

Combined Micro-Needling with Lyophilized Platelet-Rich Plasma versus Micro-Needling Monotherapy in The Treatment of Atrophic Post-Acne Scars: Split-Face Study

May H. El-Samahy, Reham Gamal Abbas Ibrahim, Mona A. Ibrahim*

Department Dermatology, Venereology, and Andrology, Faculty of Medicine, Ain Shams University, Egypt

*Corresponding author: Mona Abdel-Halim Ibrahim, Mobile: (+20) 01006228698, E-mail: monaabdelhalim@med.asu.edu.eg

ABSTRACT

Background: Combined micro-needling with platelet-rich plasma (PRP) is an effective treatment option for atrophic post-acne scars. Lyophilized PRP (L-PRP) is a novel, simpler, standardized preparation of PRP. The combined treatment of post-acne scars with micro-needling and L-PRP hasn't been previously investigated.

Objectives: This study aimed to compare the effectiveness of the combined use of micro-needling and L-PRP versus micro-needling only in treating atrophic post-acne scars. **Patients and methods:** This randomized controlled split-face study included 20 adult patients with post-acne atrophic scars. One side of the face was treated with micro-needling. The other side was treated with micro-needling and L-PRP. The treatment was applied at 2 weeks intervals for 3 sessions. The assessment was done with Antera 3D[®] camera analyzer. The mean indentation index of each side of the face was calculated before and two weeks after the last treatment.

Results: Our study showed that the mean age of patients was 28.35 ± 4.87 years, 90% were females, and 20% were males. 50% had Fitzpatrick skin type III, while the other half had skin type IV. Both micro-needling monotherapy and combined micro-needling with L-PRP produced significant improvement in the mean indentation index of atrophic post-acne scars. However, the mean percentage of improvement was higher in the combined treatment group. Side effects were minimal and transient with both treatment modalities.

Conclusion: Combined treatment with micro-needling and L-PRP showed superior results in improving atrophic post-acne scars and is regarded as a safe, simple, and cost-effective treatment modality.

Keywords: L-PRP, Post-acne scars, Micro-needling, Dermapen, PRP.

INTRODUCTION

Acne vulgaris is a highly prevalent skin condition that affects virtually all teenagers and adults at some point in their lives. The general state of health is unaffected, but acne can leave both physical and mental scars that last a lifetime resulting in loss of self-esteem. Inflammatory acne lesions might leave lifelong scars, and the severity of scarring may rely on delaying the treatment of acne patients⁽¹⁾. Acne scarring is the result of skin damage that occurs throughout the healing process. Scars are classified into two main categories: atrophic and hypertrophic or keloid scars. Most patients have atrophic scars. Atrophic acne scars are sub-categorized into ice pick, boxcar, and rolling scars⁽²⁾.

There are numerous treatment options for atrophic post-acne scars. Chemical peeling, microdermabrasion, dermabrasion, laser therapy, punch techniques, dermal grafting, tissue-augmenting substances, subcision, micro-needling, and platelet-rich plasma (PRP) are some of these. These treatment modalities show variations in their effectiveness and side effects. Generally, invasive techniques showed a greater response rate with longer downtime and more side effects. On the other hand, non- or less-invasive techniques are less effective but more comfortable for patients with shorter downtime. This fact leads to the adoption of the concept of combination therapy, which shows effectiveness with high safety profile⁽³⁾.

Micro-needling is found in many combination treatments for post-acne scars. It can be combined with other treatments, such as subcision and chemical peels⁽⁴⁾. Micro-needling is a minimally invasive technique. It

is done by using a sterile dermaroller or dermapen, which is made up of a number of fine and sharp needles that penetrate the skin. Multiple microbruises form in the dermis triggering a complex cascade of growth factors that results in collagen production^(5,6).

Micro-needling can also be combined with PRP⁽⁷⁾. The latter contains a high concentration of platelets. There are several growth factors in the α -granules of the platelets, and these granules are secreted after platelets' activation by aggregation initiators. The secreted growth factors can cause fibroblastic stimulation, inducing collagen production⁽⁸⁾. Lyophilized PRP (L-PRP) is a novel technique of PRP that show similar effectiveness as the conventional PRP. However, it is more time-saving and comfortable for the patients. It can also deliver a standardized amount of growth factors per treatment session⁽⁹⁾. To the best of our knowledge, combined micro-needling with L-PRP has not been assessed before in the treatment of atrophic post-acne scars. Therefore, we aimed to assess the effect of this combined treatment and compare it with micro-needling monotherapy in a split-face study.

