Original Article

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A Comparative Study of Fractional CO_2 Laser versus Intradermal Injection of Autologous Platelet Rich Plasma in Melasma

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ABSTRACT

Introduction: Melasma is a common acquired hyperpigmentation disorder of the face involving the cheeks, forehead, and commonly the upper lips. This condition is more common in women. The objective of this study was to compare the efficacy of fractional CO_2 laser and intradermal platelet rich plasma (PRP) in melasma and to note down any effects of fractional CO_2 and autologous PRP in a prospective long term follow up study.

Methodology: A total of 60 patients with melasma attending the OPD of the Department of Dermatology were recruited. Half of study participants were treated with fractional CO_2 laser treatments while the other half were treated with intradermal autologous PRP once every two weeks for eight weeks. MASI score, visual analogue scale, objective and subjective assessment were done immediately before each session and two weeks after treatment.

Results: The CO_2 laser treatment created more variability in MASI score due to effective treatment, while the PRP showed very little variability due to ineffective or less effective treatment results.

Conclusion: Fractional CO_2 laser is less invasive and more effective as compared to intradermal injection of PRP in melasma patient.

INTRODUCTION

Melasma is a common acquired hyperpigmentation disorder of the face involving the cheeks, forehead, and commonly the upper lips. This condition is more common in women accounting for 90% of all cases.[1] Men have been reported to represent only 10% of the cases.[2,3,4] Melasma is more common in individuals with Fitzpatrick skin types IV-VI than those with fairer skin.[2,5] In present era, platelet rich plasma (PRP) is also getting attention in melasma treatment. In PRP, most important contents of platelets are contained in the α-granules. There are >30 bioactive substances in these granules. Some of the bioactive substances present in the α-granules include platelet-derived growth factor (PDGF), transforming growth factor (TGF)-β1 and β2, epidermal growth factor, and mitogenic growth factors such as platelet-derived angiogenesis factor and fibrinogen. In literature, only TGF-β1 has been investigated about its relation with melanogenesis. TGF-β1 decreases melanogenesis via delayed extracellular signal-regulated kinase activation. PRP has new good autologous growth factors supplement having very good efficacy in so many dermatology indications with zero side effects.

Efficacy of fractional photothermolysis **(**CO_2 laser-10,600 wavelength**)** in melasma-microthermal zones (MTZ) creation and tissue destruction by fractional photothermolysis (FP) results in elimination of melanocytes and keratinocytes containing melanin granules through a "melanin shuttle". This melanin shuttle formation results in significant improvement in epidermal and dermal pigmentation associated with conditions such as melasma and dyschromia of photoageing.[6] CO_2 laser is a noble emerging interventional study for literature as well as cosmetic dermatology. It is highly efficacious than other conventional modality e.g. Kligman formulae which has so many disfiguring side effects like bleaching,

hirsutism of face etc. This present study was aimed to compare the efficacy of fractional CO_2 laser and PRP in melasma and to note down any adverse effects of fractional CO_2 and autologous PRP.

METHODS

The prospective interventional comparative study conducted in the Department of Dermatology was carried out from June 2017 to June 2018 at a government medical college and associated hospitals in Rajasthan, after taking approval from the ethical committee. The study participants included were aged 18 years and above, both sexes, those willing to give written informed consent and follow up. The excluded ones were those who had collagen or elastin disorders, on drugs stimulating cutaneous malignancies and photosensivity, photo-dematoses, usage of topical or oral retinoids and steroids, pregnant or immuno-suppressed, HIV, hepatitis B and C, any active infection or bleeding disorders. A total of 60 patients were enrolled and randomized with computer generated randomized sequence into two group of 30 each i.e. group A (CO_2 laser) and group B (autologous intradermal injection of PRP).

Procedure of fractional CO_2 laser: Treatment area was disinfected by povidone iodine solution. Topical anaesthetic cream i.e. EMLA (Lidocaine 2.5% + Prilocaine 2.5%) was applied under occlusion for 45-60 minutes and disinfected again. The ablative fractional CO_2 laser (10,600 nm wavelength) with point energy between 70 to 120 mJ, duration 3 minutes, interval 10 ms was used.

