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Efficacy of Autologous Injectable Platelet Rich Fibrin in Facial Atrophic Acne Scars in Combination with Microneedling: A Randomized Clinical Trial

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Abstract

Introduction: Several modalities for treating acne scars exist. The combination of microneedling and injectable platelet-rich fibrin (i-PRF) is a synergistic approach.

Objective: The aim was to compare the efficacy of microneedling alone versus microneedling with iPRF in post acne atrophic scars.

Materials and Methods: This study was a hospital-based randomized clinical trial conducted at B P Koirala Institute Health Sciences, Dharan, Nepal. Twenty patients with postacne atrophic scars underwent four sessions of microneedling with-iPRF and microneedling alone, monthly. The Goodman and Baron quantitative score and Goodman and Baron qualitative scores were assessed at zero, four, eight, twelve, and sixteen weeks. The Facial Acne Scar Quality of Life questionnaire (FASQoL) was also evaluated.

Result: The Goodman and Baron quantitative score was reduced from 23 to 14 in microneedling + i-PRF group (p=0.005) and from 16 to 11.50 for microneedling only group (p=0.005)

The percentage reduction in the Goodman and Baron quantitative score after the 16th week was 39.13% for group A and 28.12 % for group B. There was a statistically significant difference in the net reduction of the Goodman and Baron quantitative score from the baseline to the 16th week between group A and group B (p=0.004).

Conclusion: Injectable platelet rich fibrin (i-PRF) in combination with microneedling was found effective in reducing lesion count, Goodman and Baron quantitative score, and qualitative grade.

Keywords: Atrophic scars; Platelet rich fibrin; Microneedling

Introduction

Acne is a common disorder experienced by up to 80% of people between 11 and 30 years of age and by up to 5% of older adults.1 Inflammatory acne lesions can result in permanent scars, the severity of which may depend on delays in treating acne patients. 2

The treatment options for atrophic acne scars can be broadly categorized into energy-based and non-energy-based. Commonly used energy-based technologies include ablative and non-ablative lasers, fractional radiofrequency, intense pulsed light, and plasma skin regeneration. Non-energy-based devices include platelet-rich plasma (PRP), subcision, microdermabrasion, microneedling, dermal fillers, and chemical peels. 3

i-PRF use has been published as a case series and a few clinical trials for the treatment of various oral and maxillofacial procedures, alopecia, and aesthetic skin rejuvenation with favorable outcomes and improved patients' satisfaction. [4–8] This study was done to provide information regarding the efficacy of i-PRF and

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compare it in combination with other popularly sought after methods of microneedling.

Material and methods

This study was a randomized control trial done over a period of one year (April 2022 to April 2023) on twenty patients to compare the efficacy of microneedling alone versus microneedling with i-PRF on post acne atrophic scars. Patients having active inflammatory acne lesions, under oral isotretinoin use within the last 6 months, undergoing ablative or non-ablative laser skin resurfacing within the preceding 12 months, history of keloid, autoimmune diseases or immunosuppressive drugs, diabetes mellitus/ medical illness, HIV-seropositive status, collagen vascular disease, pregnancy, lactation, and chronic and granulomatous infectious conditions like tuberculosis were excluded. Patients with platelet dysfunction syndrome, critical thrombocytopenia, hemodynamic instability, septicemia, and patients on anticoagulant therapy or aspirin were also excluded.

This study was approved by the institutional review committee of the B. P. Koirala Institute Of Health Sciences, Dharan, Nepal. Informed written consent was obtained from all the participants.

A detailed clinical history and examination findings were recorded in preset proforma. An examination of the facial scars was done in terms of their number, type and distribution. The grading of the acne scars was done according to Goodman and Baron Qualitative grading and quantitative score 9,10 Facial Acne Scar Quality of Life (FASQoL), 11 a self-reported questionnaire, was used as a patient reported outcome measure, which comprises ten questions with the given parameters.