PATIENTS AND METHODS

Patients: A randomized-controlled open-label split-face study was done on 20 adult patients having post-acne atrophic scars. Patients aged 20 - 36 years old (80% females, 20% males) with Fitzpatrick skin types III (50%) and IV (50%). The study was done at the Dermatology Department of Ain Shams University.

Exclusion criteria: Patients with active acne, active skin infection, current pregnancy, severe systemic

illness, malignancy, a history of syncopal attack, hypertrophic scars, or keloids. Patients having previous treatment with topical/systemic isotretinoin or facial procedure in the last 6 months or anticoagulants in the last 2 weeks were also excluded.

The patients were randomly allocated to two groups using simple random sampling to receive combined micro-needling (dermapen) and L-PRP (L-GF[®]) on one side and dermapen only on the contralateral side of the face.

Assessment of results: Baseline and post-treatment assessments (2 weeks after the last treatment session) were done with Antera 3D[®] imaging system (Miravex Ltd., Dublin, Ireland). It is an effective assessment tool for measuring the changes in acne scars before and after treatment⁽¹⁰⁾. A high-resolution color image was first captured using the color mode. Then to assess the degree of acne scars, the camera was switched to the wrinkle mode, which can measure the skin depressions from the surface. A large filter (3 mm) was used as a threshold value to assess the size, width, and depth of individual scars. The latter parameters were displayed on the display bar and represented as a false color map. To measure the degree of acne scars in a selected area, the indentation index was calculated. The indentation index measures the total depressions in the skin in a selected area. The value is measured in arbitrary (au) value. The indentation index was calculated for 6 areas (Right forehead, right cheek, right lower face, left forehead, left cheek, left lower face). Then the mean of the indentation index on each side of the face was calculated (i.e., the mean indentation index on the right side of the face equals the sum of the right forehead indentation index, right cheek indentation index, and right lower face indentation index divided by three. The same applies to the left side of the face).

Procedure

The whole face was disinfected with alcohol. A thick layer of anesthetic cream (EMLA cream) was applied under occlusion to the whole face for 45 minutes, then gently removed just before the application of treatment. One side of the face was treated with dermapen with needle lengths of 150 mm and 12 needle tips. One hand was used to stretch the skin, and with the other hand, the dermapen was applied perpendicular to the skin surface in horizontal, vertical, and oblique directions. The therapeutic endpoint was determined as a uniform pin-point hemorrhage that was easily controlled. The other side was treated with a dermapen plus intradermal injection of L-GF[®] (CMC, Cairo). One vial was injected for each patient per session at 1cm equidistant injection points with a 23-gauge needle. Each vial contains 1 million platelets concentrate. The vial was first diluted with 2 cm distilled water.

L-GF[®] was prepared from heterologous donors, then leuko-depleted and disinfected to avoid allergic reactions and possible infections. It was then tested for bacterial and viral antigens, and nucleic acid sequencing was done to ensure sterilization. The platelet

concentration was adjusted to $1 \times 10^6/\mu\text{l}$, and the growth factors were measured using by ELISA technique^(11,12).

After the procedure, a saline solution was used to cleanse the face, and cold packs were applied. Patients were told to use sunscreen every day before going out in the sun and to reapply it every two hours.

The side effects were recorded for each type of treatment during and after the procedure. The treatment was applied at 2 weeks intervals for 3 sessions.

Ethical consent: Informed written consents were obtained from all patients, and The Research Ethical Committee, Faculty of Medicine, Ain Shams University approved the study. This study was conducted in compliance with the code of ethics of the world medical association (Declaration of Helsinki) for human subjects.

Statistical analysis:

A statistical software for social sciences was used to code, tabulate, and transfer the data to a computer (IBM SPSS 20.0). For descriptive statistics, median and interquartile range (IQR) were used for nonparametric data whereas mean \pm standard deviation, and range were used for parametric numerical data. An independent sample t-test was used to assess the statistical significance of the difference between the two independent means of the two study groups. The statistical significance of the difference between two study groups in a parametric variable was assessed using a paired t-test. The one-way ANOVA test was used to assess the statistical significance of the difference in a parametric variable between more than two study groups. A linear link between two quantitative variables was evaluated using the Pearson correlation coefficient. To determine whether there was a correlation between two quantitative, non-parametric, continuous variables, Spearman correlation was utilised. $P \leq 0.05$ was regarded as being significant, and $P \leq 0.001$ as being extremely significant.

