

Original Research Article

Laser for post acne scars with or without growth factors: a comparative clinical trial

Lakkireddygaru Sujana^{1*}, Balachandra S. Ankad², Savitha L. Beergouder²

¹Department of Dermatology, Venereology, and Leprology, Santosh Medical College and Hospital, NCR, Delhi, India

²Department of Dermatology, Venereology and leprosy, S Nijalingappa Medical College and Hospital, Navanagar, Bagalkot, Karnataka, India

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*Correspondence:

Dr. Lakkireddygaru Sujana,

E-mail: dr.sujana@gmail.com

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ABSTRACT

Background: Treatment of acne scars presents a considerable challenge to dermatologists. But with advent of fractional CO₂ (FCO₂) laser and platelet-rich plasma (PRP), new avenues can be explored. PRP provides various growth factors, so that the healing of laser-damaged skin is accelerated. The aim of this study was to assess the efficacy and safety of FCO₂ laser alone and in combination with PRP in patients with post-acne scars.

Methods: Eighty patients with acne scars were counseled and randomly assigned into two groups of 40 each. Group A was treated with FCO₂ laser alone, while Group B was treated with FCO₂ laser and PRP for 6 months. Primary objective was assessment of efficacy of both treatment modalities. Secondary objective was evaluation of safety of treatments.

Results: At the end of 6 months, group A showed about 18% reduction, while group B showed about 33% reduction in acne scars on objective assessment. Patient satisfaction as assessed by subjective assessment was greater in group B than in group A. Duration of erythema, edema and crusting was lesser in group B compared to group A.

Conclusions: Combination of FCO₂ and PRP was found to be more efficacious as compared to FCO₂ laser alone. Combining the treatment modalities can provide a new strategy for treating the post-acne scars.

Keywords: Fractional CO₂ laser, Post-acne scars, Platelet-rich plasma

INTRODUCTION

Acne vulgaris is a common chronic inflammatory condition of pilosebaceous unit affecting adolescents and young adults psychologically. Acne (especially inflammatory) results in scars which are often distressing and challenging to treat if left untreated.¹ This presents a considerable challenge to the dermatologist, because of the disfigurement it produces on the face, which is socially and psychologically the most significant body part. All types of acne can resolve with sequelae.¹ All acne lesions leave a transient macular erythema after resolution but in dark skin types, post inflammatory

hyperpigmentation persists months after resolution.^{2,3} In some, acne lesions result in scarring.

Acne scar prevalence is not well understood. A study reported acne scars in 11% in men and 14% in women.⁴ Cheeks being most common site for post-acne scarring was seen in 39.5% with icepick scars being most common.⁵ Scars can occur as a result of inflammation due to self-manipulation or due to aggressive procedural approach for management of acne.⁶ Acne scars are the result of damage in and around the pilosebaceous follicle during inflammation.⁷ Causes of acne scar formation can be broadly categorized as either the result of increased

tissue formation or due to loss or damage of local tissue.⁸ Clinical manifestations and severity of scarring of acne scars are related to the degree of inflammatory reaction, to tissue damage, and to time elapsed since the onset of tissue inflammation.^{9,10} Broad Classification of acne scars

is shown in (Table 1).¹¹ In addition to suffering from acne, the actual presence of acne scars is a risk factor for suicide and is linked to low self-esteem, depression, anger, anxiety, altered social interactions, decreased academic performance, and unemployment.^{8,12-14}

Table 1: Classification of acne scars.

Based on colour	Based on depth	
Hyperpigmented	Depressed	Elevated
Hypopigmented	Ice-pick scars	Hypertrophic scars
	Boxcar scars	Keloid
	Rolling scars	
	Atrophic scars	
	Follicular elastolysis	
	Stellate scars	
	Crateriform scars	

Prevention of acne scars by early effective treatment of acne is most effective approach.¹⁵ Goal of any intervention should be improvement of scars and not total cure.¹⁵ Management of scars is a staged process involving combination of different modalities with multiple sittings. Available treatment options include topical application of agents like benzoyl peroxide, retinoids, exfoliants; chemical peeling, dermabrasion, laser ablation etc. Dermatologists are encountered frequently with challenge of evaluating and proving treatment recommendations to patients with acne scars. Fractional CO₂ (FCO₂) laser and PRP are now available, and combination therapy with the two may provide synergistic effect, leading to better efficacy and faster skin recovery. Hence, the aim of this study is to compare the efficacy of FCO₂ laser alone and in combination with PRP therapy in treatment of acne scars and also to evaluate synergistic effect of combination modality.