		Extremely (4)	Very much (3)	Somewhat (2)	A little (1)	Not at all (0)
1	Feeling self conscious of acne scars on the face					
2	Feeling less attractive because of scars					
3	Annoyed by scars					
4	Worried that the scars will not go away					
5	Sad because of the scars					
6	Upset by negative comments from others					
7	Avoiding going out with friends/ family					
8	Bothered by having to hide scars on the face					
9	Impact of scars in personal relationships					
10	Impact of scars on participation at work/School					

Pretreatment photographs of the patient were taken at enrolment, before each treatment session, and 4 weeks after the last session in identical lighting conditions with the same digital camera (Canon PowerShot 730 HS).

The face was mapped into five zones [central forehead, lateral forehead, and temporal area, chin, and cheeks] and further divided into 10 grids (Figure 4). 0.1 ml (4 U) of the distilled water, or i-PRF was administered in each grid. A 40 U insulin syringe with a 27G needle was used for the injection purpose. The treatment was provided by the same dermatologists (specialists in dermatology and aesthetic medicine) as follows:

Group A: Injectable PRF+ microneedling

These patients received intradermal injections of i-PRF in combination with microneedling.

Group B: Microneedling + distilled water

These patients received microneedling with intradermal distilled water.

Prior to microneedling, a thick application of topical anesthesia cream (eutectic mixture of prilocaine 2.5% w/w and lignocaine 2.5% w/w) was applied for 30-45 minutes. Dermarollers with 192 needles with a length of 1.5 mm were used for microneedling. The rolling was done 5 times each in the horizontal, vertical, and oblique directions with the other hand till uniform pinpoint bleeding points were seen all over the scarred area.

For the preparation of i-PRF, 10-40 ml of peripheral venous blood was collected from the antecubital vein,

kept in 5 ml sterile plastic centrifuge tubes without added anticoagulants, and centrifuged immediately at room temperature. The centrifuge used was a REMI R- 8C, and the centrifugation speed was 800 rpm, 60g RCF for 4 minutes. The upper 0.5- 0.75 ml of the preparation tube was removed by an insulin syringe and injected within 5 minutes of extraction.

i-PRF injection was done after microneedling in the treatment A group. Whereas in the other group (Group B), intradermal distilled water injection was injected after performing the microneedling. The post procedure area was cleaned with normal saline, and ice packs were kept for 10 minutes to comfort patients. Patients were advised to use sunscreen >30 SPF regularly and to follow sun protective measures. The treatment was given for a total of 4 sessions, and assessment were done at every visit and 4 weeks after the final session.

An objective assessment was done using the Goodman and Baron qualitative and quantitative global scar grading system by an independent dermatologist. The Goodman qualitative scale is a 4-point objective assessment of patient photographs that incorporates three scar morphologies and areas of involvement. The Goodman quantitative postacne scarring grading system is a photographic assessment that results in a more detailed global severity score ranging from 0 to 84 points.

The improvement was rated as poor, good, and excellent depending upon the change in grade of the acne scars. An improvement of two grades was considered excellent; 1 grade was rated as good; and no improvement was labeled as a poor response. Facial acne scar quality of life (FASQoL)[11] self-reported questionnaires were administered to the patients as a patient reported outcome measure.

The presence or absence of adverse events like postprocedural erythema, edema, pain, pigmentation, etc. was assessed. The down time of the treatment was also recorded at each visit. Data was entered in Microsoft Excel 2019 (Microsoft Corporation, Redmond, Washington, USA), and statistical analysis was done using Statistical Package for the Social Sciences version 25 (Chicago, Inc.). For descriptive statistics, percentage, mean, S.D., and median, were calculated along with graphical and tabular presentation. For inferential statistics, Fischer's exact test, the Paired Wilcoxon signed rank test, and the Mann- Whitney U test were performed.

Results:

The clinical data of the study participants is illustrated in Table 1.

