

CLINICAL EVALUATION OF MESOTHERAPY ON THE IMPROVEMENT OF FACIAL SCARS (RANDOMIZED CONTROLLED CLINICAL TRIAL)

Dina M. Omara¹* *BDS*, Ahmed M. Shaaban² *PhD*,
Marwa G. Noureldin³ *PhD*

ABSTRACT

INTRODUCTION: If a tissue's integrity has been compromised, most body tissues can go through wound healing and leave behind scars when they recover. Mesotherapy is a non-invasive transdermal injection into the skin which stimulating fibroblasts for collagen and elastin biosynthesis and facilitating cell-to-cell communication that can be used to heal face scars.

OBJECTIVE: This study evaluated the efficacy of mesotherapy using both qualitative assessment and quantitative measurements in comparison to control group.

MATERIALS AND METHODS: Twenty-four patients with oblique or vertical forehead lacerations who underwent primary closure within five days. Randomly divided into two groups: Group 1 (n=12) was given mesotherapy (microneedling) and group 2 (n=12) was given no further treatment. At the 1, 3, and 6-month follow-up appointments, the Vancouver scar scale (VSS) scores and wound diameter were assessed, along with clinical pictures and an assessment of the scar's pigmentation.

RESULTS: At the 1-month follow-up, both groups had significantly improved. After 3 months, follow-up, the mesotherapy (microneedling) group displayed more significant changes in VSS, wound breadth, and color difference scores than the control group. Patients from both groups relapsed to their original records during the follow-up at 6 months.

CONCLUSION: Significant progress was achieved in the VSS and in the wound width with Mesotherapy (microneedling) group compared to the control group. All the major changes were observed in the 3 and 6-month visits.

KEYWORDS: Wound healing, facial scars, mesotherapy.

RUNNING TITLE: Evaluation of mesotherapy in improving facial scars.

1 B.D.S Faculty of Dentistry Alexandria University

2 Professor of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University, Alexandria, Egypt

3 Assistant Professor of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University, Alexandria, Egypt

* Corresponding Author:

E-mail: dinaomara2017@gmail.com

INTRODUCTION

The human face plays a crucial role in one's identity and conception of oneself, and a visible deformation can have a profound psychological effect on the person in question (1). These include acute facial injuries and iatrogenic facial disfigurements caused by surgical operations. After face trauma, post-traumatic stress disorder has been documented in 10–70% of patients. This disorder shows up as anxiety and despair (2, 3). Injuries to the skin, whether from trauma or surgical procedure, will leave scars.

Several physiological systems are coordinated in the complex process of wound healing to effectively respond to tissue injury. Scar formation is the typical outcome of this process, which involves numerous separate yet interlocking phases including hemostasis, inflammation, proliferation, and maturation (4) A range of consequences brought on by tissue injury result in normal wound repair. They range from pathologic excess healing (such as hypertrophic scars and keloids) to pathologic under healing (such as

chronic, non-healing wounds), Physiologic healing, which includes the development of scars, falling somewhere in between.

Throughout the past few years, additional therapies and methods have been created to get around these restrictions. Collagen induction therapy, sometimes referred to as microneedling therapy, is one of these methods. There are some pathological and clinical investigations that have shown that microneedling produces a positive clinical and histological response in the skin. Microneedling (mesotherapy) treatment for face and other types of scars has not been subjected to any objective clinical trials, which is glaringly absent.

The AQ (Ahmed Qahtani) recovery serum is a growth factor created to support the skin's natural healing mechanisms, which repair and regenerate skin tissue by enhancing circulation, antioxidant activity, and cellular regeneration (5).

Therefore, this study was showing efficacy of mesotherapy using both qualitative assessment and quantitative measurements to verify its positive effects on facial scarring.

MATERIALS AND METHODS

The study was performed as a randomized clinical trial with a 1:1 allocation ratio that was carried out upon approval of the Research Ethics Committee at the Faculty of Dentistry, Alexandria University, on 20/03/2022. Ethics Committee No: 0410-03/2022. Prior to the procedure, all patients signed an informed consent form at Alexandria University's Faculty of Dentistry's Oral and Maxillofacial Surgery Department, to ensure and confirm their understanding of the procedure's outcome and the risks associated with this intervention.