METHODS

This was a prospective, single-centered, randomized study conducted from December 2017 to November 2018 and was aimed at comparing the efficacy of FCO₂ laser alone and in combination with PRP in treatment of post-acne scars. The study was approved by ethics committee before commencement. Eighty patients with post acne scars attending dermatology outpatient department of Hanagal Shree Kumareswar Hospital, Bagalkot were included in the study.

Patients aged 18 years or more, who had post-acne scars and were willing to provide informed consent, were included in this study. Patients with active acne, keloid formation, active herpes infection, HIV/HBV infection, platelet dysfunction, unrealistic expectations, pregnant women and lactating mothers, and those who had taken isotretinoin within 6 months before the start of the study were excluded from the study.

After screening against inclusion and exclusion criteria, the patients were divided into two groups. Group A was given FCO₂ laser alone, while group B was given FCO₂ laser along with PRP therapy. A total of 6 similar sittings were done in each group at intervals of 4 weeks. Digital photographs were taken before and 4 weeks after the procedure. Before the procedure, all the treatment areas were gently cleansed and a topical anesthetic cream, EMLA (lidocaine + prilocaine), was applied for 45 minutes and then washed off with sterile water, then covered with 1% betadine. Eye shields were used to cover eyes.

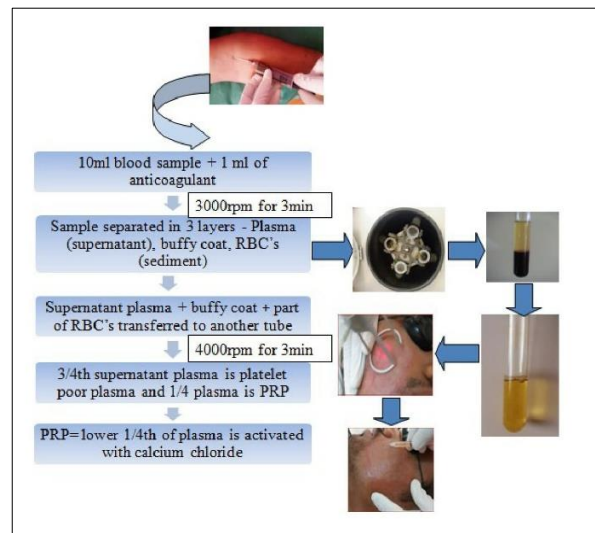


Figure 1: Method of preparation of platelet-rich plasma.

In group A, FCO₂ laser was delivered to post-acne scars in scan mode with 25-30 mJ of energy, density of 4-5 PPA and dot repeat of 3, in square shape and in sequential way. A single pass was used on scars. Pre-cooling and post-cooling was done with ice cubes to prevent post-procedural burning and pigmentation. After

the procedure, a thin layer of sunscreen was applied. Patients were advised to use sun protection measures and to avoid scrubs and soap for 1 week. For group B, similar procedure was followed for FCO₂ laser therapy as described for group A after which PRP pre-packed with growth factors was injected intradermally. Method of preparation of PRP is shown in (Figure 1).

Primary objective of the study was evaluation of efficacy of both the treatment modalities in post-acne scars with the help of Goodman’s global acne scarring scoring system and subjective assessment by patients. Secondary objective involved evaluation of safety of the treatment. Scores obtained by objective assessment with Goodman’s quantitative global acne scarring scoring system and patient’s subjective assessment at baseline and end of treatment (Table 2) were compared. Photographs were again taken at the end of the treatment period and compared with those taken at baseline. The individual lesion score was defined as score of the lesion for depth multiplied by its score for size. Total score for any particular case was calculated as the sum of individual scores of all the lesions in the patient. Improvement was calculated in percentage change in patient’s score during treatment period. Subjective assessment was done by patients themselves on a 5-point visual analog scale. Appropriate statistics were applied using OpenEpi software.

