A Comparative Study to Assess the Efficacy of Fractional Carbon Dioxide Laser and Combination of Fractional Carbon Dioxide Laser with Topical Autologous Platelet-rich Plasma in Post-acne Atrophic Scars

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Abstract

Context: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit prevalent in adolescent population. Atrophic acne scarring negatively affects the quality of life. Although challenging to treat, the introduction of fractional carbon dioxide (CO₂) laser and platelet-rich plasma (PRP) therapy for atrophic scars has opened up new avenues. Aim: The aim of this study was to evaluate and compare the efficacy of fractional CO₂ laser alone and in combination with topical PRP in treating post-acne atrophic scars. Subjects and Methods: A hospital-based prospective, double-blinded, randomized, and comparative study was conducted. A total of 33 cases with post-acne atrophic scars of moderate to severe grade were randomly allotted into Group A and Group B who were treated for three monthly sessions of fractional CO₂ laser followed by topical PRP and fractional CO₂ laser monotherapy, respectively. Evaluation at baseline and every visit was carried out and compared at the end of 12 weeks. Results: Of the 33 patients, 25 completed the study. The mean change in score was higher in subjects of Group A. The mean scar score significantly reduced in both groups. The mean visual analog scale was higher in Group A. The reduction in scar score was significantly higher in patients with rolling scars and boxcar scars and least in ice pick scars. Erythema, edema, pain, and hyperpigmentation were higher in Group B. Conclusion: Combination therapy with PRP is more efficacious in reducing post-acne atrophic scars and reducing adverse effects of laser therapy as compared to fractional CO₂ laser monotherapy.

Keywords: Fractional carbon dioxide laser, platelet-rich plasma, post-acne atrophic scars

Introduction

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit. In a world where both women and men are conscious about their appearance, acne poses as a psychological and social burden of high gravity.[1] Inflammatory acne can produce permanent facial scarring by the healing of all forms of active acne,[2] which is an element of peril for low academic performance, unemployment, depression, and dysmorphophobia, leading to suicide. Broadly, acne scars are classified into atrophic and hypertrophic scars. Atrophic acne scars have been additionally categorized as ice pick, rolling, and shallow or deep boxcar scars.[3]

Although challenging to treat, various non-energy-based techniques and energy-based modalities can be used for improvement of acne scars.[3] However, the introduction of fractional carbon dioxide (CO₂) laser and platelet-rich plasma (PRP) therapy for atrophic scars has opened up new avenues for management of acne scars.
The fractional CO₂ laser thermally modifies a portion of the skin, leaving intervening zones of normal skin intact, which rapidly regenerates the ablated columns of tissue. In spite of being unparalleled in results, fractional CO₂ laser is followed by side effects such as erythema, edema, infections, and risk of developing hyper- or hypopigmentation making it unappealing for patients. Autologous PRP provides with a full array of potential bioactive growth factors and chemokines released on platelet activation, which aid in quick wound healing and actively reduce atrophic acne scarring making these two modalities synergistic in nature.

This study aimed to gauge and compare the effectiveness and safety of fractional CO₂ laser resurfacing and combination of fractional CO₂ laser resurfacing and topical PRP to provide the best possible treatment and relief to patients anguished by post-acne atrophic scars.

**SUBJECTS AND METHODS**

A total of 33 patients with post-acne atrophic scars of moderate to severe grade were included for a hospital-based prospective study from November 2017 to June 2019. Exclusion criteria comprised patients with active acne, patients with macular or mild atrophic acne scars, predisposition to keloidal or hypertrophic scarring tendency, and patients with active bacterial or viral infections. Detailed history with respect to the onset and duration of acne and scarring, any treatment for acne or acne scars received within past 6 months, and preexisting medical conditions were recorded.

Initial clinical examination of the patient was carried out to determine the grade and score of acne scars using Goodman and Baron qualitative grading and quantitative scoring chart and was recorded. Informed consent for the study was obtained from all the patients. Patients were randomly allotted into Group A and Group B, and were treated for three monthly sessions of fractional CO₂ laser followed by topical PRP and fractional CO₂ laser monotherapy, respectively. Baseline investigations and clinical photographs were taken. The end point of the study was three laser ablation sessions.

**Equipments**

1. eCO₂ laser: The fractional CO₂ laser (Lutronic, Goyang, Korea) system with a wavelength of 10,600 nm was used with treatment settings of a pulse energy of 50–100 mJ, and a spot density of 50–100 spots cm⁻² in the static mode; 1–2 passes were delivered using a 120-density tip with beam size of 120 μm and peak power of 30 W. The laser was irradiated to the entire area containing acne scars.

2. Method of PRP preparation: Two-stage centrifugation process (double-spin method) was used in the preparation of PRP. Whole blood samples (10mL) was drawn from the patient and transferred into a tube prefilled with citrate anticoagulant solution. The mixture was centrifuged at 1600 rpm for 7 min (first spin). After the first spin, the lower red blood cell portion was discarded and supernatant containing platelet-poor plasma and Buffy coat was centrifuged again at 4000 rpm for 5 min (second spin). The lower one-third of this solution provided approximately 2 mL of autologous PRP for topical application.

