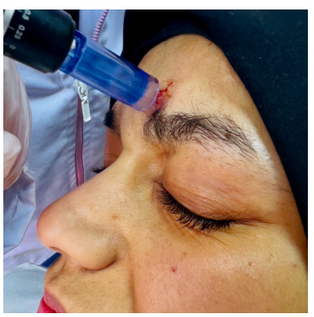


Figure 2: Mesotherapy using the derma pen on the scar line for micro-needling the AQ recovery serum

6- After that, another final layer of the recovery serum (0.1 ml) was administered.
7- Patients were instructed to avoid washing the face for 6-8 hrs.
8- The sessions were repeated once a week for up to 6 sessions.
9- In cases where ecchymosis developed, the surgeon kept a cold compress or manual gentle compression at the area of injured arteries.

Group C (Control group)

It involved 11 patients who received no further treatment after primary closure. However, scar evaluation was performed on 1,3 and 6 months follow ups.

III- Postoperative phase

Post-operative medications and instructions

• For the first 14 days, till wound closure, patients were instructed to apply Jacy topical cream (SAbSHiRe pharmaceuticals, Egypt) two to three times a day for skin renewal.
• Over the closed scar area, Scaro gel which contains silicone fluid, vitamins A and E, almond oil, and polydimethylsiloxane. (Macro Group Pharmaceuticals, Egypt) was applied. Application was in one direction, twice daily for two to six months. This is for improvement of the color and texture of the skin.
• Patients were informed to sit upright for 6 hours without interference with the operated area.
• Patients were informed to avoid exposure to the sun for the first 24 hours.
• All patients were advised to apply sunscreen daily for six months (17).

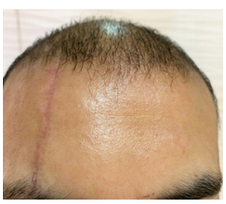
IV- Clinical follow-up phase

Patients were followed up clinically at 1, 3 and 6 months postoperatively. (Figure 3,4,5) The evaluation was performed by two trained surgeons (inter-examiner reliability). The inter-reliability was determined by comparing the session ratings of both surgeons. Intra-reliability was assessed by re-examination of 10 of the participants, in two subsequent times at a 2-day interval.

Clinical examination will evaluate:

1- The Vancouver Scar Scale (VSS) was measured by two surgeons in an independent, blinded manner to calculate scar appearance. The mean values for both surgeons on the different time intervals were calculated and tabulated. [18]

2-The mean wound widths were measured on the different time intervals using a digital Vernier caliper. [19]



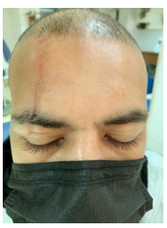


Figure 3a: Follow up at 1 month for BTA patient

Figure 3b: Follow up at 3 months for BTA patient

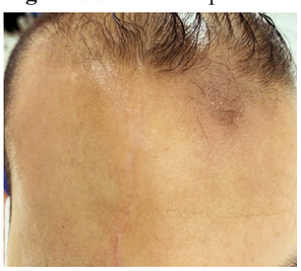
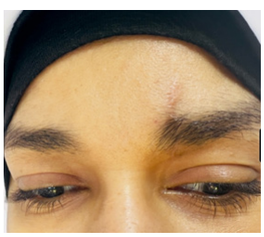


