Original Article

A Split-Face Comparison Study between the Effects of Microneedling Combined with Topical Application of Autologous Platelet-Rich Plasma and the Effect of Microneedling Alone in the Treatment of Atrophic Post Acne Scars

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Abstract

Background: A permanent cosmetic disfigurement is produced due to acne scarring, which is linked to great psychological distress and low self-esteem. It is a significant cosmetic problem that poses a chief challenge to dermatologists. Skin micro puncturing technique called microneedling (MN) involves the body's self-healing mechanism to rejuvenate scars. It is believed that the different growth factors of platelet rich plasma (PRP) can stimulate wound healing and collagen regeneration. Therefore, we decided to conduct split face study to compare the efficacy of MN with PRP and MN alone. **Material and Methods:** This study was a split face comparative study of 30 patients with moderate to severe atrophic post-acne scars. The right half of the face was treated with MN plus topical PRP, and the left half was treated with MN alone. The treatments were given four times at monthly intervals. Final evaluation done six months from last session (9th month of treatment) by Goodman and Baron quantitative and qualitative acne scar grading scales. Photographic assessment of overall scar improvement was carried out by a blind observer, and patient self-assessment scores were recorded. The patients were followed on day 3and day 7 after the procedure and adverse effects were noted. **Results:** Noteworthy improvement in scar quality of both sides was detected. The qualitative grades for Goodman and Baron were both greatly lowered on each side separately and the difference between the two sides was not statistically significant at 9th month. Mean scores decreased significantly on both sides, in terms of quantitative scoring. At 9th month, there was a statistically significant scar improvement of 42.38% on the MN+PRP side ($P<0.0001$) and 38.08% on the MN side ($P<0.000$); however, there was no statistically significantly greater improvement on the MN+PRP side, as compared to the MN side ($P=0.532$), suggesting that MN+PRP is not superior to MN in scar reduction. There was a marked reduction in erythema and oedema on MN+PRP side than on MN side. **Conclusion:** Both of these modalities were successful and had similar outcomes. There was no improvement in scar improvement when PRP was combined with microneedling, while the downtime and discomfort were better with adding PRP.

Keywords: Acne, Scars, Microneedling, Platelet rich plasma.

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Introduction

Acne is an inflammatory disease of the pilosebaceous unit that occurs in most people. One of the most common problems with acne is the presence of acne scars which is the result of abnormal acne resolution. Acne scars can be broadly classified into atrophic and hypertrophic.[1] They affect both genders equally and occur to varying extents in up to 95% of acne sufferers. Atrophic Scars from acne can be ice-pick, rolling, or boxcar type and can cause serious psychological distress often accompanied by depression, anxiety and low self-esteem.[2] Acne scars can negatively impact quality of life, and in some severe and longstanding cases, patients have been reported to be severely depressed, with suicidal tendencies.[3,4]

Multiple treatment modalities have been used in the treatment of atrophic acne scars, such as subcision, punch techniques (punch excision and closure, punch grafting, punch elevation), resurfacing procedures (dermabrasion, ablative lasers, chemical peels), non-ablative lasers, microneedling radiofrequency (MNRF), as well as soft-tissue augmentation with dermal fillers or autologous fat transfer.[5] It is often necessary to use a combination of these treatments to address the various types of scars and achieve optimal results. One of the

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most popular modalities for percutaneous collagen induction is microneedling (MN).[6] It is a minimally invasive technique where tiny holes are made in the epidermis and dermis using microneedles. In dermatology, MN is used for scar improvement, striae, photoaging, wrinkles, periorbital hypermelanosis, melasma, and other skin imperfections, and it allows for a better transdermal delivery of topical agents through the micro channels created.[7,8]

Platelet-rich plasma (PRP) is the concentration of platelets in a small volume of plasma in an autologous manner. Platelets have several key growth factors in their α-granules, such as platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor-β1 (TGF-β1), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), and fibroblast growth factor (FGF). These growth factors are several times higher in concentration in PRP than in normal plasma and when released, they bind to transmembrane receptors on mesenchymal stem cells, fibroblasts, epidermal cells and endothelial cells.[9] The receptor mediated signaling cascade is believed to act on genes associated with cell proliferation, migration and differentiation, leading to tissue repair and extracellular matrix deposition.[10,11] Several studies have been performed on autologous PRP therapy, which yielded promising results in conditions like androgenetic alopecia, non-healing ulcers, skin rejuvenation and striae distensae.[12-15] Microneedling is an established technique for scar regeneration and PRP with its growth factor profile is believed to improve wound healing. PRP has been investigated in isolation and when combined with fractional CO_2 laser (FCL), or microneedling, and the results have been mixed. This split face study was thus conducted to assess the possible synergistic effect of topical application of PRP with MN and MN alone.