Table 1 : Baseline characteristics of Group A (i-PRF+ microneedling) and Group B (microneedling+ distilled water) patients

Variables	Group A (iPRF+MN)	Group B (MN+ distilled water)	P value
Age Mean Median	 24.50± 5.46 24.00	 23.60±4.19 23.00	0.676*
Sex (n, %) Female Male	 9 (90%) 1 (10%)	 8 (80%) 2 (20%)	1.000**
Onset of acne Mean±SD Median	 15.30±2.12 15.00	 14.90±1.60 15.00	0.907*
Duration of scars Mean±SD Median	 47.40±23.05 60.00	 46.40±27.40 42.00	0.909*
Family history (n, %) Yes No	 1 (10%) 9 (90%)	 3 (30%) 7 (70%)	0.582**
Fitzpatrick skin type (n,%) 3 4	 5 (50%) 5 (50%)	 3 (30%) 7 (70%)	0.650**
Icepick Mean±SD Median	 19.40±8.11 19.50	 19.70±15.80 13.50	0.596*
Rolling Mean±SD Median	 11.70±11.36 7.50	 8.70±7.43 6.00	0.622*
Boxcar Mean±SD Median	 18.40± 9.16 16.50	 19.80±11.063 16.50	0.970*

*Mann Whitney U test **Fischer's exact test

The baseline Goodman and Baron qualitative grading and quantitative score are illustrated in Table 2. The groups were comparable in terms of their lesion count, scores, and grading.

Table 2: Goodman and Baron Quantitative score and qualitative grade in both groups prior to treatment

	Group A (N=10) (i-PRF+ microneedling)	Group B (N=10) (microneedling+ distilled water)	P value
Goodman and Baron Quantitative Score			
Mean±SD Median	22.20±7.92 23.00	19.60±10.762 16	0.384 *
Goodman and Baron Qualitative Grade			
Grade 3	1 (10%)	2 (20%)	1.00#
Grade 4	9 (90%)	8 (80%)	

*Mann Whitney U test # Fischer's exact test

In both groups, there was a statistically significant decrease in the number of icepicks, boxcars, and rolling

scars in the 16th week, as shown in Table 3.

Table 3: Reduction in the lesion count at the end of the study

		Before treatment	16th week	P value
Icepick scars	**Group A** Mean±SD Median	 19.40±8.11 19.50	 15.10±6.29 17.00	0.005@
	Group B Mean±SD Median	 19.70±15.80 13.50	 17.60±14.67 12.00	0.026@
Rolling scars	**Group A** Mean±SD Median	 11.70±11.36 7.50	 8.80±9.57 5.00	0.011@
	Group B Mean±SD Median	 8.70±7.43 6.00	 5.80±4.51 4.50	0.011@
Boxcar scars	**Group A** Mean±SD Median	 18.40±9.16 16.50	 12.90±6.95 11.50	0.005@
	Group B Mean±SD Median	 19.20±11.06 16.50	 14.60±8.73 13.50	0.004@

