

# Efficacy of fractional carbon dioxide laser versus 0.1% tacrolimus cream in the treatment of segmental vitiligo

Marrium Manzoor, Kehkashan Tahir, Uzma Amin, Sarah Bashir, Omer Altaf, Nadia Naeem

Department of Dermatology, Postgraduate Medical Institute/ Lahore General Hospital, Lahore.

## Abstract

**Objective** To compare the efficacy of fractional carbon dioxide laser versus 0.1% tacrolimus cream in the treatment of segmental vitiligo.

**Methods** The randomized controlled trial was conducted in the Dermatology department, Lahore General Hospital Lahore for duration of 6 months (June 2018 to December 2018). Total 120 patients were recruited and divided randomly in 2 equal groups. In group A; fractional CO<sub>2</sub> laser was applied once a month. In group B; 0.1% tacrolimus cream was applied twice a day. After 2 months, efficacy was measured i.e. >50% reduction in VASI score. SPSS v. 25 was used to analyze the collected information.

**Results** The mean age of patients in CO<sub>2</sub> laser group was  $41.68 \pm 14.26$  years, there were 17 (28.3%) males and 43 (71.7%) females. In tacrolimus cream group, the mean age of patients was  $38.57 \pm 12.72$  years, there were 18 (26.7%) males and 44 (73.3%) females. The mean percentage reduction in VASI score was  $53.98 \pm 18.06$  with CO<sub>2</sub> laser and  $39.18 \pm 15.01$  with tacrolimus. The difference was significant ( $p < 0.05$ ). Efficacy was achieved in 34 (56.7%) cases with CO<sub>2</sub> laser and in 19 (31.7%) with tacrolimus. The difference was significant ( $p < 0.05$ ).

**Conclusion** In conclusion, CO<sub>2</sub> fractional laser was found significantly effective in re-pigmentation of vitiligo as compared to tacrolimus.

## Key words

Vitiligo; CO<sub>2</sub> fractional laser; Repigmentation; Tacrolimus cream; Vitiligo Area Scoring Index.

## Introduction

Vitiligo is defined as a common form of localized depigmentation. It is an acquired idiopathic epidermal pigment loss which can occur anywhere on the body,<sup>1</sup> and depigmentary ailment occur due to loss of functioning of epidermal melanocytes. Globally vitiligo affects only 0.5-1% of world's population, but greatly affects quality of life of patient greatly.<sup>1,2</sup> Some populations have rates as high as 2-3%.<sup>3</sup> Males and females; both can be affected equally. About 50% cases develop vitiligo in age less than 20

and most develop it before age 40.<sup>4</sup>

Treatment of vitiligo is a challenge. Current vitiligo therapies are largely ineffective. Different options are available like topical, oral, phototherapy and fresher modalities.<sup>5</sup> The accuracy of the vitiligo assessment system used for assessing patient progress has an effect on the effectiveness of vitiligo treatment,<sup>6</sup> causing disfigurement, size of vitiligo surface areas and severe disruptions in life quality.<sup>7,8</sup>

Carbon dioxide (CO<sub>2</sub>) fractional or "pixilated" lasers are one of the most recent advancements in non-surgical skin transformation treatments. The carbon dioxide laser now has the longest wavelength, and can be used on dark skin types without any hazard with suitable adjustments.

## Address for correspondence

Dr. Marrium Manzoor  
Department of Dermatology,  
Postgraduate Medical Institute/  
Lahore General Hospital, Lahore.  
Email: marrium145@gmail.com

This is a test treatment.<sup>9</sup> CO<sub>2</sub> has also been found to be a promising treatment modality in vitiligo.<sup>8</sup> Tacrolimus can be used instead of topical steroids in vitiligo. This cream does not cause atrophy, adverse ocular effects or telangiectasia. Topical corticosteroids, which have minimal application to the face and intertriginous regions, also cause atrophy, telangiectasia, and adverse ocular effect.<sup>5</sup>