Patients

This study involved patients of both sexes who visited our emergency clinic with newly sustained traumatic vertical or oblique forehead lacerations. Patients from the emergency clinic of the Department of Oral and Maxillofacial Surgery were selected at Alexandria University's College of Dentistry.

Sample randomization

This study used computer-generated random numbers for simple randomisation in a clinical trial that was randomised with a 1:1 allocation ratio. Two equal groups of 24 patients each were formed:

Group I: Including 12 patients received (mesotherapy) growth factor AQ recovery serum with microneedling dermapen and acted as the study group. (Figure 1)

Group II: Including 12 patients that received no treatment. (Figure 2)

Inclusion criteria (6)

1. Patients aged range from 20-40 years old without scar treatment in the six months prior to the study.
2. Patient presenting with vertical or oblique forehead lacerations caused by trauma.
3. Recent and fresh wounds.
4. Atrophic scar (linear scar).
5. A healthy patient (class I classification by the American Society of Anesthesiologists).
6. The patient has no pathology or local irritation.
7. Patient who was able to understand verbal and written instructions.

Exclusion criteria (6, 7)

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

Materials (Figure 3)

Mesotherapy growth factor AQ recovery serum (AQ Skin Solutions, Irvine, California, USA). It is cosmetic therapy consisting of Active Ingredients includes: (5)

- 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.
 - Anti-Microbial agent.
- Derma pen (Derma pen Dr. Pen, China).
- Needle cartridge tips (Needle cartridge tips, China).
- Digital vernier caliper (150 mm, 6-inch, electronic, stainless steel vernier caliper).

Methods

Pre-operative assessment and examination

History and clinical examination

1. Every patient had their medical history taken, which included their name, sex, age, occupation, place of residence, primary complaint, systemic diseases, medications, and past procedures. A thorough clinical examination was performed extra orally to ascertain the following:
2. An evaluation of swelling using a 1-4 Edema scale.

1. General examination

It consists of monitoring of vital signs and observation of general state of health and asking about the history of the trauma that caused the forehead laceration.

2. Extra-oral examination

a) Inspection

To distinguish any swelling, presence of burn, and erythema.

b) Palpation

To distinguish any deformation or modification in the forehead's bone shape

Operative procedures

There are 2 groups:

Group (1) study group:

1. At Alexandria University's Department of Oral and Maxillofacial Surgery, all surgeries were carried out under local anesthetic.

2. A single surgeon performed the microneedling in the clinic for patients in the mesotherapy AQ recovery serum group.
3. The forehead area, as well as the skin beneath the healed wound, was treated with a derma pen in the intradermal layer.
4. To eliminate all oils from the skin's surface, the patient's skin was washed with ethyl alcohol and then with ether.
5. Skin was covered in topical anesthetic lotion for 30 minutes while in occlusion.
6. Insulin syringe was used to drop 0.1 ml of AQ serum as a first layer on the scar line.
7. Dermapen with 0.5-1 mm needle depth was used on the scar line for microneedling this solution at the region of the scar.
8. Another layer of AQ recovery serum was applied 0.1 ml as a final layer after microneedling by dermapen.
9. Patients avoided washing their face for 6-8 hrs.
10. The sessions were repeated once weekly for up to 6 sessions.

Group (2) control group: was composed of 12 patients in which they no mesotherapy was received and evaluation was done on 1,3 and 6 months follow ups.

Post-operative care and medication

- All groups received the following post-operative medications:
- For the first 14 days, up until the wound is closed, apply Jacy topical (SAbSHiRe pharmaceuticals, Egypt) cream two to three times daily to create the best conditions possible for skin renewal.
- Scaro gel (Macro Group Pharmaceuticals, Egypt) is applied twice daily for two to six months on closed scar sites, in one direction, to improve the texture and colour of the skin. It contains silicone fluid, vitamins A and E, almond oil, and polydimethylsiloxane.
All the patients were given the same postoperative instructions as the following:
- Patients were advised to stay in a upright position for 6 hours.
- For six months, all patients were instructed to use sunscreen every day (8).
- Throughout the first 24 hours, avoid excessive physical activity or exposure to the sun.
- For at least 6 hours following treatment, the microneedling area was kept free of manipulation.
- If ecchymosis developed, the surgeon who carried out the procedure provided a cold compress or gentle manual compression right where the arteries were pierced.