**Treatment procedure**

The face was cleaned with mild cleanser before the procedure. Topical anesthetic containing lidocaine 2.5% + prilocaine 2.5% was applied under occlusion and left for 1 h. The topical anesthetic was completely removed and affected areas were irradiated with fractional CO₂ laser using the same standard parameters in patients of both groups.

After the laser, patients in Group A received topical autologous PRP plasma application. All patients were instructed to apply topical mupirocin for 5 days, and regular use of sunscreen was advocated. They were instructed to avoid washing their face for 6 h after the procedure, direct sunlight, heat, or friction on the treated areas. Two more sessions were performed 4 weeks apart following similar protocol.

**Follow-up**

The patients in both groups were asked to follow-up for next laser session every 4 weeks up to 12 weeks. During each visit, the investigator recorded the findings related to treatment response such as reduction or improvement in acne scars (acne scar score), patient satisfaction, and general perception regarding the treatment. Clinical photographs were taken with identical settings and lighting at every follow-up before successive laser session. Any adverse effects related to therapy were recorded in the pro forma immediately after laser ablation (short term) and at each follow-up before successive session (long term). At the end of 12 weeks, the final response was evaluated according to the aforementioned procedure.

**Efficacy evaluation**

The following two primary efficacy parameters were assessed: (1) Objective assessment—Change from baseline acne scar score using Goodman and Baron quantitative scoring system at the end of 12 weeks. (2) Subjective assessment—Patient assessment of improvement of acne scars after the end of 12 weeks; patients in both the groups were asked to mark their improvement on a 10-inch long “visual analog scale (VAS).”

**Statistical analysis**

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 17,
Chicago, Illinois. Results were compared using independent $t$ test or Mann–Whitney $U$ test, paired $t$ test, repeated measures of analysis of variance (ANOVA), and one-way ANOVA. Categorical data were compared using chi-square test. For all tests, significant was achieved at $P < 0.05$.

**RESULTS**

Of the 33 patients enrolled in the study, 25 patients completed the study and 8 patients were lost to follow-up due to unknown reasons. Summary of patients characteristics are given in Table 1. The mean scar scores of patients in both groups are summarized in Table 2.

The mean change in score at the end of the study was higher in subjects of Group A (4.17) when compared to those in Group B (3.15), which was statistically insignificant [Table 3]. The mean scar score in Group A reduced significantly from 11.5 to 4, and in Group B, it reduced significantly from 12 to 3 ($P < 0.0001$) [Table 4]. The mean VAS for patient’s assessment of improvement was higher in subjects in Group A (4.08) when compared to those in Group B (3.46). However, this was not significant.

Clinical photographs taken at baseline and at the end of the study in patients of Group A are as seen in Figures 1 and 2.

Clinical photographs taken at baseline and at the end of the study in patients of Group B are as seen in Figures 3 and 4.

Immediate adverse effects were observed in 21 patients. Twenty patients developed erythema, eight patients developed edema, and one patient had pain after the procedure. Erythema, erythema with edema, and pain was more in the subjects of Group B even though there was no significant difference between two groups.

Long-term adverse effects were observed in 10 patients. Hyperpigmentation [Figure 5] was observed in three patients; pain, erythema, and acne [Figure 6] was observed in two patients each; and secondary infection was observed in one patient. Pain and hyperpigmentation was more in subjects in Group B even though no significant difference was observed between two groups.

The change in scar score irrespective of treatment was the highest in patients with rolling scars with a mean of 4.2, followed by boxcar scars with a mean of 3.89 and the lowest in ice pick scars with a mean of 2.33, which was highly statistically significant.

**DISCUSSION**

Our study enrolled 33 patients of post-acne atrophic scars, of which 25 patients completed the study. In our study,

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**Table 1: Patient characteristics (original)**

| Age          | 24.36 ± 4.37 years |
|--------------|--------------------|
| Gender       |                    |
| Males        | 21 (63.6%)         |
| Females      | 12 (36.4%)         |
| Mean duration of scars | 2.74 ± 1.57 years |
| Fitzpatrick skin type |          |
| III          | 3 (9.1%)           |
| IV           | 20 (60.6%)         |
| V            | 10 (30.3%)         |
| Type of scars |                  |
| Rolling      | 14 (42.4%)         |
| Ice pick     | 6 (18.2%)          |
| Boxcar       | 13 (39.4%)         |

**Table 2: Mean scar score at baseline (original)**

| Group | N | Mean ± SD  | $P$ value |
|-------|---|------------|-----------|
| A     | 17| 12.41 ± 3.792| 0.635     |
| B     | 16| 11.75 ± 4.139|           |

SD = standard deviation
Independent $t$ test was used for analysis. $P < 0.05$ is considered significant