RESULTS

Among 20 patients, the mean age was 28.35 ± 4.87 , with a range of 20 – 36 years. 80% of patients were females, and 20% were males. Half of the patients (50%) had Fitzpatrick skin type III, and the rest 50%, had skin type IV. The mean duration of acne scars was 6.10 ± 3.19 , with a range of 2 – 11 years.

There was a highly statistically significant difference ($P < 0.001$) between the scars indentation index before and after treatment in the side treated with dermapen only. The mean indentation index of the right side before treatment was 21.90 ± 2.69 , after treatment by dermapen only was 19.95 ± 2.72 and the mean percentage of improvement was $\downarrow 9.03 \pm 4.25$. The mean indentation index of the left side in the other group before treatment was 23.61 ± 5.49 , after treatment by dermapen only was 21.59 ± 4.83 and the mean percentage of improvement was $\downarrow 8.40 \pm 4.45$. No

significant difference was found between both sides (Figures 1, 2).

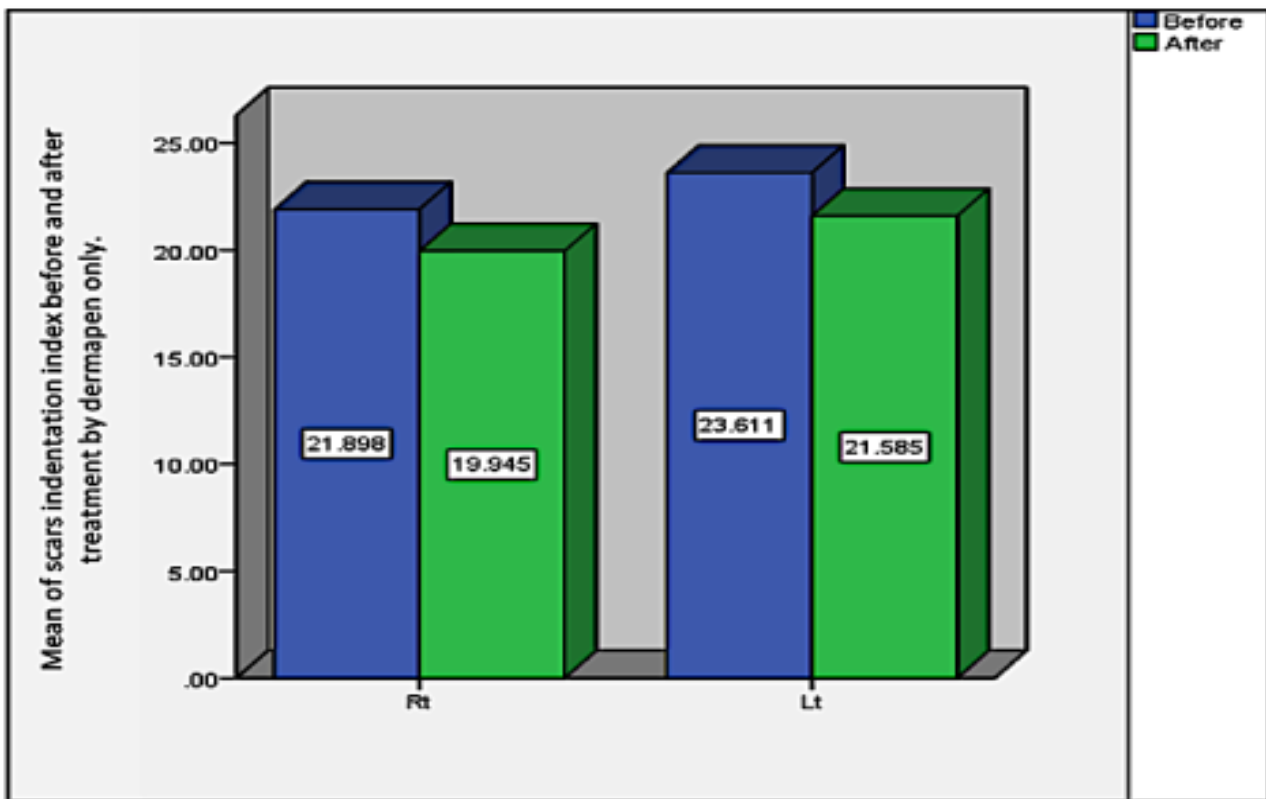


Figure (1): Comparison between scars indentation index before and after treatment by dermapen only.,