In one study, 10 vitiligo patients, fractional CO<sub>2</sub> for vitiligo was found to be successful in 60% (6/10) of the cases.<sup>10</sup> Larger, randomized controlled trials are required to determine whether fractional CO<sub>2</sub> has any utility when administered in the treatment of vitiligo.<sup>11</sup> However, one study found that fractional CO<sub>2</sub> for vitiligo had a 44 percent efficacy rate (>50 percent re-pigmentation).<sup>12</sup> One more study conducted on 30 patients of vitiligo presented that efficacy (excellent to moderate re-pigmentation) was achieved in 40% (12/30) with 0.1% tacrolimus for vitiligo.<sup>13</sup>

This study was planned to observe that the fractionated lasers represent a new modality for skin resurfacing based on the theory of fractional photo-thermolysis. Through literature it has been noticed that addition of fractional laser can be helpful in early improvement in vitiligo and patients' satisfaction level and not much literature is available in this regard as well as no local data is found in literature. Therefore, we conducted this study to find better management protocol for vitiligo in future. Currently 0.1% tacrolimus is applied, but if fractional CO<sub>2</sub> laser is more effective as compared to 0.1% tacrolimus, then in future, we will be able to use more efficacious treatment of vitiligo in local setting.

## **Methods**

This Randomized controlled trial was carried out

during June to Dec 2018 in the dermatology Department of Lahore General Hospital, Lahore. It was started after obtaining permission from the Institutional Review Board. Informed written consent was obtained from patients. Sample size of 120 patients (60 patients in both groups) was estimated keeping 80% power of study, 10% significance level and percentage of efficacy i.e. 40% with 0.1% tacrolimus cream and 60% with fractional CO<sub>2</sub> laser for segmental vitiligo.

All patients presenting with stable segmental vitiligo area severity index (VASI) score >50 and age group 18-70 years were included from the study. Patients already taking medication for vitiligo or with failed previous treatment, pregnant and lactating females. Hypertensive patients and lip tip variety of vitiligo patients were excluded from the study.

Patients fulfilled the inclusion and exclusion criteria were recruited in study from outpatient department of Department of Dermatology. Demographic data (name, age, gender, site of vitiligo, and duration of disease) was recorded. Patients were divided randomly in 2 equal groups by applying lottery method. In group A; fractional CO<sub>2</sub> laser at high-energy 10 600-nm radiation, producing fast tissue ablation with minimal bleeding once a month was applied. The parameters used were: "15-W, 500µs pulse duration, 50 µm spacing, and 1-stack." In group B; 0.1% tacrolimus cream was applied twice a day. At baseline picture of patches was obtained and were kept safe in patient's file. Then patients were followed-up till 2 months for resolution of vitiligo. After 2 months, patients were assessed by researcher herself for satisfaction of patients with treatment by using VASI and efficacy was measured. Picture was also obtained and compared with baseline picture of patient. Data was entered in SPSS 25. Chi-square test was applied to compare the efficacy of treatment in both trial

groups. P-value  $\leq 0.05$  was kept as significant.

**Results**

In our study, total 120 patients were included. In CO<sub>2</sub> laser group, the mean age of the patients was 41.68±14.26 years and in tacrolimus group, the mean age was 38.57±12.72years. There were 17 (28.3%) males and 43 (71.7%) females in CO<sub>2</sub> laser group and 18 (26.7%) males and 44 (73.3%) females in tacrolimus group. In CO<sub>2</sub> laser group, face was involved in 21 (35%), hands in 19 (31.7%), legs in 10 (16.7%) and foot in 10 (16.7%). In tacrolimus group, face was involved in 21 (35%), hands in 17 (28.3%), legs in 5 (8.3%) and foot in 17 (28.3%) (**Table 1**).

Efficacy was achieved in 34 (56.7%) cases and efficacy could not be achieved in 26 (43.3%) cases in CO<sub>2</sub> laser group. In tacrolimus cream group, efficacy was achieved in 19 (31.7%) cases and efficacy could not be achieved in 41 (68.3%) cases. The difference was significant (p<0.05) (**Table 2**).