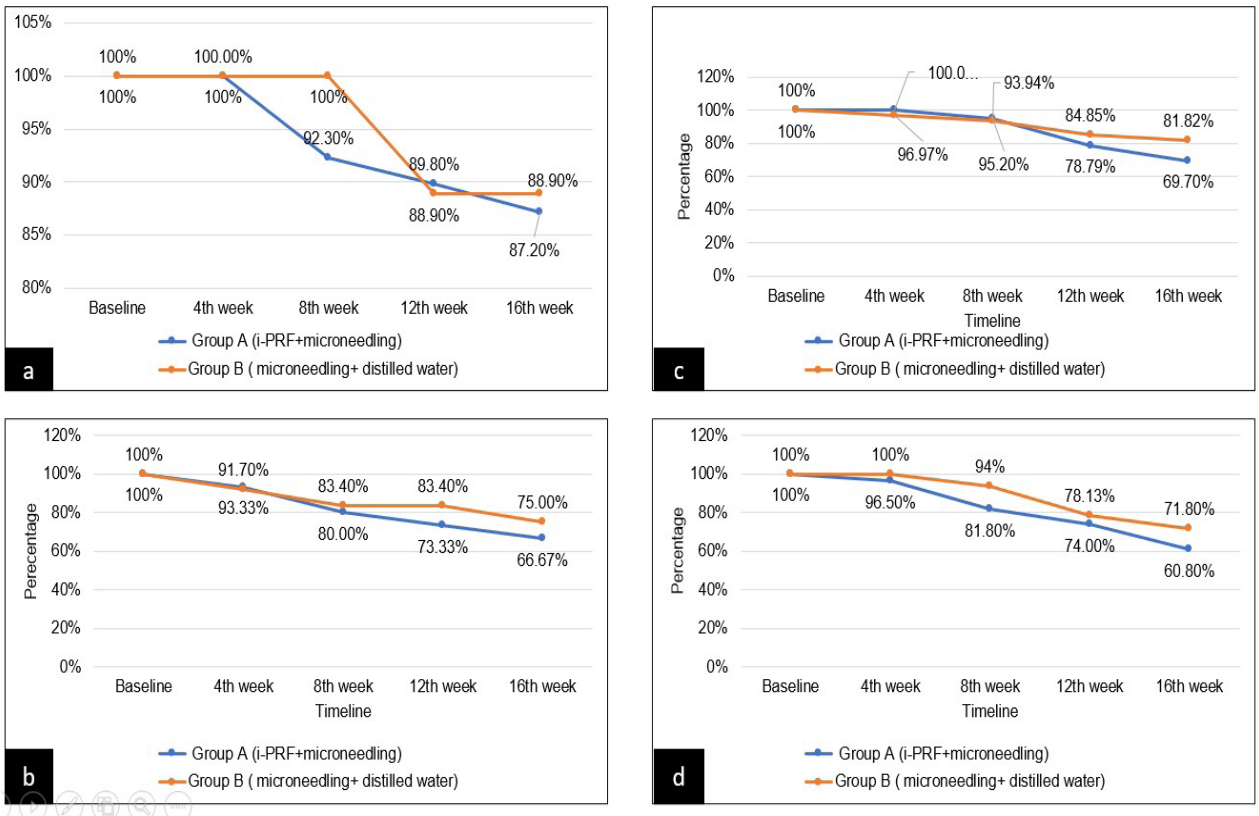


Figure 1: Percentage reduction in icepick scars (a), rolling scars (b) boxcar scars (c) and reduction in Goodman and Baron quantitative score (d)

Reduction in the Goodman and Baron Quantitative score and qualitative grade:

The decrease in the Goodman and Baron quantitative score was statistically significant for both groups (p = 0.005) as shown in Table 3 (Figures 5 and 6). The percentage reduction in the Goodman and Baron quantitative score for group A was 39.13%. Whereas, in group B, it was 28.12 %. The percentage reduction in scars has been shown in Figure 1.

Table 3: Reduction in Goodman and Baron Quantitative score at the end of assessment

Goodman and Baron quantitative score			
	Baseline	16th week	**P value**
Group A Mean±SD Median	22.20±7.92 23.00	14.70±6.03 14.00	0.005@
Group B Mean±SD Median	19.60±10.76 16.00	15.60±10.56 11.50	0.005@

The difference in numerical score between the pretreatment and 16th week was calculated for the patients in both groups, and was found to be statistically significant (p = 0.004) between group A and group B as shown in Table 4.

Table 4 : Comparison of net reductions in Goodman and Baron Quantitative score between both groups (baseline-16th week)

Net score	Group A	Group B	P value
Mean±SD Median	7.30±2.80 7.00	4.00±1.05 4.00	0.004*

*Mann Whitney U test

When comparing the Goodman and Baron qualitative grading, in Group A, 4 patients (40%) had excellent responses as compared to Group B where it was 2 patients (20%) as shown in Figure 2. However, there was no statistically significant difference in responses between the groups (p = 1.00)

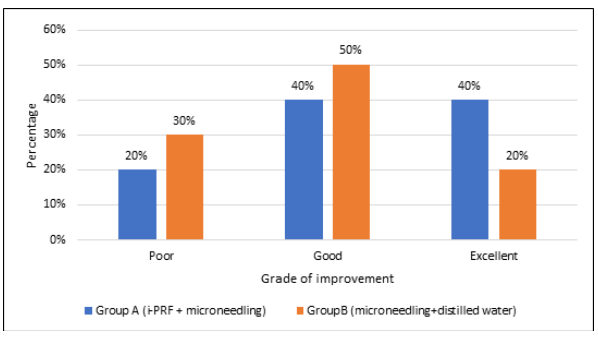


Figure 2 : Grade of improvement in group A and group B

Improvement in the FASQoL score after treatment.