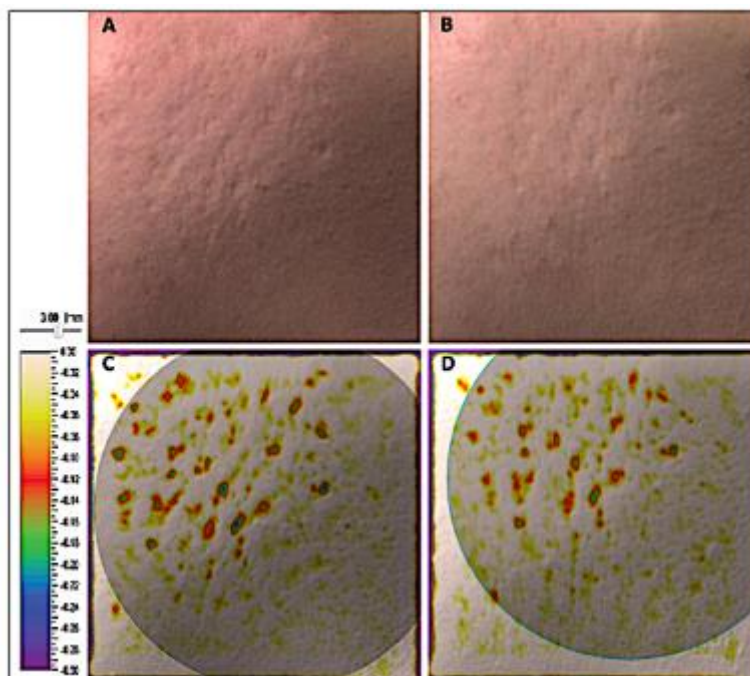


Figure (2): Left cheek treated by dermapen only. (A): Color image before treatment. (B): Color image after treatment. (C): Indentation index of acne before treatment (20.28). (D): Indentation index after treatment (19.51), the mean percentage of improvement was $\downarrow 3.8$. Large filter (3 mm) was used, and a false color map on the left reflects the size and depth of individual acne scars. The indentation index was measured in the shaded areas.

There was a highly statistically significant difference ($P < 0.001$) between acne scars indentation index before and after treatment on the side treated with dermapen plus L-GF[®] in both groups. The mean indentation index of the right side before treatment was 23.10 ± 3.61 , after treatment by dermapen plus L-GF was 18.67 ± 3.42 , and the mean percentage of improvement was $\downarrow 19.32 \pm 4.81$). The mean indentation index of the acne scars on the left side before

treatment was 23.60 ± 5.97 , after treatment was 16.03 ± 3.47 and the mean percentage of improvement was $\downarrow 30.75 \pm 10.90$. No significant difference was found between both sides (**Figures 3, 4**).