Materials and Methods

This was a split face, comparative, prospective study with 30 patients aged 18-40 years with moderate to severe atrophic post-acne scars. In each patient, he or she served as his/her own control. Patients with scars categorized as grade 2-4 (Goodman & Baron) and with identical grade on both sides of the face and only atrophic scars were included. Patients with active acne, facial infections (herpes, folliculitis and warts), bleeding or platelet disorders, collagen vascular disease, HIV infection, hepatitis B and other chronic diseases were excluded. Participants who had undergone facial surgery or laser therapy within the last 6 months, or who had been on oral isotretinoin within the last 6 months or who had unrealistic expectations were also excluded. Based on the mean improvement scores reported by Fabbrocini et al. (microneedling: 2.583 ± 0.900; microneedling with PRP: 3.5 ± 0.904), the minimum sample size was 21 per group at 90% power and 5% significance. [16] Considering the split-face design, 30 patients were included. Parallel group study design: 21 or more per group at 90% power, 2-sided 5% significance level. A split-face design was used to reduce interindividual variation and enhance statistical efficiency, and the number of patients was determined to be 30.

Prior to therapy, in each patient platelet count, total leukocyte count, bleeding time, clotting time, random blood glucose and liver function tests, HIV screening and hepatitis B surface antigen tests were performed. 17 mL of autologous venous blood was collected and PRP was prepared using a manual double spin technique, REMI-R8C centrifuge (Gonshor et al.).[17] The amount of PRP yielded in each treatment session was around 2-3 mL containing a platelet count of 8-12 lakh/mm³. Topical anaesthetic cream containing 2.5% lidocaine and 2.5% prilocaine was applied for 1 hour prior to microneedling. A derma roller containing 192 needles of 1.5-mm length was rolled six times in vertical, horizontal, and diagonal directions until uniform pinpoint bleeding appeared. The right half of the face received microneedling followed by topical PRP application in two stages, whereas the left half underwent microneedling alone.

Post-treatment, patients were counselled to use mupirocin ointment and sun screen with sun protection factor (SPF) ≥ 30. Treatment was four times at monthly interval. Post-procedural assessment was performed on day 3 and day 7 to record adverse effects, such as erythema, oedema, post-inflammatory hyperpigmentation, and acneiform eruption. Final evaluation was made at the ninth month, 6 months after the last treatment session. All the participants were offered full face microneedling with PRP after the completion of their study. The Goodman and Baron qualitative and quantitative acne-scar grading systems were used to gauge treatment response.[18,19] Independent assessment of standardized clinical photographs was done on a 0-10 improvement scale by a blinded dermatologist. A similar 0-10 self-assessment scale was used to document patient-reported improvement.

Categorical variable data were presented as frequencies and percentages, and the continuous variable data were presented as mean, standard deviation, and median. The Kolmogorov–Smirnov test was used to assess data normality. Independent t-test or Mann–Whitney U test was employed for between treatment comparisons and paired t-test or Wilcoxon signed-rank test was for within treatment comparisons, depending on data distribution. Chi-square and Fisher's exact tests were used for categorical variables. Statistically significant p values were set at < 0.05. Data was entered in the Microsoft Excel and analysed in SPSS 21.0. The study was approved by the institutional ethics committee and was not funded.

Results

30 out of 36 enrolled patients completed four treatment sessions.6 patients were lost to follow up due to migration to different places.

In our study age of patients varied from 18 – 37 years with average age of 23.23 + 4.85 years. Majority of patients were in the age group of 18-24 yrs (73.33%) followed by 25-30 years (20 %). There were 17 males (56.67%) & 13 female (43.33%) patients. Duration of scars in majority of patients was ≤2years (56.66%), followed by 2-4years (30%) and >4years (13.33%). The mean duration of the acne scars was 2.96years. The majority of patient's skin is Fitzpatrick's skin photo type 5 (53.33%), type 4 (30%) and type 3 (16.66%). Family history of acne scars seen in 17 (56.67%) patients. [Table 1]

Table 1: Characteristics of the study population.