Follow up:

Postoperative clinical evaluation

All patients were urged to show up at 1 pm for follow-up appointments.

- For a minimum of six months, all patients were requested to return for follow-up appointments at intervals of one month, at which time pictures and documentation of any potential side effects were taken (8).
- Using a typical light source box, digital photos of the scar were obtained under the same lighting and illumination settings (9).

Clinical follow-up phase (Figure 4)

Patients were followed up clinically at 1, 3 and 6 months postoperatively. Clinical examination evaluated:

Primary outcome

Wound width

The mean width of the forehead wound of each group was likewise determined for the 1-month, 3-month and 6-month visits (10).

Vancouver scar scale

The Vancouver scar scale (VSS) was assessed by two plastic surgeons in an independent, blinded fashion to quantify scar appearance at the 1-month, 3-month and 6-month visits (11).

Color differences

Quantified color differences between the scar and surrounding normal skin were measured and compared using the Commission International d'Eclairage (CIE) $L^*a^*b^*$ color coordinates for each patient. The letters L^* , a^* and b^* represent each of the three values the CIELAB color space uses to measure objective color and calculate color differences. L^* represents lightness from black to white on a scale of zero to 100, while a^* and b^* represent chromaticity with no specific numeric limits. $L^*a^*b^*$ values of the region of interest were obtained using Adobe Photoshop 7.0 (Adobe Systems Incorporated, San Jose, CA.), and the total $L^*a^*b^*$ color difference between normal skin and scar was calculated using the following equation:

$$\Delta T = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$$

The mean total $L^*a^*b^*$ color difference for each group was determined for the 1-month, 3-month and 6-month visits (12).

Cheon YW, Lee WJ, Rah DK. Objective and quantitative evaluation of scar color using the $L^*a^*b^*$ color coordinates. J Craniofac Surg 2010;21:679-84.

Statistical analysis

Data was collected and inputted into the computer. The statistical analysis was conducted using Statistical Package for Social Sciences (SPSS/version 24) software.



Figure (1): Photograph (A) showing patient receiving Mesotherapy (microneedling with AQ recovery serum) at first session. Photograph (B) Scar at patient's 1-month visit. Photograph (C) Scar at patient's 3-month visit, and Photograph (D) Scar at patient's 6-month visit, improved scar quality and erythema were noted with subsequent patient satisfaction.



Figure (2): Photograph (A) showing patient receiving no treatment of scar on day of removing sutures. Photograph (B) showing scar at patient's 1-month visit. 6-month visit showing Scar at patient's 3-month visit, and Photograph (D) showing scar at patient's 6-month visit, widened and erythematous scar continues to be problematic.



Figure (3): AQ recovery serum GF, Derma pen and needle cartridge tips.



Figure (4): Comparison between Mesotherapy (microneedling) group and Control group at 6 months follow up.

RESULTS

Twenty-four patients were placed into two groups for this study: group I “mesotherapy (microneedling)treatment group” and group II “control group”. The mean age in group I was 31.5 ± 6.84 years with range 20-40 and in group II the mean age was 30.6 ± 5.99 with range 21-38 years, there was no discernible difference between the two groups when the two groups' ages were compared ($p > 0.05$).

The patient gender was nearly similar in the two groups; group I had 58.3% men and 41.7% women, while group II had a male to female ratio of 1:1. There was no statistically significant difference in sex between the two groups ($P > 0.05$).

Two groups of patients with recent traumatic vertical or oblique forehead lacerations were selected from the Emergency Clinic at the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University.

Postoperative results

Clinical result

1. Wound width (mm)

The Wound width (mm) at base line in group I was 25.75 ± 17.00 and decreased by insignificant value ($p > 0.01$) after 1 month to be 20.97 ± 13.88 , while The wound's width greatly decreased to 17.71 13.75 and 12.61 11.47 at 3 and 6 months, respectively, while in group II the base line Wound width (mm) was 25.45 ± 8.11 while after 1, 3 and 6 months the change was insignificant ($p > 0.05$) to be 24.30 ± 8.01 , 23.33 ± 8.18 and 20.42 ± 7.99 respectively (Figure 1) .On comparing the two group at different period of follow up, it was found that there was no significant difference at base line regarding Wound width (mm), while after 1, 3 and 6 months there was a significant improve in mesotherapy group more than control group ($p < 0.05$). Table (1) (Figure 3)