For group A, the mean FASQoL[11] score was17.70±3.46 with a range of 11 to 22 (median 18). In group B, the mean FASQoL score was 13.50±3.92 with a range of 6 to 19 (median 13.00) as shown in Table 5. The difference between the baseline FASQOL scores between the two groups was statistically significant (p = 0.030). The reduction in the FasQoL score is illustrated in Table 5.

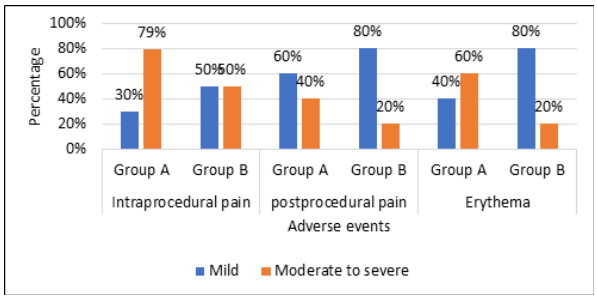
Table 5 : Comparison of FASQoL score at baseline and at 16th week (Group A and Group B)

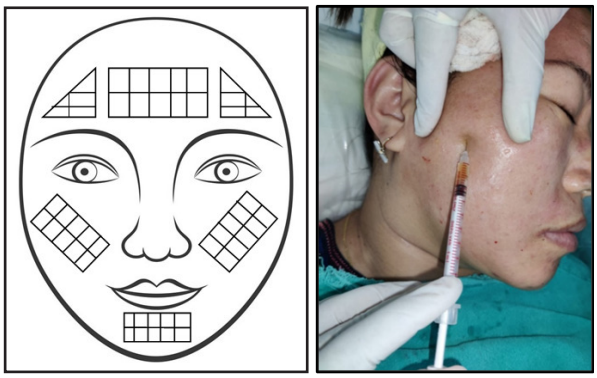
Group A			
Score	**Baseline score**	**16th week**	**P value**
Mean±SD Median	17.70± 3.46 18.00	12.20±3.29 12.50	0.004@
Group B			
Mean±SD Median	13.50±3.92 13.00	9.500±3.65 9.00	0.005@

@Wilcoxon signed rank test

Pain (intraprocedural and post procedural) was the most common adverse event, followed by erythema as shown in Figure 3. The occurrence and severity of the adverse events between the groups were statistically insignificant.

Fig 3: Adverse events between group A and group B





A B

Figure 4 : Division of face into zones and grids for injection (a). Intradermal injection of i-PRF (b)