Table 2: Assessment of degree of objective and subjective improvement.

Grade	Points	Improvement
Nil	0	No improvement
Satisfactory	1	Up to 25% improvement in score
Good	2	26-50% improvement in score
Very good	3	51-75% improvement in score
Excellent	4	>75% improvement in score

RESULTS

A total of 80 patients with acne scars who fulfilled the criteria were randomized into two groups of 40 each. Baseline characteristics are given in (Table 3).

Table 3: Baseline characteristics of patients enrolled in the study.

	Group A (FCO ₂ laser alone)	Group B (FCO ₂ laser + PRP)
Mean age (years)	24.9±4.41	26.28±5.36
Gender	Male: 22 (55%) Female: 18 (45%)	Male: 20 (50%) Female: 20 (50%)
Mean duration of acne scars (years)	4.4±2.34	5.6±2.55

Figure 2 shows, patients treated with FCO₂ laser as well as PRP responded better to treatment than those treated with FCO₂ laser alone. More number of patients in combination group had good response, and one patient in this group showed excellent response. Along with overall objective score, there was greater reduction in mild, moderate and severe acne scars in group-B in comparison with group-A, as shown in (Figure 3). For subjective assessment, patients were asked to rate the efficacy of the treatment on a scale of 0 to 4, where 0 meant no improvement and 4 meant excellent improvement. As shown in (Figure 4), patients in group B rated the treatment better than those in group A.

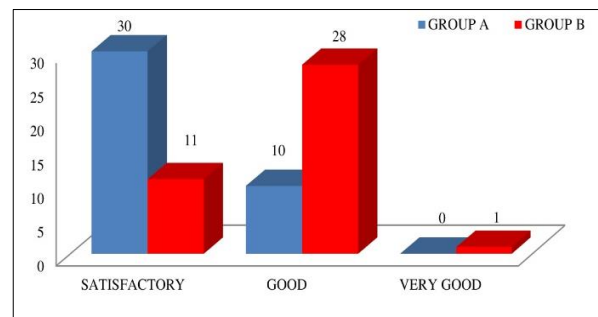


Figure 2: Comparison of objective assessment scores between treatment groups.

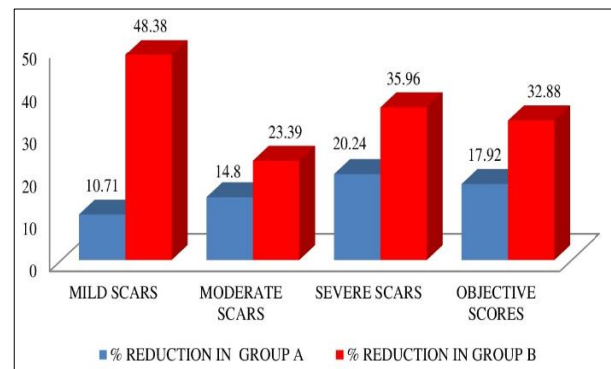


Figure 3: Comparison of objective improvement in mild, moderate and severe scars between treatment groups.

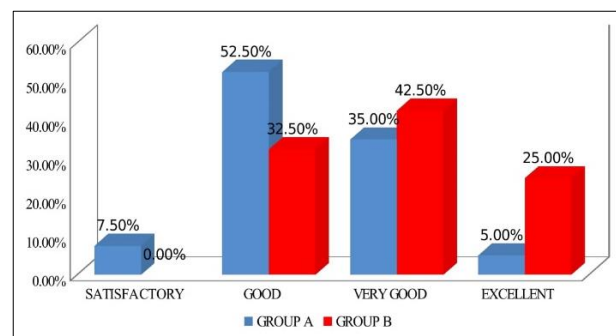


Figure 4: Comparison of subjective assessment scores between treatment groups.

Complications analyzed were erythema, crusting, edema, pain and pigmentation. Duration of erythema, edema and crusting was less in group B than in group A, as shown in (Table 4). Pain was scored on a scale of 0-3. In group A, 23 patients (57.5%) experienced mild pain, 17 patients (42.5%) experienced moderate pain. In group B, 4 patients (10%) experienced mild pain, 27 patients (67.5%) experienced moderate pain, and 9 patients (22.5%) experienced severe pain. In overall comparison, group B patients experienced more pain. Presence or absence of hyperpigmentation after treatment was also examined in both groups. In group A, 20 patients (50%) developed hyperpigmentation, whereas in group B, 18 patients developed hyperpigmentation.