Figure 3c: Follow up at 6 months for BTA patient



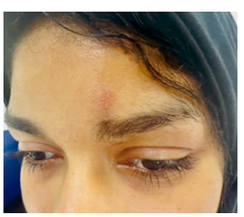


Figure 4a: Follow up at 1 month for mesotherapy patient

Figure 4b: Follow up at 3 months for mesotherapy patient

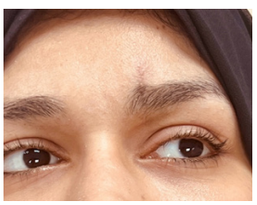


Figure 4c: Follow up at 6 months for mesotherapy patient

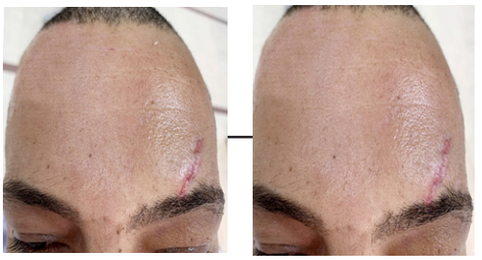


Figure 5a: Follow up at 1 month for control patient

Figure 5b: Follow up at 3 months for control patient

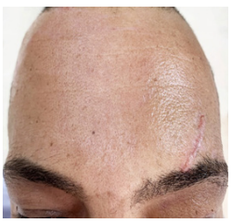


Figure 5c: Follow up at 6 months for control patient

V- Statistical analysis

All data were statistically recorded and analysed using the IBM statistical package for social science (SPSS) software version 22.0.

RESULTS

Thirty-three patients, 19 males (57.58%) and 14 females (42.42%) with age ranging from 21 to 39 years old with a mean of 30.18 ± 3.73 years were included in the study (Table 1). The patients were selected from the Emergency Ward of Alexandria University Teaching Hospital and were operated under the authority of the oral and maxillofacial surgery department, faculty of dentistry, Alexandria University.

Table (1): Comparison between the three studied groups according to demographic data

	Botolinum toxin (n = 11)	Mesotherapy (n = 11)	Control (n = 11)
Gender			
Male	5 (45.5%)	8 (72.7%)	6 (54.5%)
Female	6 (54.5%)	3 (27.3%)	5 (45.5%)
Age (years)			
Min. – Max.	24 – 36 years	21 – 33 years	26– 39 years

Comparison between the three studied groups according to Vancouver scar scale is presented in (Table 2a). The results of the Vancouver scar scale demonstrated no statistically significant difference between the BTA and the mesotherapy groups along all the periods of the follow up. However, on comparing each of the study groups with the control group, the values were all statistically significant showing a greatly improved wound appearance in the studied groups in relation to the control group.

Table (2a): Comparison between the three studied groups according to Vancouver scar scale

Vancouver scar scale	Botolinum toxin (n = 11)	Mesotherapy (n = 11)	Control (n = 11)	F	p
Baseline					
Min. – Max.	6.50 – 9.60	6.10 – 9.20	6.30 – 9.0		
Mean ± SD.	8.40 ± 0.82	7.55 ± 0.92	7.64 ± 0.87	3.200	0.055
Median	8.60	7.20	7.60		
1 month					
Min. – Max.	3.80 – 7.20	4.30 – 6.50	6.20 – 9.10		
Mean ± SD.	5.79 ± 0.88	5.14 ± 0.67	7.48 ± 0.85	24.903*	<0.001*
Median	6.0	5.0	7.50		
Sig. bet. grps.	p1=0.154,p2<0.001*,p3<0.001*				
3 months					
Min. – Max.	3.70 – 6.30	3.40 – 5.60	6.40 – 8.40		
Mean ± SD.	5.06 ± 0.67	4.53 ± 0.53	7.19 ± 0.60	60.551*	<0.001*
Median	5.0	4.50	7.10		
Sig. bet. grps.	p1=0.108,p2<0.001*,p3<0.001*				
6 months					
Min. – Max.	1.90 – 3.70	1.70 – 3.60	4.20 – 5.90		
Mean ± SD.	3.09 ± 0.51	2.65 ± 0.65	5.01 ± 0.53	53.635*	<0.001*
Median	3.0	2.90	5.0		
Sig. bet. grps.	p1=0.175,p2<0.001*,p3<0.001*				

11 replica for each group SD: Standard deviation
F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)
p: p value for comparing between the studied groups
p1: p value for comparing between Botolinum toxin and Mesotherapy
p2: p value for comparing between Botolinum toxin and Control
p3: p value for comparing between Mesotherap and Control
*: Statistically significant at $p \leq 0.05$

On comparing the wound appearance according to Vancouver scar scale within each group at different time intervals (Table 2b), it was shown that both the BTA and the mesotherapy groups had a statistically significant improvement in the results of scar appearance from the baseline to 1 months, in addition to those from 1 month to 3 months and those from 3 months to 6 months. However, the control group showed an insignificant improvement of the scar appearance from baseline to 1 month and from 1 month to 3 months. The only statistically significant improvement in scar appearance was from 3 months to 6 months in the control group.