2. Vancouver scar scale

The Vancouver scar scale at base line in group I was 7.17 ± 1.85 and decreased by a significant value ($p < 0.01$) after 1, 3 and 6 months to be 2.17 ± 1.34 , 1.92 ± 1.31 and 1.0 ± 0.43 respectively, while in group II the base line Vancouver scar scale was 7.33 ± 1.15 ,

after 1 month the Vancouver scar scale was 7.00 ± 1.04 with no significant change in comparing with the base line value, after 3 and 6 months there was a significant decrease to be 5.67 ± 1.87 and 5.50 ± 1.68 . On comparing the two group at different period of follow up, it was found that there was no significant difference at base line regarding Vancouver scar scale, while after 1, 3 and 6 months there was a significant improve in mesotherapy group more than control group ($p < 0.05$). Table (2)

3. Color difference

The Color difference at base line in group I was 57.21 ± 13.24 and decreased by a nonsignificant value ($p > 0.05$) after 1 month to be 55.93 ± 13.48 , while the decrease after 3 and 6 months was significantly ($p < 0.05$) in comparing with base line to be 38.79 ± 9.08 , and 23.64 ± 8.75 respectively, while in group II the base line Color difference was 64.73 ± 14.84 while after 1 month the color difference was 63.19 ± 15.37 with no significant change, after 3 and 6 months there was a significant decrease to be 55.56 ± 12.06 and 41.07 ± 15.45 . On comparing the two group at different period of follow up, it was found that there was no significant difference at base line and 1st months post treatment regarding Color difference, while after 3 and 6 months there was a significant improve in mesotherapy group more than control group ($p < 0.05$). Table (3)

Table 1: Comparison between the two studied groups regarding Wound width (MM) at different period of follow up.

	Wound width (MM)			
	Baseline	1 month	At 3- months	At 6 months
Mesotherapy group				
Range	16.45-75.99	14.4-63.75	10.45-59.66	5.8-47.8
Mean	25.75	20.97	17.71	12.61
SD	17.00	13.88	13.75	11.47
Median	18.47	16.59	12.91	8.79
P1		0.229 N.S.	0.018*	0.019*
Control group				
Range	14.71-35.6	14.29-34.48	13.1-34.21	10.8-32.61
Mean	25.45	24.30	23.33	20.42
SD	8.11	8.01	8.18	7.99
Median	27.07	25.61	24.62	20.86
P 2		0.361 N.S.	0.260 N.S.	0.072 N.S.
P 3		0.365 N.S.	0.012*	0.008*

P1 Comparison between baseline and different interval time in the mesotherapy group
 P2 Comparison between baseline and different interval time in the control group.
 P3 comparison between mesotherapy group and control group at the same time.
 P was significant if < 0.05
 * Significant difference
 N.S. Not significant

Table 2: Comparison between the two studied groups regarding Vancouver scar scale at different period of follow up.

	Vancouver scar scale			
	Baseline	1 month	At 3- months	At 6 months
Mesotherapy group				
Range	4-10	1-5	1-5	0-2
Mean	7.17	2.17	1.92	1.00
SD	1.85	1.34	1.31	0.43
Median	7.0	2.0	1.5	1
P1		0.001*	0.001*	0.001*
Control group				
Range	6-9	6-8	3-8	3-7
Mean	7.33	7.00	5.67	5.50
SD	1.15	1.04	1.87	1.68
Median	7.5	7.0	6.0	6.0
P2		0.233 N.S.	0.028*	0.003*
P3	0.397 N.S.	0.001*	0.001*	0.001*

P1 Comparison between baseline and different interval time in the mesotherapy group
 P2 Comparison between baseline and different interval time in the control group.
 P3 comparison between mesotherapy group and control group at the same time.
 P was significant if ≤ 0.05
 * Significant difference
 N.S. Not significant

Table 3: Comparison between the two studied groups regarding color difference at different period of follow up.