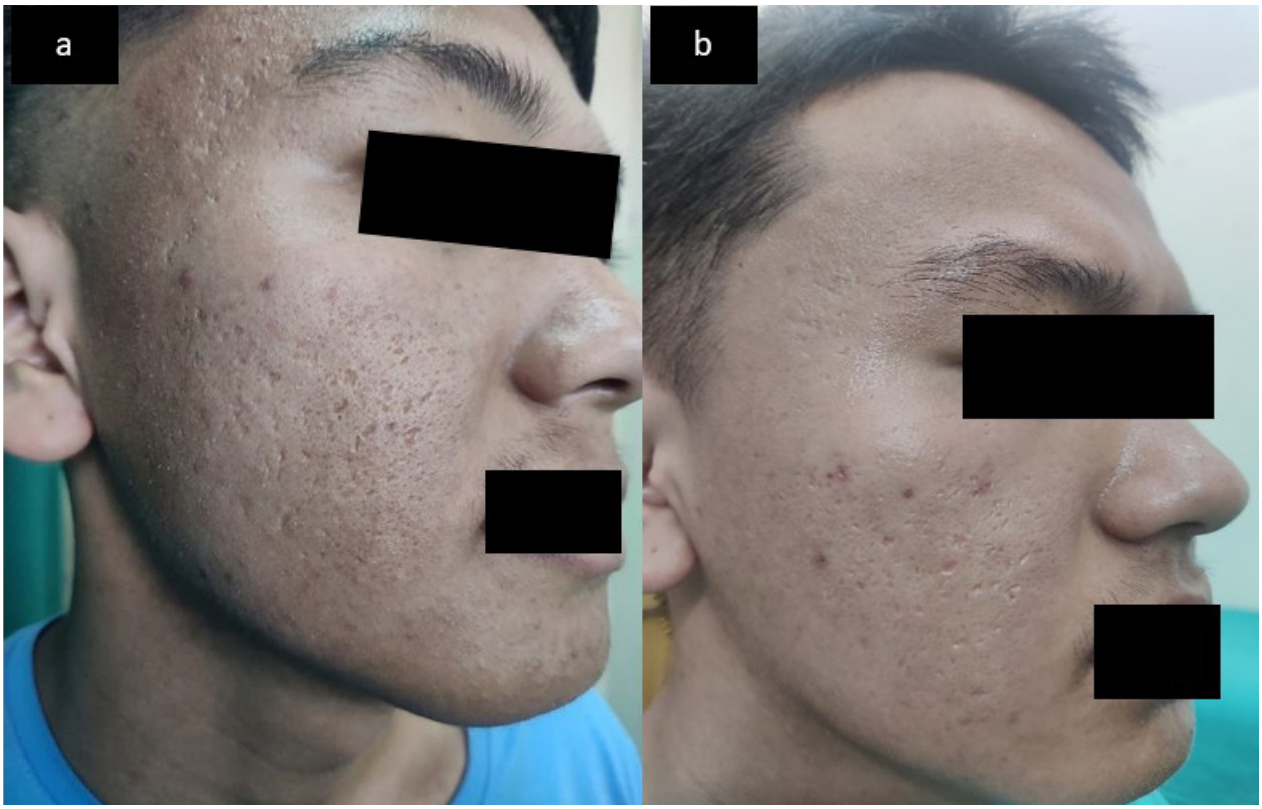


Figure 5: An 18 year old male with atrophic acne scars before treatment (a) and after fourth session of treatment with i-PRF with microneedling (b)