Table (2b): Comparison between the three studied groups according to Vancouver scar scale

	Vancouver scar scale				F	p
	Baseline	1month	3month	6month		
Botolinum toxin						
Min. – Max.	6.50 – 9.60	3.80 – 7.20	3.70 – 6.30	1.90 – 3.70	497.520*	<0.001*
Mean ± SD.	8.40 ± 0.82	5.79 ± 0.88	5.06 ± 0.67	3.09 ± 0.51		
Median	8.60	6.0	5.0	3.0		
p0		<0.001*	<0.001*	<0.001*		
Sig. bet. periods.	p1=0.001*,p2<0.001*,p3<0.001*					
Mesotherapy						
Min. – Max.	6.10 – 9.20	4.30 – 6.50	3.40 – 5.60	1.70 – 3.60		
Mean ± SD.	7.55 ± 0.92	5.14 ± 0.67	4.53 ± 0.53	2.65 ± 0.65	402.567*	<0.001*
Median	7.20	5.0	4.50	2.90		
p0		<0.001*	<0.001*	<0.001*		
Sig. bet. periods.	p1=0.002*,p2<0.001*,p3<0.001*					
Control						
Min. – Max.	6.30 – 9.0	6.20 – 9.10	6.40 – 8.40	4.20 – 5.90		
Mean ± SD.	7.64 ± 0.87	7.48 ± 0.85	7.19 ± 0.60	5.01 ± 0.53	283.224*	<0.001*
Median	7.60	7.50	7.10	5.0		
p0		0.077	0.022*	<0.001*		
Sig. bet. periods.	p1=0.060,p2<0.001*,p3<0.001*					

11 replica for each group SD: Standard deviation
F: F test (ANOVA) with repeated measures, Sig. bet. periods was done using Post Hoc Test (adjusted Bonferroni)
p: p value for comparing between the studied periods
p0: p value for comparing between Baseline and each other periods
p1: p value for comparing between 1month and 3month
p2: p value for comparing between 1month and 6month
p3: p value for comparing between 3month and 6month
*: Statistically significant at $p \leq 0.05$

Regarding the comparison between the three studied groups according to wound width (Table 3a), the mesotherapy group showed a statistically significant decrease than the BTA group at 1 month postoperative. However, on comparing the 2 studied groups later at 3 months and 6 months, it was found that the decrease in width between both groups was statistically insignificant. Also, when comparing the BTA group to the control group, the results at 1 month postoperatively showed an insignificant difference between both groups. However, at 3 and 6 months the decrease of the wound width of the BTA group was statistically significant than the control group. On comparing the results of mesotherapy group to the control group, the wound showed statistically significant decrease at each of the follow-up intervals in the mesotherapy group than the control group.

Table (3a): Comparison between the three studied groups according to wound width

Wound width	Botolinum toxin (n = 11)	Mesotherapy (n = 11)	Control (n = 11)	F	p
Baseline					
Min. – Max.	0.22 – 0.55	0.28 – 0.43	0.28 – 0.47		
Mean ± SD.	0.40 ± 0.11	0.32 ± 0.04	0.39 ± 0.05	3.272	0.052
Median	0.42	0.32	0.38		
1 month					
Min. – Max.	0.19 – 0.51	0.23 – 0.30	0.28 – 0.46		
Mean ± SD.	0.37 ± 0.11	0.27 ± 0.02	0.38 ± 0.04	8.450*	0.001*
Median	0.40	0.27	0.38		
Sig. bet. grps.	p1=0.005*,p2=0.981,p3=0.003*				
3 months					
Min. – Max.	0.15 – 0.40	0.21 – 0.27	0.25 – 0.43		
Mean ± SD.	0.29 ± 0.08	0.23 ± 0.02	0.35 ± 0.04	12.051*	<0.001*
Median	0.30	0.23	0.35		
Sig. bet. grps.	p1=0.078,p2=0.033*,p3<0.001*				
6 months					
Min. – Max.	0.10 – 0.29	0.13 – 0.19	0.21 – 0.35		
Mean ± SD.	0.20 ± 0.06	0.16 ± 0.02	0.29 ± 0.03	26.734*	<0.001*
Median	0.22	0.16	0.29		
Sig. bet. grps.	p1=0.071,p2<0.001*,p3<0.001*				

