

Efficacy of fractional carbon dioxide laser and platelet rich plasma versus fractional carbon dioxide laser alone in patients of vitiligo

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Abstract

Background Vitiligo is an acquired pigmentary disorder caused by loss of epidermal melanocytes. Several treatments using laser and surgical techniques provide hope for patients with vitiligo who have not shown re-pigmentation with traditional therapies. Fractional CO₂ lasers and PRP are latest advances in non-surgical skin rejuvenation treatments.

Objective To compare the efficacy of fractional carbon dioxide laser and platelet rich plasma versus fractional carbon dioxide laser alone in patients of vitiligo.

Methods After meeting the inclusion criteria, 60 patients (30 in each group) were randomly allocated by lottery method. Group A received sessions of fractional CO₂ laser + PRP at three weeks interval and group B received only fractional CO₂ laser at three weeks interval for total three months. VASI score was calculated at baseline and three weeks after end of treatment. Efficacy was assessed by calculating decrease of VASI score from baseline till three weeks after end of treatment and >50% reduction in VASI score from baseline was termed as efficacious.

Results Mean age of patients was 33.58±11.75 years. There were 34 (56.67%) male and 26 (43.3%) female patients. In group A, efficacy was achieved in 17 (56.7%) patients and in group B, efficacy was achieved in 7 (23.3%) patients (p-value=0.008).

Conclusion Results of our study concluded that fractional CO₂ laser combined with PRP has statistically significant better efficacy than fractional CO₂ laser alone in treating vitiligo.

Key words

Fractional Carbon Dioxide (FCO₂); Platelet Rich Plasma (PRP); Vitiligo; VASI.

Introduction

Vitiligo is an acquired pigmentary disorder caused by loss of melanocytes from the epidermal cells.¹ It presents as well circumscribed depigmented milky white macules and patches on the skin.² Vitiligo affects about 0.5%-1% of the population.³ It seriously impacts the quality of life, leading to

self-isolation and loss of self-esteem especially if lesion are on sites of cosmetic concern like face and extremities.⁴ Vitiligo is generally classified into segmental and non-segmental vitiligo. Treatment of vitiligo includes topical corticosteroids, calcineurin inhibitors, vitamin D analogues, narrow band UVB or psoralen and ultraviolet A and surgical techniques like tissue and cellular grafts.⁵ Despite many treatment options available for vitiligo, the response to treatment is variable, requires a prolonged course and is unsatisfactory. Therefore, new therapeutic approaches are required.⁶

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Platelet rich plasma (PRP) is a new treatment modality in vitiligo. It is composed of high concentration of platelets, growth factors and plasma proteins including fibrin and fibronectin. PRP stimulates melanocytes proliferation in vitiligo.⁷ Another treatment modality is the fractional CO₂ laser (FCO₂). FCO₂ laser causes photothermolysis and releases different types of growth factors and cytokines that can stimulate melanocytes migration into the vitiligo patches. FCO₂ laser has advantage over traditional ablative laser as there is a lowered chance of scar formation and recovery time is short.⁷ According to a study done by Abdelghani *et al.*, combination of FCO₂ laser with Intradermal PRP injection in vitiligo showed more than 75% repigmentation in 40% patients while in FCO₂ laser group only 10% patients achieved more than 75% repigmentation.⁸ Another study by Kadry *et al.*, indicated combined FCO₂ laser with PRP achieved highest significant improvement while FCO₂ alone showed mild improvement.⁶

The rationale of this study was to determine the best treatment modality in patients of vitiligo, as despite the numerous conventional treatments, patients remain in refractory state. Variation of response in various geographical and ethnic groups, cosmetic concern and lack of local literature warrants a study to evaluate the efficacy of combined FCO₂ laser and PRP versus FCO₂ laser alone in vitiligo. As no local

study was available in this regard, this study was planned to determine the best treatment option between combined FCO₂ and PRP alone for vitiligo patients.

Methods

It was a randomized study done at Department of Dermatology, Lahore General Hospital for 6 months, June 2021 to November 2021 after taking permission from the hospital's ethical committee. Total 60 patients (30 in each group) of vitiligo were taken. Patients with both segmental and non-segmental vitiligo of any severity (assessed by VASI), of either gender, age between 18- 60 years and vitiligo of more than 3 months duration were included in the study after taking written consent. Patients receiving any kind of vitiligo treatment during last 2 months and those having acral type or genital vitiligo were not included in the study. Patients having history of photosensitivity, hypertrophic scars, keloids and Koebner phenomenon were also excluded from study.

Patients were randomly allocated in to two groups by lottery method. Information was noted in the pre designed proforma regarding their demographic data. The VASI score was calculated at baseline at follow up visits (3rd, 6th, 9th, 12th weeks) and 3 weeks after last treatment (15th week) (Table 1).