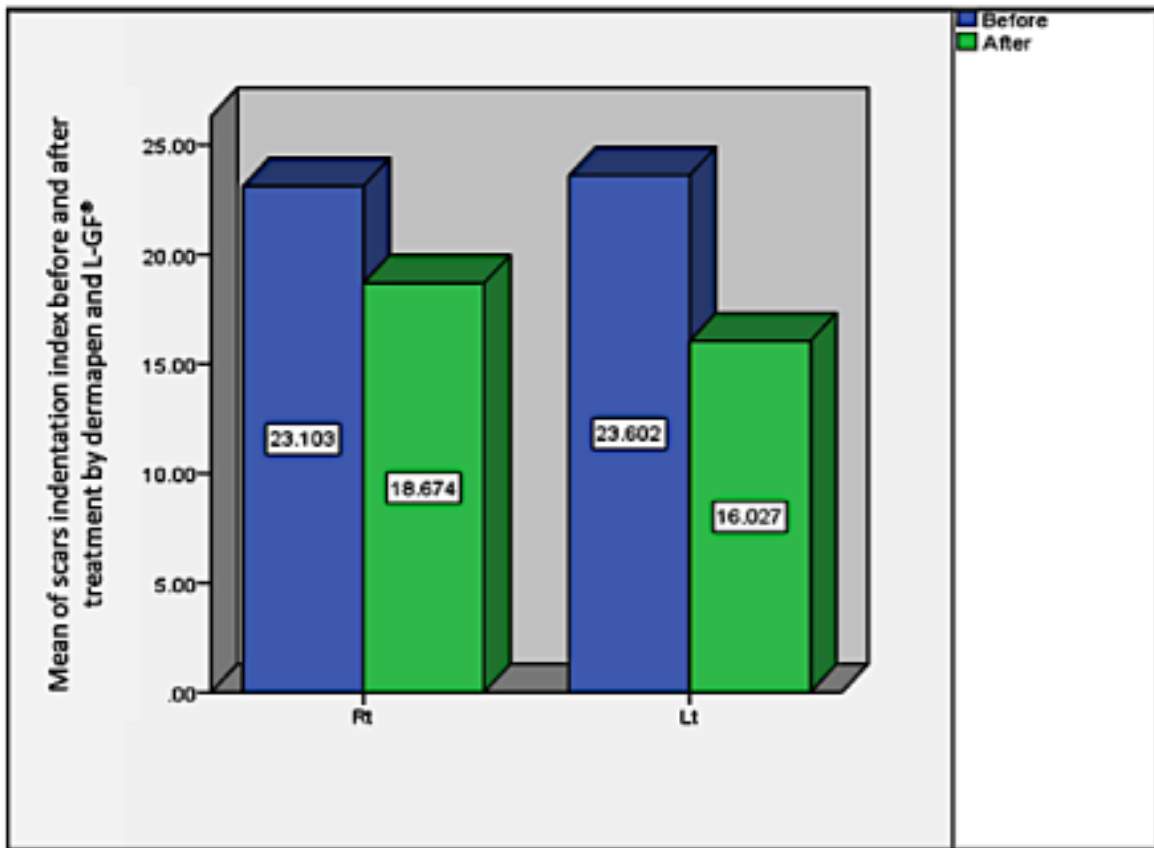


Figure (3): Comparison between scars indentation index before and after treatment by dermapen and L-GF®

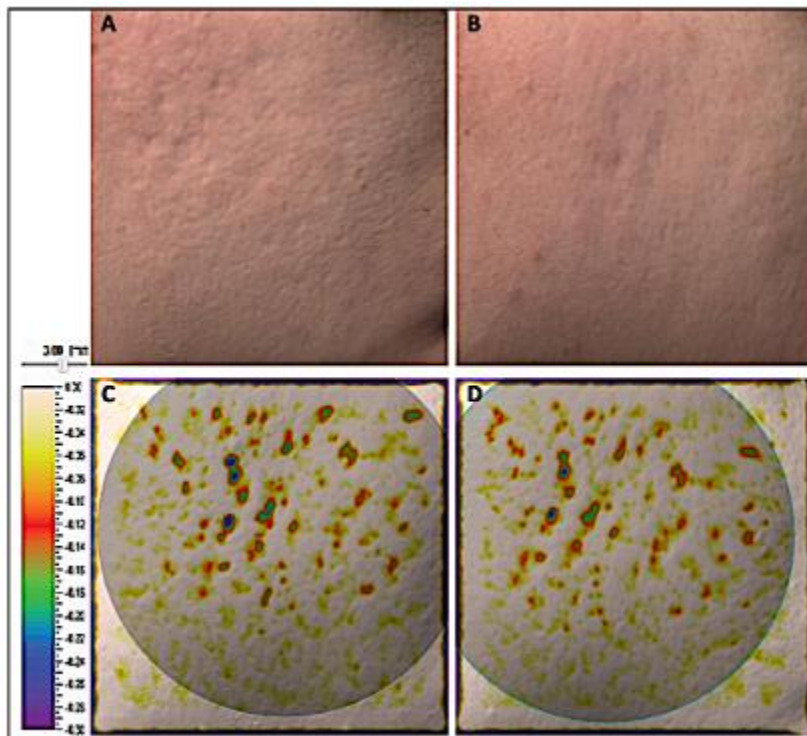


Figure (4): Right cheek treated by dermapen and L-GF®. (A): Color image before treatment. (B): Color image after treatment. (C): Indentation index of acne scars before treatment (20.17). (D): Indentation index of acne scars after treatment (15.63), the mean percentage of improvement was $\downarrow 22.5$. Large filter (3 mm) was used, and a false color map on the left reflects the size and depth of individual acne scars. The indentation index was measured in the shaded areas.