Table 4: Comparison of erythema, edema and crusting (downtime) after treatment in group A and group B.

	Group A (FCO ₂ alone)	Group B (FCO ₂ + PRP)
Erythema (days)	7.05±0.904	5.48±0.64
Edema (days)	7.00±0.847	5.48±0.64
Crusting (days)	7.05±0.904	5.48±0.64

Photographic assessment

Group A and group B showed good results; but Group B showed more clearance of scars, improvement of skin texture and decreased down time (Figure 5).

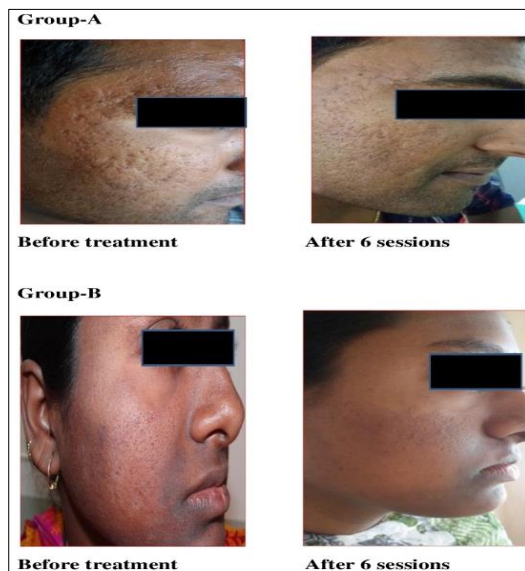


Figure 5: Comparison of improvement by photographic assessment between treatment groups.

DISCUSSION

Although acne scars are common, there has been no single effective modality in the management of this problem. With newer insights into scar remodeling and healing, new modalities of treatment have also been

employed in the management of acne and acne scars. FCO₂ and PRP are recently introduced innovative techniques for treatment of acne scars, with the aim to achieve best results with minimal side effects.

Fractional photothermolysis is a technology that removes fractions of the skin instead of wiping away the entire layer.¹⁶ Laser resurfacing involves monochromatic light delivery into the scars, and resultant heat initiates collagen injury and neocollagenesis.¹⁷ Fractional resurfacing (FR) leads to formation of MTZ (micro-thermal zones) by ablation of epidermal and dermal tissue without injuring the adjacent skin, which leads to rapid wound healing in ablated area.¹⁷ Delivery of laser beam causes ablation where most superficial layer undergoes vaporization and creates a zone of vaporization. High heat below this zone causes tissue necrosis, creating a zone of irreversible damage. Further below this zone, lower heat results in formation of zone of reversible damage which results into shrinkage of collagen. This is followed by skin tightening, collagen remodeling, and re-epithelialization.

At present, the most popular media for fractional resurfacing are CO₂ and erbium. Both CO₂ and erbium target water and vaporize the skin. CO₂ laser penetrates deeper than erbium.¹⁸ CO₂ laser has a wavelength of 10,600 nm. It targets 20-60 µm depth of epidermal and papillary dermal layers; 20-50 µm of surrounding area undergoes thermal damage. Thermal injury generates coagulation and denaturation of collagen and re-epithelialization ensues. Due to fractional ablation of epidermis and dermis, the adjoining non-ablated skin and appendages assist re-epithelialization.¹⁷

Platelet-rich plasma (PRP) is an autologous blood plasma containing 4-7 times the baseline concentration of platelets and is pre-packed with growth factors.¹⁹ Autologous growth factors and secretory proteins, chemokines, and cytokines released on platelet activation facilitate wound repair and rejuvenation in cosmetic dermatology, they act by stimulation of dermal fibroblast proliferation and increase type I collagen synthesis.¹⁷ GFs and cytokines are released from platelets during clot formation at wound site.²⁰ Different growth factors and their biological roles are summarized in (Table 5).¹⁹

The aim of the present study was to assess the synergistic efficacy of FCO₂ and PRP in post- acne scars. Majority of patients in both the groups were aged between 21 and 30 years. Acne and its complications are noted mainly in this age group. Also, awareness of new treatment modalities like PRP and lasers is greater in this age group. So, greater amount of participants of this age group is of relevance. Two methods of treatment were evaluated to know the efficacy by using objective and subjective parameters. Scars were evaluated using Goodman's quantitative global acne scarring grading system. The scores were noted before and after 6 sessions of treatment and were used for statistical analysis.