Data was split for effect modifiers. In patients aged 18– 40 years, with CO<sub>2</sub> laser, efficacy was

**Table 1** Basic demographics of patients with vitiligo (n = 120).

	CO <sub>2</sub> laser (n=60)	Tacrolimus Cream (n=60)
Age (years)	41.68 ± 14.26	38.57 ± 12.72
Duration of vitiligo (months)	6.22 ± 3.45	5.85 ± 3.25
Gender		
Male	17 (28.3%)	16 (26.7%)
Female	43 (71.7%)	44 (73.3%)
Lesion site		
Face	21 (35%)	21 (35%)
Hands	19 (31.7%)	17 (28.3%)
Legs	10 (16.7%)	5 (8.3%)
Foot	10 (16.7%)	17 (28.3%)

achieved in 15 (50%) cases. With tacrolimus, efficacy was achieved in 13 (36.1%) cases (p>0.05). In patients aged 41-70 years, with CO<sub>2</sub> laser, efficacy was achieved in 19 (63.3%) cases. With tacrolimus, efficacy was achieved in 6 (25%) cases (p<0.05). Similarly data was stratified for Gender, duration of vitiligo and site of lesion and age groups. The difference was significant in female patients, and patients having vitiligo from 7-12 months (P< 0.05). In patients having vitiligo on back, with CO<sub>2</sub> laser, efficacy was achieved in 7 (70%) cases. With tacrolimus, efficacy was achieved in 5 (29.4%) cases (p<0.05) (**Table 3**).

**Table 2** Comparison of outcome in both groups.

	CO <sub>2</sub> laser	Tacrolimus Cream	p-value
VASI at baseline	67.90 ± 10.62	70.25 ± 10.38	0.223
Percentage decrease (%)	53.98 ± 18.06	39.18 ± 15.01	0.0002
Efficacy			
Yes	34 (56.7%)	19 (31.7%)	0.006
No	26 (43.3%)	41 (68.3%)	

**Table 3** Comparison of outcome in both group stratified for effect modifiers.

		Efficacy	CO <sub>2</sub> laser	Tacrolimus Cream	P value
Age (years)	18-40	Yes	15 (50%)	3 (36.1%)	0.256
		No	15 (50%)	23 (63.9%)	
	41-70	Yes	19 (63.3%)	6 (25%)	0.005
		No	11 (36.7%)	18 (75%)	
Gender	Male	Yes	8 (47.1%)	8 (50%)	0.866
		No	9 (52.9%)	8 (50%)	
	Female	Yes	26 (60.5%)	11 (25%)	0.001
		No	17 (39.5%)	33 (75%)	
Duration of Vitiligo (month)	1-6	Yes	19 (55.9%)	12 (36.4%)	0.109
		No	15 (44.1%)	21 (63.6%)	
	7-12	Yes	15 (57.7%)	7 (25.9%)	0.01

## Discussion

Skin and mucous membrane disorders can be acquired, including vitiligo. Despite the fact that there are many possible therapies for vitiligo, many individuals still have the condition that is known as refractory. For patients with vitiligo, a number of combination therapies have already been tried in an effort to increase effectiveness.<sup>14</sup> Because cell migration is essential for vitiligo re-pigmentation, the laser treatment was applied across the vitiligo lesion as well as a thin rim of healthy skin that was about 2 mm in diameter surrounding the lesion.<sup>15</sup> Additionally, it is known that matrix metalloproteinase-2 promotes melanocyte migration from nearby normal skin. In vitro melanocytes have been shown to exhibit a negligible increase in matrix metalloproteinase-2 activity in response to narrow-band ultraviolet-B radiation.<sup>16</sup>

New treatment methods, like intradermal 5-fluorouracil injections combined with Narrow-band UV-B and micro-dermabrasion combined with 5-fluorouracil, have been studied and have shown positive results. The regulation of resurfacing depth & wound care has become more difficult as a result of dermabrasion or reappearing, despite the combination treatments' promising results. Due to severe skin damage, there is also a chance of scarring during treatment.<sup>17,18</sup>