By comparing both treatment modalities, there was a highly significant difference between the mean percentage improvement of the combined treatment with dermapen and L-GF[®] and dermapen monotherapy. The mean percentage improvement was significantly greater on the sides treated by the combined treatment (Table 1).

Table (1): Comparison between the mean percentage of improvement by the combined treatment (dermapen with L-GF[®]) and monotherapy (dermapen)

Percentage of Improvement	Scars indentation index by		Independent sample t-test	P
	Dermapen only (n = 20)	Dermapen plus (L-GF) (n = 20)		
Min. – Max.	↓1.12 – 16.17	↓11.65 – ↓45.79	-6.674	0.001*
Mean ± SD.	↓8.72 ± 4.25	↓25.04 ± 10.08		
Median	↓8.46	↓23.01		

*Highly statistically significant at P ≤ 0.001

There was no statistically significant correlation between age, duration of scars, and the mean percentage of improvement of indentation index either with combined or monotherapy. Moreover, there was a statistically insignificant relationship between skin types III and IV and the total mean percentage of improvement of scars indentation index in cases treated with either treatment.

Regarding side effects, only transient symptoms of pain, erythema, edema, and bruising were found. No difference was found between both treatment modalities.

DISCUSSION

Atrophic acne scars are one of the cosmetic concerns in dermatologic practice. Most patients prefer combined treatments of minimally invasive techniques as they have a high response rate with minimal downtime and side effects ⁽⁴⁾. The combined use of micro-needling with PRP offers an additive or even a synergistic positive effect on improving acne scars ⁽¹³⁾. PRP can be applied either topically or injected intradermally after micro-needling. Microneedles open narrow channels through the skin, increasing the delivery of topical PRP and inducing collagen synthesis by a dual mechanism. This combination is safe for all skin phototypes, cost-effective and with minimal downtime ⁽¹⁴⁾. Lyophilized PRP is another method of PRP that have many advantages over fresh preparations. It has simpler steps as it doesn't require centrifugation, and each vial has a constant concentration of growth factors, therefore overcoming the variation in platelet counts between patients. Additionally, it has a longer shelf life (12 months) ⁽⁹⁾.

No studies have investigated combined micro-needling with L-PRP in the treatment of atrophic post-acne scars. However, there is a split-face study that compared the combined application of L-PRP versus saline after fractional carbon dioxide (CO₂) laser. The patients received 4 sessions, and the post-treatment

assessment was done one month after the last session using subjective questionnaires and Visia analysis. This study showed a significant improvement on the side treated with L-PRP, with improvement in the pore size and skin texture and with more rapid healing ⁽¹⁵⁾. Additionally, **Neinaa et al.** ⁽¹⁶⁾ showed, in a split-face study, superior results of L-PRP versus conventional PRP when topically applied after fractional CO₂ laser. The patients received 3 treatment sessions, and the assessment was done by dermoscopy, Goodman's and Baron scale, and Echella d'Évaluation Clinique des Cicatrices d'Acné (ECCA) scale.

Out of the statistical results of the current study, a significant increase in the mean percentage of improvement of the indentation index was found in the side treated by dermapen only. This is in agreement with **Sitohang et al.** ⁽¹⁷⁾, who performed a systematic review of randomized controlled trials on the use of micro-needling for treating post-acne scars. These clinical trials showed consistently positive results. Micro-needling was found to be a relatively safe and effective treatment for acne atrophic scars, either used as monotherapy or in combination. Micro-needling resulted in persistent clinical improvement in which the skin got thicker, with significantly greater collagen deposition and significantly higher elastin concentration ⁽¹⁸⁾. It can also seve the old collagen fibers of the scars in the superficial dermal layers ⁽¹⁹⁾.