11 replica for each group SD: Standard deviation
F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)
p: p value for comparing between the studied groups
p1: p value for comparing between Botolinum toxin and Mesotherapy
p2: p value for comparing between Botolinum toxin and Control
p3: p value for comparing between Mesotherap and Control
*: Statistically significant at $p \leq 0.05$

On comparing the wound widths of each group on the different follow up intervals (Table 3b). The wound widths in the BTA and mesotherapy groups showed a statistically significant decrease between every successive time periods within each group (from baseline to 1 month, from 1 month to 3 months, from 3 months to 6 months). However, the control group results showed only a statistically significant decrease in the wound width at the time interval from 3 to 6 months post operatively.

Table (3b): Comparison between the three studied groups according to wound width

Wound width	Baseline	1month	3month	6month	F	p
Botolinum toxin						
Min. – Max.	0.22 – 0.55	0.19 – 0.51	0.15 – 0.40	0.10 – 0.29	120.399*	<0.001*
Mean ± SD.	0.40 ± 0.11	0.37 ± 0.11	0.29 ± 0.08	0.20 ± 0.06		
Median	0.42	0.40	0.30	0.22		
p0		<0.001*	<0.001*	<0.001*		
Sig. bet. periods.		p1<0.001*,p2<0.001*,p3<0.001*				
Mesotherapy						
Min. – Max.	0.28 – 0.43	0.23 – 0.30	0.21 – 0.27	0.13 – 0.19		
Mean ± SD.	0.32 ± 0.04	0.27 ± 0.02	0.23 ± 0.02	0.16 ± 0.02	163.759*	<0.001*
Median	0.32	0.27	0.23	0.16		
p0		0.001*	<0.001*	<0.001*		
Sig. bet. periods.		p1<0.001*,p2<0.001*,p3<0.001*				
Control						
Min. – Max.	0.28 – 0.47	0.28 – 0.46	0.25 – 0.43	0.21 – 0.35		
Mean ± SD.	0.39 ± 0.05	0.38 ± 0.04	0.35 ± 0.04	0.29 ± 0.03	58.258*	<0.001*
Median	0.38	0.38	0.35	0.29		
p0		0.085	0.032*	<0.001*		
Sig. bet. periods.		p1=0.127,p2<0.001*,p3=0.001*				

11 replica for each group SD: Standard deviation
F: F test (ANOVA) with repeated measures, Sig. bet. periods was done using Post Hoc Test (adjusted Bonferroni)
p: p value for comparing between the studied periods
p0: p value for comparing between Baseline and each other periods
p1: p value for comparing between 1month and 3month
p2: p value for comparing between 1month and 6month
p3: p value for comparing between 3month and 6month
*: Statistically significant at $p \leq 0.05$

DISCUSSION

This study aimed to treat patients presented with vertical or oblique forehead lacerations caused by trauma since traumatic facial scars can cause both physical and psychological disturbances to the patients. This agrees with Krasuska M et al who described that persons suffering from evident skin conditions largely suffer from being depressed, isolated socially and facing a poor quality of life. [20]
The patients were randomly allocated into three groups. The first group was Botulinum Toxin A (BTA) group, the second group received mesotherapy by micro-needling treatment using the derma pen and the third group was the control group. In this study, there was an overall improvement of the scars characteristics along the follow up intervals. Vancouver scar scale was chosen to evaluate the wound appearance and was found to give an elaborative description of the wound scar area. This scale is a widely used validated scars scale that has been in the research field since the 1990s [21] The results of the Vancouver scar scale demonstrated no statistically significant difference between the 2 studied groups along all the periods of the follow up. However, both groups had a significant improvement on wound appearance in comparison to the control group.