Characteristics	Number	Percentage (%)
Age (years)		
18-24	22	73.33
25-30	6	20
>30	2	6.67
Gender		
Male	17	56.67
Female	13	43.33
Duration of Acne scars		
< 2 years	17	56.66
2-4 years	9	30
>4 years	4	13.33
Family history of acne scars		
Positive	17	56.67
Negative	13	43.33
Fitzpatrick skin phototypes		
III	5	16.66
IV	9	30
V	16	53.33

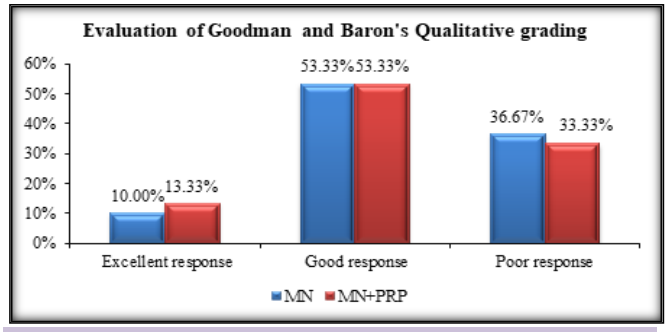

Figure 1: Goodman and Baron's Qualitative acne scar grading scores

Both the sides at baseline had 4 patients (13.33%) in grade 2, 8 patients (26.66%) in grade 3, and 18 patients (60%) in grade 4 on evaluation using Goodman & Baron qualitative scale. Both sides had a mean baseline score of 3.47 ± 0.73. By the 9th month, mean scores had reduced to 2.67 ± 0.92 on the MN+PRP side ($p < 0.0001$) and 2.73 ± 0.83 on the MN side ($p < 0.0001$). On MN+PRP side Improvement of two grades (excellent response) was observed in 4 (13.33%) patients, one grade (good response) in 16 (53.33%) patients and none (poor response) in 10 (33.33%) patients. Excellent, good and poor responses were seen in 3 (10%), 16 (53.33%) and 11 (36.67%) patients, respectively on MN side. In both treatments, there was significant scar improvement to lower grades of severity. The clinical response difference between the two sides was not statistically significant, however (MN vs. MN+PRP, $p = 0.909$) (Fig. 1).

When tested on the Goodman and Baron quantitative scale, the mean score on the MN+PRP side at baseline was 12.67 ± 3.6 and was lowered to 7.27 ± 2.92 at 9th month ($p < 0.0001$). Similarly, on the MN side, the mean score reduced from 12.53 ± 3.6 at baseline to 7.73 ± 2.9 at the 9th month (baseline vs. 9th month, $p < 0.0001$). At baseline there were no significant differences between the mean quantitative scores on both sides. At 9th month, there was a significant decrease of scores in both groups, MN+PRP group 42.38% and MN group 38.08%. But no statistically significant difference between the two sides was observed ($p = 0.537$) suggesting that PRP does not provide any further improvement as compared to MN alone [Figure 2].

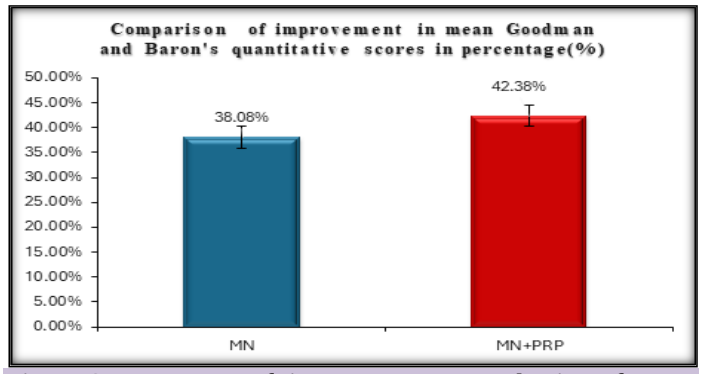

Figure 2: Percentage of improvement on evaluation of mean Goodman and Baron's quantitative scores

The MN+PRP side had excellent, good, fair and poor response in 3 patients, 8 patients, 13 patients and 6 patients respectively on the evaluation of blinded dermatologist scores. The MN side showed similar responses in 2 patients (6.66%), 9 patients (30%), 11 patients (36.66%), and 8 patients (26.66%), respectively. The mean score of scar improvement at the 9th month was 5.17 ± 1.72 on the MN+PRP side and 4.93 ± 1.66 on the MN side. The results reflect a great improvement on both sides on their own. But this difference was not statistically significant at the 9th month (p value MN vs MN+PRP is 0.595) [Figure 3].

