ABSTRACT

Background: A proposal has recently been made regarding the potential adjuvant use of platelet-rich plasma (PRP) with microneedling for the correction of acne scars. Aim and objective: To evaluate the efficacy and safety of autologous PRP combined with microneedling in the treatment of atrophic acne scars. Materials and methods: 30 patients were enrolled in the study. They were treated with intradermal autologous PRP followed by microneedling using 1.5mm diameter dermaroller and then topical application of PRP. Each patient underwent 4 sittings at an interval of 4 weeks. Photographic assessment was done at each visit and then after 3 months. Quantitative global acne scarring assessment tool based on the type and number of scars was used to assess the severity. The response to treatment was evaluated by objective and subjective methods. Results: On a four-point scale for quantitative assessment of clinical improvement of skin smoothness, out of 30 patients, 6 patients showed very good reduction, 14 patients showed moderate and 1 patient showed minimal reduction. Rolling and superficial box scars showed higher significant improvement when compared with ice pick and deep box scars (p=0.0006). Patient’s satisfaction of improvement was comparable with physician’s observations. No serious adverse effects were noted during the study. Conclusion: Autologous platelet rich plasma with microneedling is both effective and safe treatment for atrophic acne scars in Indian skin. What’s known? 1. Microneedling is an established treatment modality for the treatment of acne scars. 2. Platelet rich plasma (PRP) has recently gained utility in cosmetic dermatology including treatment of acne scars and facial rejuvenation.

INTRODUCTION

Acne scars is a common dermatological condition, occurring as a sequel of inflammatory acne.

Severe scarring is associated with substantial psychological and social distress, particularly in adolescents. Dark-skinned individuals are at higher risk for developing atrophic scars. 1 Many treatment options, such as topical retinoids, chemical peels, dermabrasion, scar revision, punch grafting, microneedling, fillers and lasers, have been used to improve acne scars, with variable results. 2 Platelet-rich plasma (PRP) is an autologous concentration of human platelets contained in a small volume of plasma. It contains various growth factors (GFs) that are secreted from the alpha granules of platelets. 3 These GFs play a pivotal role in modulation of tissue repair and regeneration. 4 Microneedling using dermaroller is a collagen induction technique used for the treatment of scars, especially acne scars. It is a simple and relatively cheap modality that can also be used for transdermal drug delivery. 5

MATERIALS AND METHODS

This prospective clinical trial was conducted with an aim of assessing the efficacy and safety of combining autologous PRP with microneedling in the treatment of atrophic acne scars and to estimate the improvement with respect to type, grade and duration of acne scars.

30 patients (18 females and 12 males) with mild to severe atrophic acne scars were enrolled in the study during a period of June 2013 to May 2014. Exclusion criteria were known photosensitivity, pregnancy, lactation, keloidal tendency, use of oral retinoids or other treatment modality for acne scars in last 6 months, any active infection, bleeding diathesis or anticoagulant medication and unrealistic expectations.

A written and signed informed explanatory consent was taken from all the patients before initiation of therapy. This clinical study was performed in accordance with the declaration of Helsinki after approval by the ethic committee of our hospital.

Patient’s demographic data (age, sex, Fitzpatrick skin type, duration and grading of scars, past medical and surgical treatment history) was recorded. Predominant scar type (Rolling, icepick, Superficial or deep boxcar) was noted in each patient before the initiation of treatment.

Procedure

1. Preparation of Platelet Rich Plasma Manual double spin method was used. 20 mL blood was drawn by venipuncture and collected into tubes containing acid-citrate-dextrose (ACD). It was centrifuged at 1500 rpm for 10 minutes. The supernatant fluid (plasma and Buffy coat) was aspirated and centrifuged at 2800 rpm for another 10 minutes. Through this method, 4 – 5 mL of platelet rich plasma was obtained. Estimation of platelet count was carried out in both serum and PRP and an approximate 10 fold rise in platelet count was noted (average platelet count in PRP varied from 10 – 15 lac).

2. Microneedling

Microneedling was done using 1.5 mm diameter, 192 needles dermaroller.

3. Treatment protocol

Local anesthetic cream (7% lidocaine + 7% tetracaine) was applied to the area to be treated under occlusion for 45 - 60 minutes before the procedure to minimize pain or discomfort. Then the whole face was cleansed using a mild cleanser and dried with sterile gauze. Autologous platelet rich plasma was injected intradermally using an insulin syringe into the scars. This was followed by microneedling using dermaroller. The endpoint for treatment session was the presence of uniform bleeding points over the scarred area. PRP was then applied topically to the treatment area. It was kept for 5 minutes and then the patient was asked to wash face gently with water.
Strict photoprotection and use of sunscreens was advised as a routine and topical antibiotic was applied for 3 days post-procedure.