Table 1

Vitiligo Area Scoring Index (VASI)

Patient's body is divided into five regions. VASI is determined by measuring in hand units (1% per unit), the area of vitiligo, and multiplying it with extent of depigmentation.

Pattern of depigmentation is expressed by the following percentages: 0 %, 10%, 25%, 50%, 75%, 90%, 100%.

At 100% depigmentation, no pigment

90%, specks of pigment

75%, depigmented area exceeds the pigmented area

50%, depigmented and pigmented areas are equal

25%, pigmented area exceeds the depigmented area

10%, specks of depigmentation

The VASI is derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and summing the values of all body sites together.

$VASI = \sum [\text{Hand units}] \times [\text{Residual depigmentation}]$

Group A received sessions of fractional carbon dioxide laser followed by PRP at three weeks interval for total three months and group B received fractional carbon dioxide laser alone at three weeks interval for total three months. Blood sample of eight milliliters was withdrawn from the patient's peripheral vein. Sample was centrifuged for 5 minutes at 1500 rpm. Superficial intradermal (ID) microinjections of 0.1 mL each spaced about 1 cm apart were given by 30-G needle in lesions of vitiligo.⁸ FCO2 laser at 50-100 mJ, spot density 150-200 spots/cm² with pulse duration of 5-6 ms, two passes with minimal overlap were delivered to the lesions of vitiligo and the surrounding thin rim of healthy skin (2 mm).⁹

Photographs were taken before procedure, at baseline and at follow up visits (3rd, 6th, 9th, 12th, 15th weeks). Efficacy was assessed at 15th week, that was 3 weeks after the end of treatment at 3 months, by calculating decrease of VASI score from baseline. >50% reduction in VASI from baseline VASI score was termed as efficacious. All data was noted in the pre designed proforma.

Data analysis was done using SPSS version 24.0. Quantitative variables i.e., age, duration of disease, VASI score at baseline and 3 months were summarized as mean and standard deviation. Frequency and percentages were used for presentation of qualitative variables like gender, site of lesion and efficacy. Data was stratified for age, gender, site of lesion and duration of vitiligo. Chi square test was applied to compare efficacy in both groups and for post stratifications keeping p value of ≤ 0.05 as significant.

Results

A total of 60 patients were included in this study. Mean age of patients were 33.58±11.75 years with minimum age 18 years and maximum age 60 years. In group A mean age was

Table 2 Clinico-demographic data.

	Group A n=30	Group B n=30
Age	34.80±13.31	32.37±10.03
Gender		
Male	20 (66.7%)	14 (46.7%)
Female	10 (33.3%)	16 (53.3%)
Number of lesions	3.53±2.43	3.83±1.86
Duration of vitiligo	13.47±8.15	14.40±7.63
Lesion Site		
Back	4 (13.3%)	1 (3.3%)
Chest	3 (10%)	6 (20%)
Face	2 (6.7%)	1 (3.3%)
Forehead	3 (10%)	4 (13.3%)
Hands	13 (43.3%)	11 (36.7%)
Feet	3 (10%)	2 (6.7%)
Lt medial malleolus	1 (3.3%)	2 (6.7%)
Left leg	1 (3.3%)	1 (3.3%)
Rt forearm	0 (0.0%)	2 (6.7%)

34.80±13.31 and in group B mean age was 32.37±10.03. In this study, 34 (56.67%) patients were male and 26 (43.33%) patients were females (**Table 2**).

In group A, mean number of lesions was 3.53±2.43 while in group B, mean number of lesions was 3.83±1.86. Mean duration of lesion in group A was 13.47±8.15 mon. and in group B, mean duration of lesion was 14.40±7.63 mon. (**Table 2**).

Distribution of lesions according to site showed that the maximum number of lesions, which was 24 (40%), were on hands. In group A, 13 (43.3%) patients and in group B, 11 (36.7%) patients had lesions on hands. Frequency distribution according to site of lesions is shown in (**Figure 1**).