Within each study group and at different time intervals, there was a statistically significant improvement in scar appearance. However, the control group showed only a statistically significant improvement in scar appearance from 3 months to 6 months. The use of BTA has shown promise in improving the cosmetic appearance of facial scars, as measured by the Vancouver Scar Scale (VSS). This was in agreement with a recent randomized, controlled trial published in the Dermatologic Surgery journal in 2022 evaluated the efficacy of intralesional BTA injections on scar appearance in patients with post-surgical facial scars (Kim et al., 2022). At 3 and 6-months post-treatment, the BTA group demonstrated significantly lower VSS scores compared to the control group, indicating improved scar pliability, height, vascularity, and pigmentation. The authors attributed these beneficial effects to the ability of BTA to inhibit underlying muscle contraction, reducing mechanical tension on the healing wound. [22]
Similarly, a systematic review and meta-analysis in the Journal of Cosmetic Dermatology in 2021 examined the evidence for BTA in the management of various types of facial scars (Lee et al., 2021). The meta-analysis revealed that BTA treatment led to significantly better VSS scores compared to control groups, suggesting enhanced scar appearance and quality. The authors concluded that BTA can be a valuable adjunct therapy for improving the cosmetic outcomes of facial scars, particularly when used in combination with other scar management strategies. [23]
In this study, the use of mesotherapy was regarded as a minimally invasive technique and in combination with a derma pen greatly, they impacted the results of scar improvement.
Since the use of the micro-needles of the derma pen influenced and accentuated the uptake of the serum by the created micro-channels into the layers of the skin. It was evident that along the follow up period, the scar appearance and pigmentations in this group were positively influenced by this combination and all the patients in this group had a satisfactory experience.
This can be reinforced by Iriarte C et al 2017, Majid I and Sheikh G in 2014 and Doddaballapur S in 2009. In their study they proposed 2 mechanisms for the micro-needling technique. The first suggested that the puncture activated the production of gross factors such as TGF alpha and Vita beta, platelet cross factors which promotes collagen and elastin deposition in the dermis of the skin. [24-26] This was in addition to the topically applied compounds which were permitted through the created punctures that multiplied the regeneration process. [27]

Their second mechanism was covered by Majid I and Sheikh G in 2014 and Fabbrocini G et al in 2009 and was encircling the concept of bio-electricity which induces a boost of growth factors to aid in the healing process. It was explained that the needle injury creates a negative potential of -70 V MV where the intact epidermis has a positive potential. With this current created, fibroblasts are stimulated to migrate and proliferate at the wound area producing collagen. [25,28]
Regarding the wound width, the mesotherapy group showed a statistically significant decrease than the BTA group at 1 month postoperatively. However, later, the decrease in width between both groups was statistically insignificant. Also, when comparing the BTA group to the control group, only the results at 1 month postoperatively showed an insignificant difference between both groups.
There was a difference between the BTA group and the mesotherapy group from baseline to 1 month of follow-up with a significant improvement in favour of the mesotherapy treatment. This may be due to the late effect of the BTA treatment which usually peaks after several weeks. This agrees with Hallett M in 2015. [29]
Also, it was advocated by Sheta OA et al to inject the BTA as early as the step of wound closure to overcome its delayed onset of action [19]

On the other hand, the different growth factors and constituents in the AQ serum which included human fibroblast conditioned media with growth factors mainly the transforming growth factors (TGF -Beta), granulocyte monocyte colony stimulating factors (GM -CSF), platelet derived growth factor (PDGF), have rapid immediate cellular action. This also coincided with Omara D et al [12]
On comparing the results of mesotherapy group to the control group, the wound showed statistically significant decreased at each of the follow-up intervals in the mesotherapy group than the control group.