Each patient underwent 4 sittings at an interval of 4 weeks and then was followed after 3 months.

**Qualitative assessment**

**Table 1: Goodman And Barron (gb) Qualitative Global Scarring Grading System**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Level of disease</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Macular</td>
<td>These scars can be erythematous, hyper- or hypopigmented flat marks. They do not represent a problem of contour like other scar grades but of color.</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by makeup or the normal shadow of shaved beard hair in men or normal body hair if extrafacial.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin. (if atrophic).</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial and is not able to be flattened by manual stretching of the skin.</td>
</tr>
</tbody>
</table>

Qualitative assessment was done using Goodman and Barron (GB) qualitative global scarring grading system which has four grades viz., macular, mild, moderate and severe [Table 1]. Pre and post treatment grading were noted and the reduction in scar grading was recorded. Grade 4 scars can show a reduction by 3, 2 or 1 grade. Similarly, Grade 3 scars can show a reduction by 2 or 1 grade. But, grade 2 scars can reduce by only 1 grade.

**Quantitative assessment**

**TABLE 2: Goodman and Baron’s quantitative acne scar grading system**

<table>
<thead>
<tr>
<th>Grade or type</th>
<th>Improvement Status</th>
<th>Number of lesions (1-10)</th>
<th>Number of lesions (11-20)</th>
<th>Number of lesions (&gt;20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milder scarring (1 point each) Macular erythematous pigmented Mildly atrophic dish-like</td>
<td>Improvement Status</td>
<td>1 point</td>
<td>2 points</td>
<td>3 point</td>
</tr>
<tr>
<td>Moderate scarring (2 points each) Moderately atrophic, dish like</td>
<td>Improvement Status</td>
<td>2 points</td>
<td>4 points</td>
<td>6 points</td>
</tr>
<tr>
<td>Punched out with shallow bases small scars (&lt;5 mm) Shallow but broad atrophic areas</td>
<td>Improvement Status</td>
<td>3 points</td>
<td>6 points</td>
<td>9 points</td>
</tr>
<tr>
<td>Punched out with deep but normal bases, small scars (&lt;5 mm) Punched out with deep but abnormal bases, small scars (&lt;5 mm) Linear or troughed dermal scarring Deep, broad atrophic areas</td>
<td>Improvement Status</td>
<td>2 points Area&lt;5 mm2</td>
<td>4 points Area 5-20 mm2</td>
<td>6 points Area &gt;20 mm2</td>
</tr>
<tr>
<td>Hyperplastic popular scars</td>
<td>Improvement Status</td>
<td>6 points</td>
<td>12 points</td>
<td>18 points</td>
</tr>
<tr>
<td>Keloidal/Hypertrophic scars</td>
<td>Improvement Status</td>
<td>2 points Area&lt;5 mm2</td>
<td>4 points Area 5-20 mm2</td>
<td>6 points Area &gt;20 mm2</td>
</tr>
</tbody>
</table>

The patients were asked to quantify their percentage of improvement at each visit. An improvement of ≥75%, 50 - 75%, 25 - 50% and 0 - 25% was graded as excellent, good, fair and poor improvement respectively.

**Subjective assessment**

Statistical analysis

The results were statistically analyzed using SPSS version 11.0 (SPSS, Inc., Chicago, IL, USA).

Differences were considered statistically significant when p < 0.05.

**RESULTS**

30 patients of acne scars with Fitzpatrick skin phenotypes III to V were included in the study. It comprised of 18 females (60%) and 12 males (40%). The mean age was 24.6 years (range 18 – 33 years).

Photographs were taken at each visit with identical patient positioning, lighting, and camera settings. Serial photographs were assessed by two unbiased, certified dermatologists.

**Assessment of efficacy**

The assessment of improvement was done qualitatively, quantitatively and subjectively.

The duration of scars ranged from 8 months to 15 years. Superficial box, deep box, rolling, ice pick scars were present predominately in ten, six, nine, and five cases, respectively. 4 patients had received treatment in the form of TCA CROSS (2 patients), subcision (1 patient) and fractional CO2 laser (1 patient) in past (1-3 years back).

Estimation of improvement with Goodman and Baron’s Global Qualitative Acne Scarring System was done. Majority of patients had grade 4 acne scars constituting 63.33% (19 patients) of the study population followed by grade 3 (10 patients, 33.33%), grade 2 (1 patient, 3.33%), and nil in grade 1.