**Table 3: Mean change in scar scores at the end of the study**

| Type of treatment | N     | Mean ± SD   | $P$ value |
|------------------|-------|-------------|-----------|
| Change in score  | Group A| 12 | 4.17 ± 1.528| 0.129     |
|                  | Group B| 13 | 3.15 ± 1.676|           |

SD = standard deviation
Independent $t$ test was used for analysis. $P < 0.05$ is considered significant

**Table 4: Baseline scar scores and change in the scar scores study**

| Groups | Baseline scar score | Scar scores at the end | $P$ value |
|--------|----------------------|------------------------|-----------|
|        | Mean ± SD | Mean ± SD |                  |
| A      | 11.08 (11.5) | 4.17 (4.0) | 1.53 | $P < 0.0001$ HS |
| B      | 12.08 (12)  | 3.15 (3.0) | 1.68 | $P < 0.0001$ HS |

HS = highly significant, SD = standard deviation
males were predominant. As acne is more severe in boys than that in girls, it may have probably resulted in severe acne scarring in males.[1]

Where type of acne scars of the patients was simplified as mixed type in a study conducted by Layton et al.,[8] the majority of our patients presented with rolling type of scars ($n = 14$) followed by boxcar ($n = 13$) and ice pick type ($n = 6$). The skin type distribution showed that the majority were type IV ($n = 20$), followed by type V ($n = 10$), and least were type III ($n = 03$), which form the predominant skin types found in south India.

In this study, a statistically significant improvement was observed in scar score in the patients treated with fractional CO$_2$ laser ablation followed by topical PRP, after each sitting, as well as in the patients treated with the fractional CO$_2$ laser alone. From this observation, we inferred that fractional CO$_2$ laser with or without PRP is an effective treatment modality for post-acne atrophic scars as confirmed by similar studies.[9-11]

On comparison of the mean scar scores improvement at each visit between the two groups, the mean change in scar scores was higher in the fractional CO$_2$ with PRP group patients compared to fractional CO$_2$ laser alone, showing an added reduction in the scar score by addition of topical PRP. In addition, there was a better mean VAS improvement of the patient after fractional CO$_2$ laser ablation followed by topical PRP ($4.08 \pm 1.44$) than that after CO$_2$ laser ablation alone ($3.46 \pm 1.05$). Subjective improvement in the post-acne atrophic scars was better where fractional CO$_2$ laser treatment was followed by topical PRP as corroborated by various studies.[12-14]
The immediate adverse effects reported in the patients were erythema (39.4%) followed by erythema and edema (21.2%) as well as pain as documented by similar studies. Erythema, erythema with edema, and pain were more in subjects treated with fractional CO$_2$ laser only, which denotes that immediate side effects (such as erythema, edema, and pain) reduce when fractional CO$_2$ laser treatment is followed by topical application of autologous PRP probably due to the regenerative properties of PRP.

Hyperpigmentation was observed in three patients, pain, erythema, and acne was observed in two patients each, and secondary infection was observed in one patient. Treatment with fractional CO$_2$ laser had to be discontinued for one patient as she developed acne after each laser sitting as observed at follow-up. This decision was taken in view of exacerbation of acne, which was observed as an adverse effect of fractional CO$_2$ laser. Pain and hyperpigmentation were observed lesser in patients treated with fractional CO$_2$ laser followed by topical PRP. As validated by numerous studies over the last 10 years, PRP following fractional CO$_2$ laser therapy leads to a considerable reduction in long-term adverse effects such as pain and post-laser hyperpigmentation, which are commonly observed in Fitzpatrick skin type III to V owing to its richness of growth factors responsible for reducing inflammation and hastening the wound-healing process.

Moreover, we used topical PRP instead of injecting PRP intradermally, which probably prevented additional inflammation due to injection, in turn reducing pain and post-laser hyperpigmentation.

Poorer response of ice pick scars as compared to rolling and boxcar scars was observed in our study, which was
similar to a study by Imran Majid.\textsuperscript{[20]} This is probably attributed to the depth of ice pick scars and the inability of thermal effect to reach their base for dermal stimulation.

Synergizing fractional laser therapy with PRP is recognized to dynamically reduce atrophic acne scarring as documented by many authors\textsuperscript{[21, 22]} Combination of fractional CO\textsubscript{2} laser with topical PRP had synergistic positive effects on the clinical outcome for acne scars and accelerated recovery. Faster reduction of routinely encountered adverse effects such as post-laser edema, erythema, and hyperpigmentation is observed with the use of both topical and intradermal PRP. Fractional CO\textsubscript{2} laser gives better response for rolling and boxcar scars as compared to ice pick scars.

Therefore, our study concludes that although fractional CO\textsubscript{2} is an effective modality for treating post-acne atrophic scars, combination therapy with PRP is more efficacious in reducing the appearance of scars, reducing adverse effects of laser therapy, and providing better patient satisfaction by the means of subjective improvement.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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