Mean VASI score at baseline, in group A was 74.50±26.40 and mean VASI score in group B at baseline was 68.33±28.75 (p-value=0.390). In group A, mean VASI score at 3rd month was 40.03±17.28 and in group B, mean VASI score at 3rd month was 44.33±20.31 (p-value=0.381). In group A, mean change in VASI score was 37.5±15.1 while in group, mean change in VASI

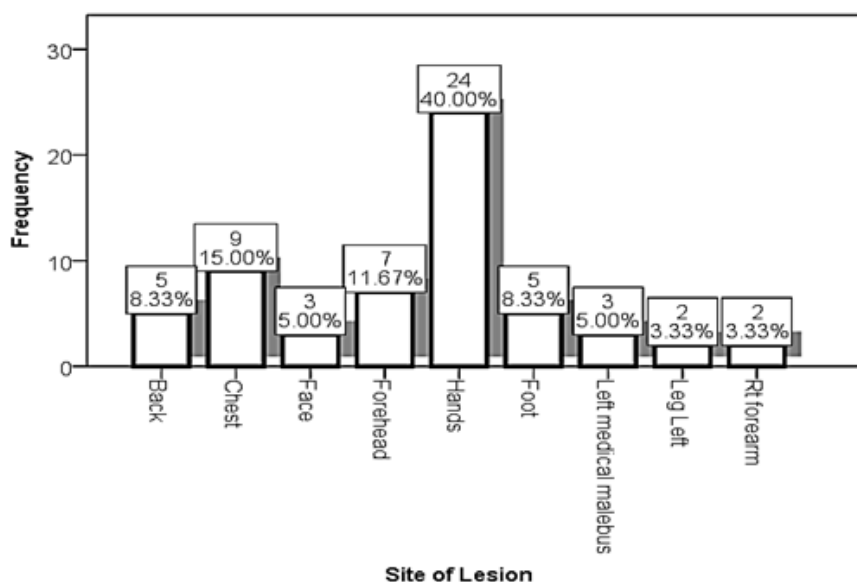


Figure 1 Frequency distribution according to site.

Table 3 Comparison of VASI between groups.

VASI at	Group A	Group B	p- value
baseline	74.50±26.40	68.33±28.75	0.390
15 th week	40.03±17.28	44.33±20.31	0.381
Change	37.5±15.1	30.1±13.2	0.048

score was 30.1±13.2. The difference was statistically significant i. e., p-value=0.0479.

Efficacy was achieved in 17 (56.7%) patients in group A and in 7 (23.3%) patients in group B. The difference was statistically significant i.e., p value=0.008 (**Table 3**).

The data was stratified for age, gender, duration of vitiligo, site of lesions and the results are shown (**Table 4**).

Data was stratified for age of patients, in patients with age ≤40, in group A efficacy was achieved in 11 (61%) patients whereas in group B, efficacy was achieved in 6 (26.1%) patients. The difference in results were statistically significant i.e., p-value=0.024. Data stratification according to gender showed that in group A, efficacy was achieved in 12 (60%) males while in group B efficacy was achieved in only 2 (14.3%) males. The difference was statistically significant i.e., p-value=0.008.

When data stratified for duration of lesion, in group A, efficacy was achieved in 10 (52.6%) and in group B, efficacy was achieved in 2 (13.3%) patients with lesions of duration ≤12 months. This difference was statistically significant i.e., p-value=0.017.

Discussion

Vitiligo is an autoimmune disorder in which immune cells target and destroy the melanocytes, leading to loss of skin pigmentation. It affects about 0.5 to 1% of the population.⁸ Vitiligo causes distress in patients as it is a highly visible condition. Various treatments for vitiligo are available: surgical and non-surgical, with variable degree of success. Use of PRP with fractional CO₂ laser in treating vitiligo is still in the early stages of investigation.¹⁰⁻¹² Introduction of these new treatment modalities may provide alternative to current available therapies (phototherapy, steroids etc.).^{13,14}

FCO₂ laser causes immediate contraction of tissue decreasing the size of vitiligo lesion and secrete cytokines and growth factors that serve as stimulants for migration of melanocytes from

Table 3 Stratification of data.

		Efficacy	Group A	Group B	p-value
Age (years)	≤40	Yes	11 (61.1%)	6 (26.1%)	0.024
		No	7 (38.9%)	17 (73.9%)	
	>40	Yes	6 (50%)	1 (14.3%)	0.119
		No	6 (50%)	6 (85.7%)	
Gender	Male	Yes	12 (60%)	2 (14.3%)	0.008
		No	8 (40%)	12 (85.7%)	
	Female	Yes	5 (50%)	5 (31.2%)	0.339
		No	5 (50%)	11 (61.8%)	
Duration of lesions (months)	≤12	Yes	10 (52.6%)	2 (13.3%)	0.017
		No	9 (47.4%)	13 (86.7%)	
	>12	Yes	7 (63.6%)	5 (33.3%)	0.126
		No	4 (36.4 %)	10 (66.7%)	
Site of lesions	Hands	Yes	8 (61.5%)	3 (27.3%)	0.093
		No	5 (38.5%)	8 (72.7%)	
	Others	Yes	9 (52.9%)	4 (21.1%)	0.047
		No	8 (47.1%)	15 (78.9%)	

Table 4 Comparison of efficacies of both groups.