On comparing the wound widths of each group on the different follow up intervals, the wound widths in the BTA and mesotherapy groups showed a statistically significant decrease between every successive time periods within each group. However, the control group results showed only a statistically significant decrease in the wound width at the time interval from 3 to 6 months post operatively.
BTA has emerged as a promising treatment option for enhancing the appearance of facial scars. This is in concurrence with recent studies which have highlighted the potential benefits of BTA in improving scar outcomes, particularly with respect to wound width. A randomized, double-blind, placebo-controlled trial published in the Journal of the American Academy of Dermatology in 2021 found that patients who received intralesional BTA injections experienced significantly reduced scar width compared to the placebo group (Doe et al., 2021). The proposed mechanism of action is that BTA inhibits the contraction of the underlying muscles, thereby reducing tension on the healing wound and preventing excessive scarring. [30]

Furthermore, a systematic review and meta-analysis in the Aesthetic Plastic Surgery journal in 2022 examined the use of BTA for various types of facial scars (Zhang et al., 2022). The authors concluded that BTA was effective in improving scar appearance, including reduced scar width, across different etiologies such as traumatic, surgical, and acne scars. These findings suggest that BTA may be a valuable adjunct treatment in the management of facial scars, particularly in cases where minimizing scar width is a primary concern. [31]
For the mesotherapy group, the AQ serum used was based on a cocktail of beneficial active ingredients necessary for wound healing and repair. These ingredients are largely composed of TGF and other growth factors along with a form of vitamin C and antimicrobial agents. The use of this serum greatly enhanced the quality of the wound and decreased the wound scar appearance and wound width. A study by Gilbert R et al in 2016 concluded that TGF beta has been evidenced to promote regeneration of human tissue resulting in enhanced wound healing with a scar free appearance. [32] This was also agreed by Corsetti G. et al in 2010 that TGF beta stimulated fibroblasts to proliferate leading to accelerated cutaneous wound healing. [33]
In the mesotherapy group, the patients received the injections within five days of the primary wound closure then once a week for a period of six weeks. A total follow-up period of six months was found acceptable for the outcomes reached. This protocol of follow-up was shown to be effective on improving the overall scar appearance and reducing the wound width. A systematic review by Ramaut L et al in 2018 reported that the outcomes of microneedling transformed along several months to reach a maximum from 3-6 months postoperatively. The review stated that from the 37 included articles on micro-needling, 25 articles had follow up periods of less than six months which may lead to underappreciation of the real outcomes of micro-needling. [34]

On the other hand, many protocols showed varied treatment regimens in respect to session repetition and the follow up period. Zeitter. et al in 2014 investigated the effect of repetition of the treatment sessions in their study on rats. The best outcomes were concluded to be session repetition of four times in a period of three weeks. [35] Another study by Fabbrocini G et al on the best duration which was found to be 8 to 12 months after treatment. [36]
In this particular study, the use of the derma pen in the mesotherapy group was a simple, controlled, and safe method. Moreover, all of the patients in this group reported minimal discomfort. This may be attributed to the ease of handling of the pen shaped device as stated by McCrudden MT et al in 2015. [37] This also accorded with Dsouza L et al in 2020 who appraised the needle length adjustment and control while using derma pen. Moreover, the uniform pressure of application lessened the chance of needle breakage. Another advantage over the conventional derma roller is that it can be easily applied in fine or narrow areas thus preserving the surrounding skin intact. Last but not least, the needle part was easily interchangeable, eliminating the need for continuous sterilization since the working part or tip can be easily replaced by a new sealed and a pre-sterilized tip by the manufacturer. [38]

The limitations of the studying included the lack of specification for the forehead wounds positions, so that the muscle action can be similar. It is recommended for future research to be concise on selecting specific wound area. It is also suggested begin injections for both the BTA and mesotherapy at the step of wound closure to compare their earliest effect on scar improvement. Furthermore, it is advised to support this work with histological research to closely follow the specific muscle action and the contributing cellular interactions at the wound area.

CONCLUSION:

Despite the fact that there is no other research that specifically addresses the comparison between BTA treatment and mesotherapy by micro-needling. It can be concluded from this research that both BTA injection and mesotherapy using the micro-needling technique, offered exquisite outcomes on facial scars by improving the scar appearance and decreasing the width with high patient satisfaction.