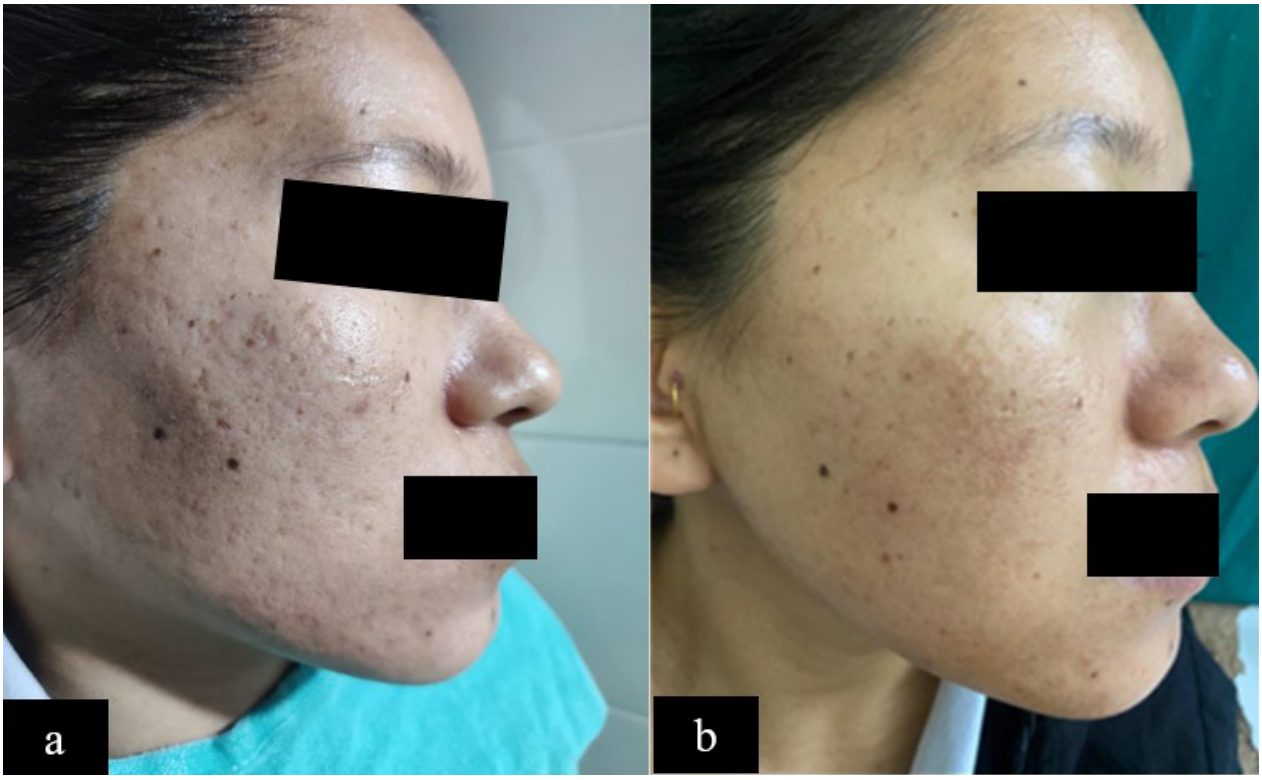


Figure 6: A 20 year old female with atrophic acne scars before treatment (a,) and after fourth session of treatment with microneedling and distilled water (b)

Discussion

Microneedling is a simple and cost-effective technique to treat acne scars where collagen synthesis is achieved by causing a minute injury to the dermis with the use of microneedles. [12] Microneedling creates micro-wounds to induce collagen production and dermal remodeling.13 Autologous platelet-rich plasma (PRP) is a plasma fraction that contains a higher concentration of platelets relative to whole blood. PRP contains a-granule, that secretes transforming growth factor-B, platelet derived growth factor, and vascular endothelial growth factor after activation. These growth factors, adhesion molecules, and chemokines interact with the local environment to promote cell differentiation, proliferation, and regeneration. [14]

The use of PRP associated with microneedling to treat acne scars has been largely studied and reported to have good results. A meta analysis in 2020, compared the effectiveness of PRP in combination with other procedures, combination procedures without PRP, and noninvasive monotherapy without PRP in the treatment of atrophic acne scars and concluded that the mean difference in percentage change in Goodman and Baron qualitative scores was more in combination therapy than monotherapy without PRP. [15]

To overcome the limitations of PRP, platelet-rich fibrin (PRF), a second-generation platelet concentrate, platelet rich fibrin (PRF), was developed in 2001. 16 It is obtained using one-step centrifugation without the use of an anticoagulant and is thereby totally autologous. The fibrin matrix is the main advantage of PRF over PRP. It acts as a 3-dimensional scaffold for the leukocytes and platelets and their release products. Miron et al,. observed that by further reducing the centrifugal force and the time duration of spin, a liquid PRF can be prepared. 17 The use of the i-PRF has been published as a case series and a few clinical trials for the treatment of various oral and maxillofacial procedures, alopecia, and aesthetic skin rejuvenation with favorable outcomes and improved patients' satisfaction.

This study was undertaken to evaluate the efficacy of i-PRF and microneedling in the treatment of postacne atrophic scars and compare them with microneedling alone.

The mean age of patients in Group A (i-PRF + microneedling) was 24.50±5.46 years and 23.60±4.19 years in Group B (microneedling + distilled water). In Group A and Group B, 70% and 80% of patients belonged to the 20-30 age group, respectively. A similar age group of 25.72 years was found in a study done by Asif et al,. 18 and a similar mean age of 26.01±3.6 years was found by Porwal et al., 19 85% of subjects were female and 15% were male. In both groups, females were predominant with a ratio of 9:1 in group A and 4:1 in group B, respectively.