**Qualitative score assessment**

**Figure 1: Clinical improvement assessment on the basis of GB qualitative acne scar grading**
The improvement based on GB Qualitative scar grading system is summarized in Figure 1. Out of 19 patients with Grade 4 scars, 3 patients (15.78%) showed improvement by 3 grades, i.e. their scars improved from Grade 4 to Grade 1 of Goodman and Baron Scale, 10 patients (52.63%) showed improvement by 2 grades [Figure 2 (a) and (b)] and 6 patients (31.57%) by 1 grade [Figure 3 (a) and (b)]. Out of 10 patients with Grade 3 scars, 4 patients (40%) improved by 2 grades and 6 patients (60%) showed improvement by 1 grade. 1 patient with grade 2 scar showed improvement by 1 grade [Figure 4 (a) and (b)].

Figure 2 (a): Grade 4 scars (b): Improvement in acne scars from Grade 4 to Grade 2 after treatment

Figure 3 (a): Grade 4 scars (b): Improvement in acne scars from Grade 4 to Grade 3 after treatment

Quantitative score assessment

Figure 5: Assessment of improvement in acne scars on the basis of GB quantitative acne scar grading

Estimation of improvement with Goodman and Baron’s Global quantitative Acne Scarring System showed that 6 patients (20%) had very good, 17 patients (56.67%) good, 6 patients (20%) moderate and 1 patient (3.33%) had minimal improvement [Figure 5].

Subjective assessment

Subjective assessment revealed that 7 patients (23.33%) had good, 15 patients (50%) moderate, 7 patients (23.33%) fair and 1 patient (3.33%) had no improvement.

Improvement according to type of scars

Rolling and superficial box showed significantly greater response when compared with icepick and deep box scars (p=.0006 and p=0.04 respectively).

Improvement according to duration and grade of scars There was no statistically significant variation of improvement with respect to duration as well as grade of acne scars.

The treatment was generally well tolerated. Side effects were minimal, that included pain, erythema and edema which subsided within 2 days post-treatment.

DISCUSSION

There has been a recent advancement in the use of platelet-rich plasma (PRP) in dermatology and aesthetic medicine, but the level of evidence from the available published data is low. PRP is a concentration of multiple growth factors (GFs), cytokines and chemokines. These GFs induces an internal signal-transduction pathway leading to cellular proliferation and collagen synthesis, thereby augmenting the natural wound-healing process. 8 Also, PRP induces synthesis of hyaluronic acid which promotes cell proliferation and extracellular matrix synthesis. 9 These pathomechanisms are helpful in atrophic scarring, which is a common sequela from loss of collagen and elastic fibers after inflammatory processes. 6

Microneedling is another modality in the treatment armamentarium of acne scars which stimulates the formation of new collagen, elastin and capillaries in the dermis. This neocollagenesis and neovascularisation leads to reduction of scars. 5 Dermal tethering which is the main obstacle in treating scars can be overcome by needling. 10 It also provides a clear channel for PRP to be absorbed more effectively through the top layer of the skin. Thus, Platelet-rich plasma by providing autologous growth factors acts synergistically with skin needling to enhance the wound-healing response. 11

Fabbrocini and colleagues 11 were the first to observe the potentiating effect of PRP on microneedling. PRP after laser resurfacing has also been found to enhance recovery of laser-damaged skin and improve the clinical appearance of acne scarring. 12-14 Further, Nofal et al 15 emphasized the effectiveness of intradermal PRP monotherapy in patients with severe acne scars.

He also reported significant improvement with combined microneedling and topical PRP.

As both topical and intradermal PRP individually have significant effect, we combined the two methods with microneedling to evaluate their effectiveness in the treatment of acne scars. While microneedling creates small pucture wounds in the epidermis and superficial dermis and creates a way for PRP absorption, intradermal PRP goes deeper in the dermis and enhances the wound healing response. In our study, majority of patients had severe acne scars (Grade 4) with the predominant type being rolling and superficial boxcar. Majority of our patients showed an improvement by 2 grades as per qualitative scoring and good reduction as per quantitative scoring. All type of scars showed improvement, with rolling and superficial boxcar scars responding better when compared with icepick and deep boxcar scars. Age of the patient, duration and pre treatment grading of scars had no significant effect on treatment outcome.

Therefore, even patients with severe acne scars of prolonged duration responded equally well with the treatment modality.

No major adverse effects were noted in any of our patients. Transient pain, erythema and edema were noted in all the patients, which subsided within 2-3 days. Bruising and post inflammatory hypo- or hyperpigmentation was not observed in any patient.
These observations are consistent with previous studies. 15,16 However, further split face study is required to ascertain the potentiating effect of PRP on microneedling.

**What's new?**

1. Microneedling creates small pucture wounds in the epidermis and superficial dermis and creates a way for PRP absorption, intradermal PRP goes deeper in the dermis and enhances the wound healing response.
2. Topical and intradermal PRP has adjuvant effect on microneedling
3. Autologous PRP with microneedling is both effective and safe treatment for atrophic acne scars especially rolling and superficial boxcar scars.

**REFERENCES:**