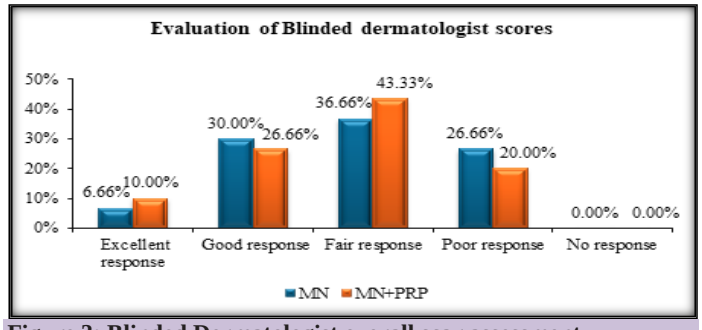

Figure 3: Blinded Dermatologist overall scar assessment

The MN+PRP side had excellent, good, fair and poor responses in 2 patients (6.66%), 11 patients (36.66%), 12 patients (40%) and 5 patients (16.66%) respectively. The MN side showed similar responses in 1 patient (3.33%), 10 patients (33.33%), 13 patients (43.33%), and 6 patients (20%), respectively. At the 9th month, the mean self-assessment scores on the MN+PRP side were 5.13 ± 1.7, and 4.9 ± 1.6 on the MN side. These results showed a significant improvement in both sides alone, but did not show a significant difference between the two sides at the 9th month (MN vs. MN+PRP, p = 0.586) [Figure 4].

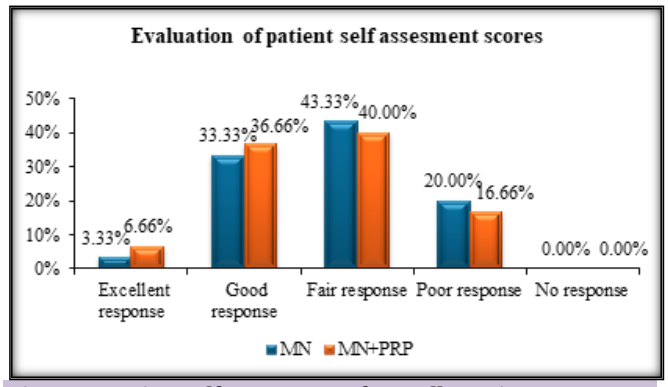

Figure 4: Patient self-assessment of overall scar improvement

Side effects noted in our study were erythema, edema, post-inflammatory hyperpigmentation (PIH), and acneiform eruptions, which were all transient. The mean duration of erythema was 4.2 ± 1.35 days (range: 2–8 days) on the MN+PRP side and 5.4 ± 1.67 days (range: 2–10 days) on the MN side. A statistically significant difference was seen between the two sides (p = 0.002). The mean duration of edema was 2.63 ± 0.76 days (range: 1 to 5 days) on the MN+PRP side and 3.47 ± 1.07 days (range: 1 to 7 days) on the MN side, which was also statistically significant (p = 0.0001). So, erythema and edema abated considerably early on MN+PRP side than MN side.

PIH developed in 4(13.33%) patients on MN+PRP side as compared to 5 patients (16.67%) on MN side. No significant difference was found in the incidence between two sides (P=1.0). Acneiform eruptions were seen in 6 patients (20%) on MN side as compared to 5 patients (16.67%) on MN+PRP side. This incidence difference between two sides was not significant (p value= 0.739).