	Color difference			
	Baseline	1 month	At 3- months	At 6 months
Mesotherapy group				
Range	38.7-77.4	37.01-78.56	25.8-55.34	11.58-34.99
Mean	57.21	55.93	38.79	23.64
SD	13.24	13.48	9.08	8.75
Median	58.6	58.4	37.0	24.0
P1		0.408 N.S.	0.001*	0.001*
Control group				
Range	33.8-83.5	31.11-82.67	34.7-77.4	16.55-69.49
Mean	64.73	63.19	55.56	41.07
SD	14.84	15.37	12.06	15.45
Median	69.8	68.0	56.6	40.4
P2		0.403 N.S.	0.055*	0.001*
P3 value	0.102 N.S.	0.116 N.S.	0.001*	0.001*

P1 Comparison between baseline and different interval time in the mesotherapy group

P2 Comparison between baseline and different interval time in the control group.

P3 comparison between mesotherapy group and control group at the same time.

P was significant if ≤ 0.05

* Significant difference

N.S. Not significant

DISCUSSION

Management of wound scars has been a difficult undertaking and a subject of attention. In comparison to other techniques with the same goal, skin microneedling has fewer adverse effects, causes less epidermal damage, and requires less recovery time following the procedure. In order to support mesotherapy's therapeutic effects on face scarring, the aim of this study was to demonstrate the therapy's effectiveness using both qualitative evaluation and quantitative data (13).

The mean age in group I was 31.5 ± 6.84 years with range 20-40 and in group II the mean age was 30.6 ± 5.99 with range 21-38 years, the gender of the patients were almost similar in the two groups; in group I 58.3% male and 41.7% female, while in group II the male: female ratio was 1:1, there was no significant difference between the two studied groups regarding basic demographic data including age and sex, this results was important to eliminate the effect of demographic data on the net results and the only affected factor was the type of treatment.

The wound width (mm) at base line in group I was 25.75 ± 17.00 and decreased but by insignificant value ($p > 0.01$) after 1 month to be 20.97 ± 13.88 , while after 3 and 6 months the wound width decreased significantly to be 17.71 ± 13.75 and 12.61 ± 11.47 respectively, while in group II the base line wound width (mm) was 25.45 ± 8.11 while after 1, 3 and 6 months the change was insignificant ($p > 0.05$) to be 24.30 ± 8.01 , 23.33 ± 8.18 and 20.42 ± 7.99 respectively. On comparing the two group at different period of follow up, it was found that there was no significant difference at base line regarding wound width (mm), while after 1, 3 and 6 months there was a significant improvement in mesotherapy group more than control group ($p < 0.05$).

Ryu et al. observed that application of epidermal growth factor (rhEGF) ointment reduced the width and length and according to Ryu et al.'s findings, which are consistent with our own, mupirocin ointment and epidermal growth factor (rhEGF) ointment produced comparable short-term cosmetic outcomes in terms of melanin index and erythema index. Their findings suggest that the usage of topical antibiotics following clean wound operations may be decreased by rhEGF (14). Also, Shin et al. demonstrated that rhEGF

significantly improved scar pliability and width and length in thyroidectomy scars after four weeks, compared with the control group (15).

Similar to our study, Castaon et al. investigated the use of microneedling and epidermal growth factor (EGF) as methods for treating acne scars. The study involved 30 patients divided into two groups: They discovered that the groups were homogeneous in terms of age, gender, and phototype when comparing (1) two microneedling treatments separated by a 30-day interval and (2) two microneedling sessions separated by the same period but linked to the release of an EGF medication. Clinical evaluations revealed that both groups' width and length of scores had decreased (16).

In our study the Vancouver scar scale at base line in group I was 7.17 ± 1.85 and decreased by a significant value ($p < 0.01$) after 1, 3 and 6 months to be 2.17 ± 1.34 , 1.92 ± 1.31 and 1.0 ± 0.43 respectively, while in group II the base line Vancouver scar scale was 7.33 ± 1.15 , after 1 month the Vancouver score scale was 7.00 ± 1.04 with no significant change in comparison with the base line value, after 3 and 6 months there was a significant decrease to be 5.67 ± 1.87 and 5.50 ± 1.68 . On comparing the two group at different period of follow up, it was found that there was no significant difference at base line regarding Vancouver scar scale, while after 1, 3 and 6 months there was a significant improvement in mesotherapy group more than control group ($p < 0.05$).