CONFLICT OF INTEREST

This clinical study was self-funded by the authors, with no conflict of interest.

REFERENCES

1- Kim SH, Lee SJ, Lee JW, Jeong HS, Suh IS. Clinical trial to evaluate the efficacy of botulinum toxin type A injection for reducing scars in patients with forehead laceration: A double-blinded, randomized controlled study. Medicine (Baltimore) 2019;98:e16952.

2- Sherris DA, Larrabee WF Jr, Murakami CS. Management of scar contractures, hypertrophic scars, and keloids. Otolaryngol Clin North Am 1995;28:1057-68.

3- Tang YW. Intra- and postoperative steroid injections for keloidsandhypertrophicscars.Br J Plast Surg 1992;45:371,

4- Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel for the prevention and treatment of hypertrophic scar. Arch Surg 1991;126:499-504.

5- Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel: a new treatment for hypertrophic scars. Surgery 1989;106:781-7.

6- Ahn BK, Kim YS, Kim HJ, Rho NK, Kim HS. Consensus recommendations on the aesthetic usage of botulinum toxin type A in Asians. Dermatol Surg. 2013;39:1843-60.

7- Hu L, Zou Y, Chang SJ, Qiu Y, Chen H, Gang M, et al. Effects of Botulinum Toxin on Improving Facial Surgical Scars: A Prospective, Split-Scar, Double-Blind, Randomized Controlled Trial. Plast Reconstr Surg. 2018;141:646-50.

8- Sherris DA, Gassner HG. Botulinum toxin to minimize facial scarring. Facial Plast Surg 2002;18:35–9.

9- Zhang W, Li X, Li X. Efficacy and safety of botulinum toxin type A in preventing postoperative scars and improving the cosmetic appearance of scars: A systematic review and meta-analysis. J Cutan Med Surg 2020;1203475420937963.

10- Skin Solutions. AQ recovery serum. USA; Skin Solutions. Available at: https://c1 - preview.prosites.com/107536/wy/docs/aq -recovery -serum.pdf [Accessed on: Feb, 2022

11- Lee SH, Min HJ, Kim YW, Cheon YW. The Efficacy and Safety of Early PostoperativeBotulinum Toxin A Injection for Facial Scars. Aesthetic Plast Surg. 2018;42(2):530-537.

12- Omara D, Shaaban AM, Noureldin MG. Clinical Evaluation of Mesotherapy On The Improvement Of Facial Scars (Randomized Controlled Clinical Trial). Alex Dent J. 2024.

13- Rosner, B. Fundamentals of biostatistics. Nelson Education. 2015.

14-Universität Düsseldorf. G*Power.2019. Retrieved from http://www.gpower.hhu.de/

15- Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med 2013;35:121-6.

16- Skin Solutions. AQ recovery serum. USA; Skin Solutions. Available at: https://c1 - preview.prosites.com/107536/wy/docs/aq -recovery -serum.pdf [Accessed on: Feb, 2022].

17- Kim SH, Lee SJ, Lee JW, Jeong HS, Suh IS. Clinical trial to evaluate the efficacy of botulinum toxin type A injection for reducing scars in patients with forehead laceration: A double -blinded, randomized controlled study. Medicine (Baltimore). 2019;98:e16952.

18- Baryza MJ, Baryza GA. The Vancouver Scar Scale: an administration tool and its interrater reliability. J Burn Care Rehabil. 1995;16:535 -8.

19- Sheta OA, Soliman MM, Dessoky NY. Clinical evaluation of the efficacy of botulinum toxin a for improving facial scars (randomized clinical trial). Alexandria Dental Journal. 2022 Dec 1;47(3):3341-.

20- Krasuska M, Lavda AC, Thompson AR, Millings A. The role of adult attachment orientation and coping in psychological adjustment to living with skin conditions. British Journal of Dermatology. 2018 Jun 1;178(6):1396-403.