Groups	Efficacy		Total	P value
	Yes n(%)	No n(%)		
Group-A (FCO2+PRP)	17 (56.7)	13 (43.3)	30	0.008
Group-B (FCO2)	7 (23.3)	23 (76.7)	30	

adjacent normal skin.⁹ Platelet-rich plasma (PRP) contains high concentrations of platelets and growth factors. It is an increasingly popular treatment modality in other dermatological conditions. Adding PRP to FCO2 laser treatment did not show any statistically significant synergistic effects according to previous studies.¹⁵ So, we conducted this study to analyze the efficacy of combining FCO2 laser and PRP versus FCO2 laser alone in vitiligo.

In the current study, the age distribution of the patients showed that out of 60 patients, mean age was 33.58 with age range of 18 to 60 years. This was comparable to a study conducted by Raizada *et al.* in which age range was 18 to 50 years.¹⁶

Gender distribution of patients in this study showed that 56.7% (n=34) patients were male

and 43.3% (n=26) were female. This was different from a study conducted by Raizada *et al.*¹⁶ in which 43% (n=13) patients were male and 56.6% (n=17) patients were female. Similarly, in another study conducted by Kadry *et al.*, 26.7% were male patients and 73.4 % were female patients. This difference in the current study may be due to social and cultural differences.⁶

In this study, duration of vitiligo in group A was 13 months and in group B it was 14 months, while in a study done by Raizada *et al.*¹⁶ duration of lesions was 18 months in CO2 laser and PRP group and 20 months in CO2 laser group. In the current study more lesions were on hands in both groups i.e., 24(40%) while in Raizada *et al.* study more lesions were on trunk in CO2 laser and PRP group 17(56%) and on limbs in PRP group 16 (57.1%).¹⁶

In the current study mean VASI score at baseline in Group A was 74.50±26.40 and in group B mean VASI score was 68.33±28.75 (p-value=0.390), while, in a study conducted by Raizada *et al.* mean VASI score in PRP+CO2 laser was 12.1±0.85 and in CO2 group was 12.7 at baseline (p-value=0.066). In the current study

we have much greater VASI score of lesions as compared to Raizada *et al.*¹⁶ This study compared efficacy of fractional CO2 laser with PRP (Group A) and Fractional CO2 laser alone (Group B). Efficacy was achieved in 56.7% patients in Group A and 23.3% in group B (p-value=0.008). Kadry *et al.* compared efficacy of fractional CO2 laser with PRP, PRP and fractional CO2 laser alone in the treatment of vitiligo. Fractional CO2 laser and PRP group showed highest improvement than fractional CO2 laser alone and PRP alone (p-value<0.001).⁶ These results were comparable to the current study as it observed that the combination group showed greater efficacy. In a study conducted by Abdelghani *et al.*, efficacy achieved in Fractional CO2 laser and PRP Group was 60%, similar efficacy was achieved in our study in fractional CO2 laser and PRP group.⁸

Mofy *et al.* and Abdelghani *et al.* found that repigmentation was seen in 10% of patients who were treated with fractional CO2 laser alone while in this study efficacy was achieved in 23% patients in fractional CO2 laser group.⁸ Shin *et al.* and Doghaim *et al.* also treated vitiligo with fractional CO2 laser and found it as effective modality similar to shown in the current study.^{16,17}

In this study greater efficacy was seen in age group ≤ 40 . It was comparable to study done by Raizada *et al.* which also showed greater efficacy achieved in age group of 18-30 years.¹⁶ This study showed that lesions having duration of ≤ 12 months showed greater efficacy while Raizada *et al.* concluded that duration of lesion did not influence efficacy in both groups.¹⁶

Side effects were pain and mild erythema, observed more frequently in combination group than fractional CO2 laser group, in the current study and those side effects resolved within 24

to 48 hours. So, results of our study revealed that fractional CO2 laser and PRP is safe and efficacious in treating vitiligo than fractional CO2 laser alone.

Limitations

This study was done on a very small sample size which is one of the limitations of the study. So, it is suggested that in the future, studies should be done with a larger sample size and should be multicentric to control the bias.

Another limitation of the study was the short follow up.

Conclusion

Results of our study concluded that combined fractional CO2 laser and PRP has statistically significant better efficacy than fractional CO2 laser alone in treating vitiligo.

Combination therapy has superior and promising results and has a synergistic effect in treating patients with lesions of vitiligo on difficult to treat areas. PRP and fractional CO2 laser as an adjuvant therapy can dramatically increase repigmentation rate of vitiligo lesions that are resistant to other conventional therapies and hence improving their quality of life.

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