In our study, total 120 patients were included. In CO<sub>2</sub> laser group, the mean age of patients was 41.68±14.26 years and in tacrolimus group, the mean age was 38.57±12.72 years. There were 17 (28.3%) males and 43 (71.7%) females in CO<sub>2</sub> laser group and 18 (26.7%) males and 44 (73.3%) females in tacrolimus group. The mean duration of vitiligo was 6.22±3.45 years in CO<sub>2</sub> laser group while 5.85±3.25 years in tacrolimus group. One population based study also showed that out of 40,888 adult patients of vitiligo, the

mean age was reported as 44.9±17.4 years, and among them 56.7% were females.<sup>19</sup> The bimodal pattern of the average age of onset shows early onset at 7.3 years and late onset at 40.5 years.<sup>20</sup> Nevertheless, in children, segmental vitiligo appears to be more prevalent than non-segmental vitiligo.<sup>21</sup>

In our study, with CO<sub>2</sub> laser, efficacy was achieved in 34 (56.7%) cases and efficacy could not be achieved in 26 (43.3%) cases. With tacrolimus, efficacy was achieved in 19 (31.7%) cases and efficacy could not be achieved in 41 (68.3%) cases. The difference was significant ( $p < 0.05$ ). As compared to others study, Li *et al*; found that efficacy (>50% re-pigmentation) was achieved in 44% with fractional CO<sub>2</sub> for vitiligo.<sup>12</sup> Helou *et al*; conducted a trial on 10 patients of vitiligo showed that efficacy was achieved in 60% (6/10) with fractional CO<sub>2</sub> for vitiligo.<sup>10</sup> Khullr *et al*; concluded that larger, randomized controlled trials are necessary to determine whether fractional CO<sub>2</sub> has any utility once administered in the vitiligo treatment.<sup>11</sup> Xu *et al*; conducted a trial on 30 patients of vitiligo showed that efficacy (excellent to moderate re-pigmentation) was achieved in 40% (12/30) with 0.1% tacrolimus for vitiligo.<sup>13</sup>

Vitiligo treatment is difficult and involves a multidisciplinary approach. While the use of a fractional carbon dioxide laser as an adjunct to conventional treatment has been confirmed to be successful, there is no consensus about how to use it. There were six studies with a total of 85 participants. The addition of fractional carbon dioxide laser to regular therapy was better to traditional therapy and in terms of  $\geq 50\%$  re-pigmentation of skin for those with refractory vitiligo (risk ratio 4.91, 95.0 percent confidence interval (95 percent confidence interval; 1.150-20.92;  $p = 0.03$ ), physician improvement scores (mean difference = 0.82, 95.0% CI 0.331-1.29;  $p < 0.001$ ), < 25.0% re-pigmentation (RR 10.64,

95.0% confidence interval;10.4910.85; p=10.002) and patient satisfaction (mean difference=1.61, 95% confidence interval; 0.73-2.49; p<10.001). These findings support the view that fractional CO<sub>2</sub> laser therapy is an effective treatment choice for vitiligo patients, especially those who have refractory vitiligo.<sup>22</sup>

Patients presented high satisfaction 'scores for the treatments. In the treatment of vitiligo, the non-ablative 1565-nm fractional laser provided no additional gain. Researchers concluded that the treatment procedure with ablative carbon dioxide laser, when combination with narrow band- ultraviolet-B and topical betamethasone solution, was appropriate for non-segmental vitiligo that was stable. The ablative fractional carbon dioxide laser is better and more effective as compared to non-ablative fractional laser in treating vitiligo.<sup>23</sup>

## Conclusion

Study results showed that 'CO<sub>2</sub> fractional laser found to be significantly' more effective in' repigmentation of vitiligo as' compared to tacrolimus. Fractional CO<sub>2</sub> laser is found more effective treatment especially in region of face and upper extremities. So in future fractional CO<sub>2</sub> laser should be 'considered as treatment modality in vitiligo.

## Limitations

During study, lost to follow-up was a major issue. Secondly financial constraints were faced during trial as trial was done for within limited resources and short period of study. Long-term outcomes could not be assessed.

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