85% of patients did not have a family history of abnormal scars. This finding is similar to a study by Porwal et al., 19 where 65.45% of participants lacked a family history of abnormal scars.

Atrophic scars can be further sub-classified into ice pick, rolling; and boxcar scars that result from dermal inflammation and overlying skin contraction. The ice pick type represents 60%–70%, of total scars, the boxcar 20%–30%, and rolling scars 15%–25% respectively. 20 In the current study, the most predominant scar type was the icepick type (40.26%), followed by the boxcar type (38.72%) and the rolling type (21%), respectively. In a study by Ibrahim et al. 2, 21 Icepick scar was the most common (37%), followed by the rolling type (29.6%) and the boxcar type (14.8%). In a hospital based, cross sectional survey by Agrawal et al., 22 icepick was the most common acne scar subtype (94%), followed by rolling (86%), and boxcar (54%).

The mean baseline FASQoL11 score in this study was was15.60 ± 4.20. In a multi country population-based survey by Tan et al., the mean FASQoL score was 11.54. 23 The most affected domain was emotional wellbeing. These findings are in agreement with the survey by Tan et al., where emotional wellbeing was the most impacted dimension. 23 Thus, in our study, there was a greater impact on quality of life among the participants.

In the assessment of Goodman and Barons qualitative grade, 9 85% patients had a grade 4 while 15% had a grade 3 scar. In a study by Ibrahim et al., 51.9% patients had grade 4 scar while 40.7% of patients had grade 3 scars. 21 Thus, in both studies, grade 4 was predominant.

In this study, the median Goodman and Baron quantitative score 10 decreased from 23.00 at baseline to 14.00 at the 16th week for group A. Meanwhile, in group B, it decreased from 16.00 to 11.5. In both groups, the reduction was statistically significant (p value = 0.005). The percentage reduction in score for group A was 39.13%, and for group B it was 28.12%. Whereas Porwal et al. found the reduction in Goodman and Baron quantitative scores10 to be 58.58% and 43.63% in PRP+microneedling and microneedling only groups. 19 The smaller number of participants in this study could have been the reason for these findings.

In this study, a reduction of 2 grades, was seen in 40% of patients in group A and 20% of patients in group B. Similarly, a reduction of 1 grade was seen in 40% of patients in group A and 50% of patients in group B respectively. Asif et al., found a reduction of 2 grades in 40% patients in intradermal PRP+microneedling group and 10% in the microneedling+ intradermal distilled water group respectively. 18

The median FASQoL score showed a reduction from 16.50 to 10.50 and was statistically significant (p = 0.001). There were no such studies that compared the FASQoL score reduction using microneedling and PRP/ i-PRF as a therapeutic modality.

Intra procedural pain was the most common adverse event, followed by erythema, both of which were more common in group A. Ibrahim et al., however, found severe pain in 64.3% of patients in the microneedling

only group versus 57.1% in the microneedling + intradermal PRP group. [17] Thus, in this study, more pain was seen in the combination of i-PRF and microneedling The percentage of severe erythema was seen in 42.9% of the microneedling + PRP group and in 21.4% in the microneedling only group respectively. Porwal et. al., reported erythema in 23.07% of patients in the intradermal PRP + microneedling group versus 15.38% of patients in the microneedling only group. [19] One of the strengths of the study is that it included both male and female participants, and it was a one-of-a-kind study that encompassed a newer therapeutic modality. However, this was a single center study with a small number of participants in each arm, and a longer follow up could not be carried out thus obscuring the long term efficacy. Thus, further multicentered, large sample size and studies with a longer follow up period are required to support the current study and eliminate potential biases.

Conclusion

Injectable platelet rich fibrin (i-PRF) in combination with microneedling was found to be more efficacious in terms of reduction of lesion count, Goodman and Baron quantitative score, and qualitative grade. Also, greater efficacy was seen in the reduction of the patient reported outcome measure; FASQoL as well as a greater reduction in the individual FASQoL parameters. Intraprocedural pain and erythema were the most common adverse events.

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