Table 5: Growth factors and their biological activity.

Growth factor	Biological activity
TGF α, β	Differentiation, Proliferation and control of many cell types. Mediates angiogenesis, Chemotactic for fibroblasts, keratinocytes and macrophages. Mitogenic for fibroblasts and smooth muscle cells. Inhibits the endothelial cells, keratinocytes and lymphocytes. Regulates matrix proteins, collagen, proteoglycans, fibronectin and matrix-degrading proteins.
PDGF- $\alpha\alpha$, $\alpha\beta$, $\beta\beta$	Mitogen for connective tissue cells, inhibitor of apoptosis, increases the motility of mesenchymal cells, fibroblasts, endothelial cells, and neurons. May be involved in physiological processes and in diseases like cancer and atherosclerosis. Fibroblast and macrophage Chemotaxis.
IGF I	Mediates various effects of growth hormone.
FGF I	Induces fibroblast, proliferation, angiogenesis, tissue organization and regeneration.
EGF	Induce differentiation of cells, mitosis of fibroblasts, endothelial cells and keratinocytes and Mediates angiogenesis.
VEGF	Induce angiogenesis by induction of mitosis in endothelial cells, and its chemotaxis and promotes alterations in vascular physiology and permeability
HGF	Mediates regeneration

As shown by objective assessment, both the treatments led to improvement in acne scars. However, improvement in dual therapy group was better than in monotherapy group. Patients on dual therapy were more satisfied with treatment than those on monotherapy.

In study conducted by Manuskiatti et al, with FCO₂ on acne scars at 6-month follow up, majority patients reported good improvement.²¹ Elcin and Yalici-Armagan showed that FCO₂ laser caused significant improvement as assessed by ECCA (échelle d'évaluation clinique des cicatrices d'acné) scale after 3 months of treatment, and the improvement continued throughout the 3-year follow-up period as assessed from self-assessment.²²

Platelet-rich plasma is another new promising treatment modality for post-acne scars. It is widely studied as an adjuvant, most notably with microneedling and ablative CO₂ laser. In a study conducted by Lee et al, with ablative CO₂ and PRP in a split face trial on 14 patients autologous PRP followed by ablative CO₂ laser showed greater improvement than with laser alone.²³ Similar results were reported by Galal et al a combination of laser and PRP being superior to laser alone.²⁴ Reduced downtime of FCO₂ laser was reported by addition of PRP. Hyperpigmentation was not developed despite darker skin type. In the present study, slightly more number of patients treated with laser alone developed hyperpigmentation. This was probably because majority of patients treated with laser alone were of darker skin type (Fitzpatrick's skin type V and VI), while patients treated with dual therapy were majorly of fairer skin types (type III and IV). A meta-analysis by Chang et al reported that the combination of PRP and FCO₂ laser synergistically improved the effect on acne scars, and also recovered the skin damaged by laser within shorter duration of time.²⁵ In the present study, FCO₂ laser combined with PRP showed better effect on acne scars

than laser alone; the finding is consistent with the studies quoted above.

CONCLUSION

This study shows that a combination of FCO₂ laser and PRP is a more efficacious treatment modality than FCO₂ laser alone.

No single treatment can treat all types of scars. Fractional resurfacing is a new concept for laser by using a fractional approach to create microscopic zones of thermal damage with controlled width, depth, and densities to targeted depths in the dermis. At the same time, autologous PRP has opened new avenues in field of acne scar due to its effect on healing and is a useful adjuvant in dermatology practice. This study implies that a combination of both these treatment modalities can achieve synergistic effect on acne scars, and thus, can work better than laser resurfacing alone.

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Conflict of interest: None declared

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