Discussion

One of the most popular modalities used for skin rejuvenation and scar remodeling is microneedling (MN).[20] Platelet-rich plasma (PRP) is a rich source of various growth factors and cytokines that stimulate angiogenesis, tissue remodeling, and wound healing processes.[11] Due to these properties, PRP has been employed in dermatology, which includes the treatment of acne scars.[12-15]

PRP has been investigated as a therapy alone and as an adjunctive treatment to traditional scar therapies. Nofal et al. found intradermal PRP injections alone to be effective in reducing acne scars.[21] However, majority of the studies have evaluated PRP in conjunction with other modalities like MN, FCL or Er:YAG laser (topically or intradermally) and the results have been inconsistent when it comes to the efficacy and any adverse effects. We chose to apply PRP topically in the present study rather than intradermal injection to reduce the pain and trauma involved in the procedure. In favour of this idea, Gawdat et al. studied topical and intradermal PRP after FCL and found no significant difference in its efficacy or downtime, while topical PRP also being significantly less painful.[22]

We included 30 patients ranging in age from 18 to 37 years with an average scar age of 2.96 years. 57% had positive family history of acne scars. Tan J. et al. found family history to be another large risk factor, with a 2-fold increased incidence of acne scars among family members.[23]

The mean score of baseline scars on either side was 3.47 ± 0.73 when compared using Goodman & Baron qualitative grading scale. At the 9th month, mean scores reduced to 2.67 ± 0.92 on the MN+PRP side and 2.73 ± 0.83 on the MN side (p < 0.0001 for each, baseline vs. 9th month). Excellent response was observed in 13.33% patients in MN+PRP arm and 10% in MN arm, and good response in 53.33% in each arm at end of follow-up. Poor responses have been reported for 33.33% and 36.67% of patients on the MN+PRP and MN sides, respectively. Scars were much better in both sides, but there were no statistical differences between the two sides (p = 0.909).

Similar trends were seen when quantitative grading was performed. At baseline, scores were comparable (MN+PRP: 12.67 ± 3.6; MN: 12.53 ± 3.6; p = 0.886). By the 9th month, scores were reduced significantly on both sides (MN+PRP: 7.27 ± 2.92, 42.38% reduction; MN: 7.73 ± 2.9, 38.08% reduction). But this difference between the two modalities was not statistically significant (p = 0.586), which means that there was no superiority of MN+PRP over MN alone.

Figure 5: Clinical Photographic Comparison of Atrophic Acne Scars at Baseline and Nine Months Following Microneedling with and Without Platelet-Rich Plasma.

These results are similar to those of Ibrahim MK et al. who investigated 35 patients that received four sessions of MN combined with topical PRP on one side and MN alone on the opposite side.[24] They found a significant improvement on both sides, and no difference between modalities. Also, in this study,

Kar et al. carried out a comparison of FCL vs FCL+PRP in 30 patients. Qualitative and quantitative scores were significantly better, and there was no difference in overall efficacy, but there was a significantly lower amount of redness, edema and pain on the PRP side.[25]

In contrast, a split face study of 50 patients by Asif et al. showed better results following intradermal PRP.[26] They had 62% improvement on the PRP side and 45.84% on the control side, better qualitative grading, blind observer scores, and patient satisfaction. Other research also showed good results on the use of PRP for acne scar reduction.[16,26-28]

In our study, scar improvement was significant with both the blind dermatologist assessment and the patient self-assessment and there was no statistically significant difference between the modalities. Remarkably, adverse effects (erythema and edema) cleared up significantly sooner on the MN+PRP side ($p = 0.002$, and $p = 0.0001$, respectively). This indicates that PRP can help in managing inflammation and speed up the healing of wounds, thus decreasing downtime. Similar reductions in downtime with PRP have been reported when combined with MN,[24,26] FCL,[25,27] and Er:YAG laser.[28] However, Faghihi G. et al. reported no added efficacy with PRP when combined with FCL, and in fact noted more severe side effects and prolonged downtime.[29]

In total, MN and MN+PRP are effective in improving atrophic acne scars; however, PRP does not provide a significant benefit in scar remodeling. One of its primary advantages seems to be its ability to speed up the resolution of any side effects of the procedure and downtime. Larger RCTs are required to further validate the efficacy and safety of PRP as a treatment for acne scars.

Conclusion

Microneedling alone and microneedling combined with topical platelet-rich plasma (PRP) produced significant improvement in atrophic acne scars over the 9-month follow-up period. However, the addition of topical PRP did not provide a statistically significant advantage over microneedling alone in terms of scar remodeling or overall clinical improvement. Nevertheless, the MN+PRP approach was associated with significantly shorter durations of erythema and edema, suggesting a potential benefit in reducing post-procedure downtime and facilitating recovery. Thus, while both approaches are effective for acne scar improvement, topical PRP may offer an additional advantage in accelerating post-treatment recovery rather than enhancing the ultimate degree of scar remodeling.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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