In the current study, there was a highly statistically significant increase in the mean percentage of improvement of the indentation index on the side treated by dermapen combined with L-GF[®] versus dermapen monotherapy. This improvement could be explained by the fact that L-PRP contains a defined amount of growth factors (e.g., EGF, VEGF, TGF-β, FGF, and PDGF) that can augment the positive effect of micro-needling on collagen remodeling and causes more acceleration of wound healing ⁽²⁰⁾. A meta-analysis was performed on 10 non-randomized and 4

randomized controlled split-face studies on atrophic acne scars comparing combined micro-needling and conventional PRP treatment with micro-needling only. There was a greater improvement with the combined treatment with more patient satisfaction and without an increase in the side effects ⁽⁷⁾. Another meta-analysis and a systemic review showed that combined micro-needling or subcision with either topical or intradermal conventional PRP showed a significantly better response than micro-needling or subcision monotherapy with validated results. Intradermal PRP is superior to topical PRP when combined with micro-needling or subcision in severe acne lesions. Adding PRP may decrease erythema duration associated with micro-needling ⁽¹⁴⁾.

Most of the studies used different treatment protocols. **Asif et al.** ⁽¹³⁾ conducted a split-face non-randomized trial to compare the efficacy of dermaroller combined with topical and intradermal injection of conventional PRP versus dermaroller with intradermal distilled water. The patients received one session per month for 3 months. The evaluation was done by Goodman's scale one month after the last treatment. They found that the side treated with dermaroller and PRP showed a significant improvement over the other side treated with dermaroller and distilled water. Another study was done on 35 patients with atrophic post-acne scars using combined micro-needling and conventional PRP. Patients received 6 sessions at 2 weeks intervals. Evaluation was done pretreatment and 6 months after the last treatment by Goodman and Baron method. There was an improvement in all acne grades. There was a reduction in the severity (grading of acne). Also, patients were satisfied with the results ⁽²¹⁾. Additionally, **Shafik et al.** ⁽²²⁾ used micro-needling with PRP gel to treat acne scars in 4 treatment sessions. The study yielded favorable results with a downgrading of different acne grades one month after treatment using Goodman and Baron scaling system.

On the other hand, few studies showed an insignificant difference between combined micro-needling and PRP versus micro-needling monotherapy. In a split-face trial comparing both treatment modalities, both the side treated with skin needling alone and the side treated with skin needling with PRP experienced a significant improvement in atrophic acne scars. However, no significant difference between both treatment modalities was found. In their study, the patients received a total of 4 treatment sessions (1 session every 3 weeks), and evaluation was done 3 months after the last treatment by Goodman's and Baron scale ⁽²³⁾.

In the present study, minimal side effects were encountered with either monotherapy or combined treatment. Mild erythema, oedema, and pain lasted a few hours after the session, and minimal bruising lasted for a few days. This is in agreement with the previous

studies ^(7, 14). Both treatment modalities are considered safe with short downtimes.

CONCLUSION

There is now cumulative evidence that combined micro-needling with PRP showed a better response rate, short downtime, and more patient satisfaction. However, there is a great discrepancy in the treatment protocols. This suggests the use of standardized regimens as L-PRP and necessitates larger-scale studies with long-term follow-up to validate the results.

Financial support and sponsorship: Nil.

Conflict of interest: Nil.

Acknowledgement: Special thanks to Professor Hossam Mostafa Fahmy, professor of clinical pathology, at Ain Shams University, for his efforts in preparing L-GF®.