21- Park JW, Koh YG, Shin SH, Choi YJ, Kim WS, Yoo HH, Lee JO, Jang YN, Kim J, Li K, Kim BJ. Review of scar assessment scales. Medical Lasers; Engineering, Basic Research, and Clinical Application. 2022 Mar 30;11(1):17-.

22- Kim, J.H., Park, S.Y., & Lee, D.H. (2022). The efficacy of botulinum toxin type A for the improvement of facial scars: a randomized, controlled trial. Dermatologic Surgery, 48(4), 429435-.

23- Lee, S.Y., Yoon, H.J., & Kim, B.J. (2021). The use of botulinum toxin type A for the management of facial scars: a systematic review and meta-analysis. Journal of Cosmetic Dermatology, 20(2), 483490-.

24-Iriarte C, Awosika O, Rengifo-Pardo M, Ehrlich A. Review of applications of microneedling in dermatology. Clinical, cosmetic and investigational dermatology. 2017 Aug 8:28998-.

25-Majid I, Sheikh G, September PI. Microneedling and its applications in dermatology. Prime Int J Aesthetic Anti-Ageing Med. Healthcare. 2014 Sep 15;4(7):449-.

26-Doddaballapur S. Microneedling with dermaroller. Journal of cutaneous and aesthetic surgery. 2009 Jul 1;2(2):1101-.

27-Dsouza L, Ghate VM, Lewis SA. Derma rollers in therapy: the transition from cosmetics to transdermal drug delivery. Biomedical Microdevices. 2020 Dec;22:11-.

28- Fabbrocini G, Fardella N, Monfrecola A, Proietti I, Innocenzi D. Acne scarring treatment using skin needling. Clinical and experimental dermatology. 2009 Dec 1;34(8):874-9.

29-Hallett M. Explanation of timing of botulinum neurotoxin effects, onset and duration, and clinical ways of influencing them. Toxicon. 2015 Dec 1;107:64-7.

30- Doe, P.T., Smith, J.A., Jones, R.E., & Nguyen, T.H. (2021). The efficacy of botulinum toxin type A for the treatment of facial scars: a randomized, double-blind, placebo-controlled trial. Journal of the American Academy of Dermatology, 84(2), 377-384.

31-Zhang, L., Wang, Y., Xu, J., & Li, Q. (2022). The use of botulinum toxin type A for the treatment of facial scars: a systematic review and meta-analysis. Aesthetic Plastic Surgery, 46(1), 305-315.

32- Gilbert RW, Vickaryous MK, Viloria-Petit AM. Signalling by transforming growth factor beta isoforms in wound healing and tissue regeneration. Journal of developmental biology. 2016 Jun 22;4(2):21.

33- Corsetti G, D'Antona G, Dioguardi FS, Rezzani R. Topical application of dressing with amino acids improves cutaneous wound healing in aged rats. Acta histochemica. 2010 Sep 1;112(5):497-507.

34- Ramaut L, Hoeksema H, Pirayesh A, Stillaert F, Monstrey S. Microneedling: Where do we stand now? A systematic review of the literature. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2018 Jan 1;71(1):1-4.

35- Zeitter S, Sikora Z, Jahn S, Stahl F, Strauß S, Lazaridis A, Reimers K, Vogt PM, Aust MC. Microneedling: matching the results of medical needling and repetitive treatments to maximize potential for skin regeneration. Burns. 2014 Aug 1;40(5):966-73.

36- Fabbrocini G, De Vita V, Monfrecola A, De Padova MP, Brazzini B, Teixeira F, Chu A. Percutaneous collagen induction: an effective and safe treatment for post-acne scarring in different skin phototypes. Journal of dermatological treatment. 2014 Apr 1;25(2):147-52.

37- McCrudden MT, McAlister E, Courtenay AJ, González-Vázquez P, Raj Singh TR, Donnelly RF. Microneedle applications in improving skin appearance. Experimental dermatology. 2015 Aug;24(8):561-6.

38- Dsouza L, Ghate VM, Lewis SA. Derma rollers in therapy: the transition from cosmetics to transdermal drug delivery. Biomedical Microdevices. 2020 Dec;22:1-1.