In agreement with our results, 60 Taiwanese women participated in a study by Kao et al. about the effects of microencapsulated rhEGF on the cutaneous scar following a caesarean section. The Vancouver Scar Scale (VSS) total score, scar elasticity, pigmentation, and scar vascularity were all considerably lower in the rhEGF group than in the silicone gel group (control group) after nine months, according to their findings (17).

In contrast with our results, 10 patients with face scars between the ages of 20 and 40 were chosen by Kalil, Frainer, and colleagues, and they had three sessions of microneedling with a 2mm needle. Digital images and anatomopathological analyses were used in the investigation. Growth factors (EGF, IGF, TGF-beta3) were administered as drugs via masks. The authors saw an overall improvement in skin texture and a minor improvement in acne scars, but they did not detect any improvement in scarring as measured by the Vancouver scar scale (VSS) (18).

In agreement with our results, Wang and colleagues demonstrated that fibroblasts obtained from hypertrophic skin and hypertrophic scar tissue produced more TGF-1 mRNA and protein than did fibroblasts derived from normal skin, indicating that TGF-1 may play a role in the development of hypertrophic scars (19). In addition to expressing more TGF-1 than normal skin, hypertrophic derived

fibroblasts have also been demonstrated to express TGF- receptors for a longer period of time.

The color difference at base line in group I was 57.21 ± 13.24 and decrease by a nonsignificant value ($p > 0.05$) after 1 month to be 55.93 ± 13.48 , while the decrease after 3 and 6 months was significantly ($p < 0.05$) in comparing with base line to be 38.79 ± 9.08 , and 23.64 ± 8.75 respectively, while in group II the base line color difference was 64.73 ± 14.84 while after 1 month the color difference was 63.19 ± 15.37 with no significant change, after 3 and 6 months there was a significant decrease to be 55.56 ± 12.06 and 41.07 ± 15.45 . On comparing the two group at different period of follow up, it was found that there was no significant difference at base line and 1st months post treatment regarding color difference, while after 3 and 6 months there was a significant improve in mesotherapy group more than control group ($p < 0.05$).

In support of our results, According to Draelos et al., epidermal growth factor (EGF) reduces follicular hyperkeratosis and sebum production while also having an anti-inflammatory impact. Additionally, it upregulates TGF-beta1, which has a pro-fibrotic effect, while upregulating the creation of organised collagen and dermal matrix components. It is anticipated that scars and skin tone will improve with its use in drug delivery (20).

Also, in agreement with our results, in their investigation of the effects of epidermal growth factor on wound healing and hyperpigmentation, Techapichetvanich et al. discovered that the incidence of hyperpigmentation was assessed by a dermatologist who was blinded using photographs at follow-up visits at 2, 3 weeks, and 1, 2 months. On the same follow-up visits, the melanin index was measured using a mexameter (Mexameter®MX18 Cutometer DualMPA580, Enviro Derm Services (UK) Ltd.) to provide an objective assessment of hyperpigmentation. At the conclusion of the investigation, the other negative effects were gathered using a questionnaire (21).

The topical application of TGF significantly decreased healing time, scarring pigmentation, scar pliability, height, and vascularity in patients with partial-thickness burns, according to a meta-analysis of published randomised controlled trials (22).

This research may have some limitations. For starters, there was no restriction on how exactly the wound inside the forehead may be placed. There could be different levels of distracting pressures acting on the skin, depending on where exactly on the forehead they are. less obtrusive, for instance. It would have been best to pick patients who had obvious wound positions. We were unable to do histopathologic analyses for this study, which is the second drawback.

The recommendations in our research are continuation of using Mesotherapy (microneedling) as the approach of treatment of facial lacerations for layers follow up periods. Further studies on larger sample of population to approve the convenience and acceptance of the usage of Mesotherapy (Microneedling) in the elimination of facial scars.

CONCLUSION

The microneedling using AQ proved effective on scar improvement since there was significant improvement in the VSS and in the wound width in the patients treated with Mesotherapy (microneedling with AQ recovery serum) compared to the control group. On the 3 and 6-month visits, all the significant changes were observed, but not on the 1-month visit. All cases showed uneventful healing.

CONFLICT OF INTEREST

There are no conflicts of interest, according to the authors.

FUNDING STATEMENT

To carry out this work, the authors received no specific funding.

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