REFERENCES

1. **Ghods S, Orawa H, Zouboulis C (2009):** Prevalence, severity, and severity risk factors of acne in high school pupils: a community-based study. *The Journal of Investigative Dermatology*, 129 (9): 2136–2141.
2. **Jacob C, Dover J, Kaminer M (2001):** Acne scarring: a classification system and review of treatment options. *Journal of the American Academy of Dermatology*, 45 (1): 109–117.
3. **Taylor M, Koron N (2021):** Combined Treatment of Rolling Acne Scars in Ethnic Skin Using Extensive Subcision, Trichloroacetic Acid Peel, and Fractional Ablative Erbium Laser. *Dermatologic Surgery*, 47 (4): 496–499.
4. **Garg S, Baveja S (2014):** Combination therapy in the management of atrophic acne scars. *Journal of Cutaneous and Aesthetic Surgery*, 7 (1): 18–23.
5. **Fernandes D (2005):** Minimally invasive percutaneous collagen induction. *Oral and maxillofacial surgery clinics of North America*, 17 (1): 51. <https://doi.org/10.1016/j.coms.2004.09.004>
6. **Juhasz M, Cohen J (2020):** Microneedling for the Treatment of Scars: An Update for Clinicians. *Clinical, Cosmetic and Investigational Dermatology*, 13: 997–1003.
7. **Kang C, Lu D (2022):** Combined Effect of Microneedling and Platelet-Rich Plasma for the Treatment of Acne Scars: A Meta-Analysis. *Frontiers in Medicine*, 8: 788754. <https://doi.org/10.3389/fmed.2021.788754>
8. **Kakudo N, Minakata T, Mitsui T et al. (2008):** Proliferation-promoting effect of platelet-rich plasma on human adipose-derived stem cells and human dermal fibroblasts. *Plastic and Reconstructive Surgery*, 122 (5): 1352–1360.
9. **Kieb M, Sander F, Prinz C et al. (2017):** Platelet-Rich Plasma Powder: A New Preparation Method for the Standardization of Growth Factor Concentrations. *The American Journal of Sports Medicine*, 45 (4): 954–960.
10. **Tanizaki H, Tanioka M, Yamashita Y et al. (2020):** Quantitative evaluation of atrophic acne scars using 3D image analysis with reflected LED light. *Skin Research and Technology*, 26 (1): 20–24.

11. **Dohan Ehrenfest D, Andia I, Zumstein M *et al.* (2014):** Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. *Muscles, Ligaments and Tendons Journal*, 4 (1): 3–9.
12. **Bausset O, Giraudo L, Veran J *et al.* (2012):** Formulation and storage of platelet-rich plasma homemade product. *BioResearch Open Access*, 1 (3): 115–123.
13. **Asif M, Kanodia S, Singh K (2016):** Combined autologous platelet-rich plasma with microneedling versus microneedling with distilled water in the treatment of atrophic acne scars: a concurrent split-face study. *Journal of Cosmetic Dermatology*, 15 (4): 434–443.
14. **Long T, Gupta A, Ma S *et al.* (2020):** Platelet-rich plasma in noninvasive procedures for atrophic acne scars: A systematic review and meta-analysis. *Journal of Cosmetic Dermatology*, 19 (4): 836–844.
15. **Huang C, Thong H (2021):** Rapid wound healing and acne scar improvement after ablative fractional carbon dioxide laser treatment combined with the application of Platelet-Lyophilized Treatment (PLT). *Clinical, Cosmetic and Investigational Dermatology*, 14: 715–721.
16. **Neinaa Y, Al-Khayat L, Suliman G *et al.* (2020):** Fractional carbon dioxide laser-assisted delivery of lyophilized-growth factors is a promising treatment modality of post-acne scars. *Dermatologic Therapy*, 33(6): e14488. <https://doi.org/10.1111/dth.14488>
17. **Sitohang I, Sirait S, Suryanegara J (2021):** Microneedling in the treatment of atrophic scars: A systematic review of randomised controlled trials. *International Wound Journal*, 18 (5): 577–585.
18. **Fabbrocini G, Fardella N, Monfrecola A (2009):** Acne scars classification and treatment. *Clin Exp Dermatol.*, 34 (8): 874-9.
19. **Leheta T, Abdel Hay R, El Garem Y (2014):** Deep peeling using phenol versus percutaneous collagen induction combined with trichloroacetic acid 20% in atrophic post-acne scars; a randomized controlled trial. *The Journal of Dermatological Treatment*, 25 (2): 130–136.
20. **Arshdeep A, Kumaran M (2014):** Platelet-rich plasma in dermatology: boon or a bane?. *Indian Journal of Dermatology, Venereology and Leprology*, 80 (1): 5–14.
21. **Yaseen U, Shah S, Bashir A (2017):** Combination of platelet rich plasma and microneedling in the management of atrophic acne scars. *International Journal of Research in Dermatology*, 3 (3): 346-350.
22. **Shafik E, Nassar A, Tawoos A *et al.* (2021):** Treatment of Atrophic Acne Scars with Platelet Rich Plasma Gel and Micro-needling. *The Egyptian Journal of Hospital Medicine*, 85 (2): 4323-4327.
23. **Ibrahim M, Ibrahim S, Salem A (2018):** Skin microneedling plus platelet-rich plasma versus skin microneedling alone in the treatment of atrophic post acne scars: a split face comparative study. *The Journal of Dermatological Treatment*, 29 (3): 281–286.