Platelet rich plasma preparation: A two-stage (separation and concentration) centrifuging process was employed in the preparation of platelet-rich plasma. PRP centrifuge machine was pre-cooled upto 20ºC for 10 minutes. 8.5 ml of whole blood was drawn from the patient by venipuncture and transferred into vaccutainer containing 1.5 ml of ACD-A (acid citrate dextrose-A) anticoagulant. The vaccutainer was labelled and centrifuged at 2500 rpms for 7 minutes. After the centrifugation, the plasma, buffy coat and superficial RBC layer were aspirated and transferred to a plain vacutainer (not having anti-coagulant). This was again centrifuged at 3000 rpms for 6 minutes. After the centrifugation, about upper 3/4th of platelet poor plasma was discarded and the concentrated PRP at the lower 1/4th was resuspended and obtained in a sterile insulin syringe. For each patient, 1.5 ml PRP was prepared. An insulin syringe was used for superficial microinjections via the mesotherapy technique, and the injections were administered into the papillary dermis (1.5~2.0 mm deep). Approximately 1.5 ml of PRP was injected in to the dermis of the face at each session with 15 days interval. Whole procedure was carried out under aseptic conditions. Four sessions were done at 15 days interval alongwith photographic assessment. Final assessment was done two weeks after completion of these four sessions. Only physical sunscreen lotion containing zinc oxide and ferric oxide was given to every patient for photoprotection.

Assessment: Melasma Area and Severity Index (MASI score), Visual Analog Scale (VAS), objective and subjective assessments were performed by two blinded dermatologists (other than who delivers the therapy) at baseline, 2nd visit, and 2 weeks after the 4th visit. Total MASI score: Forehead 0.3 (D+H) A + right malar 0.3 (D+H) A + left malar 0.3 (D+H) A + chin 0.1 (D+H) A.

RESULTS

The study was conducted on 60 patients aged 18 years and above. Figure 1 depicts graph of the trend line of difference of baseline MASI score and MASI score at follow up for CO_2 laser and PRP. The difference of baseline MASI score of CO_2 laser showed zig-zag trend where the trend line of PRP dropped to zero level meaning that CO_2 laser treatment created more variability in MASI score that might have been due to the treatment pattern and medication. Conversely, the MASI score of PRP showed very little variability caused by ineffective or less effective treatment results. A five point likert type grading scale was used by two blinded dermatologists (other than

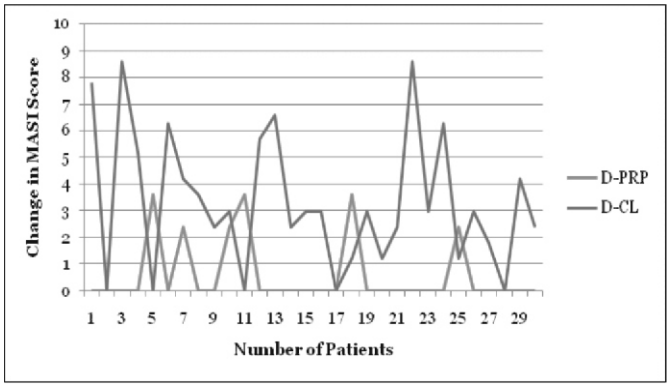


Figure 1: Comparison of changes in MASI scores of CO_2 laser and platelet rich plasma (PRP).

Table 1: Visual Analogue Scale (VAS) score distribution at baseline in study participants

VAS	VAS Observer 1				VAS Observer 2			
	CO_2 Laser		PRP		CO_2 Laser		PRP	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Poor	0	0	0	0	3	10	0	0
No Change	8	26.7	27	90	2	6.7	23	76.7
Fair	5	16.7	3	10	11	36.7	7	23.3
Good	12	40	0	0	10	33.3	0	0
Excellent	5	16.7	0	0	4	13.3	0	0

(PRP) Platelet Rich Plasma

Table 2: Clinical improvement at follow up in study participants

Clinical Improvement	at 2nd session				at 2.5 months			
	CO_2 Laser		PRP		CO_2 Laser		PRP	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Poor	0	0	0	0	3	10	0	0
No Change	5	16.7	27	90	2	6.7	25	83.3
Fair	21	70	3	10	14	46.7	5	16.7
Good	4	13.3	0	0	7	23.3	0	0
Excellent	0	0	0	0	4	13.3	0	0

(PRP) Platelet Rich Plasma

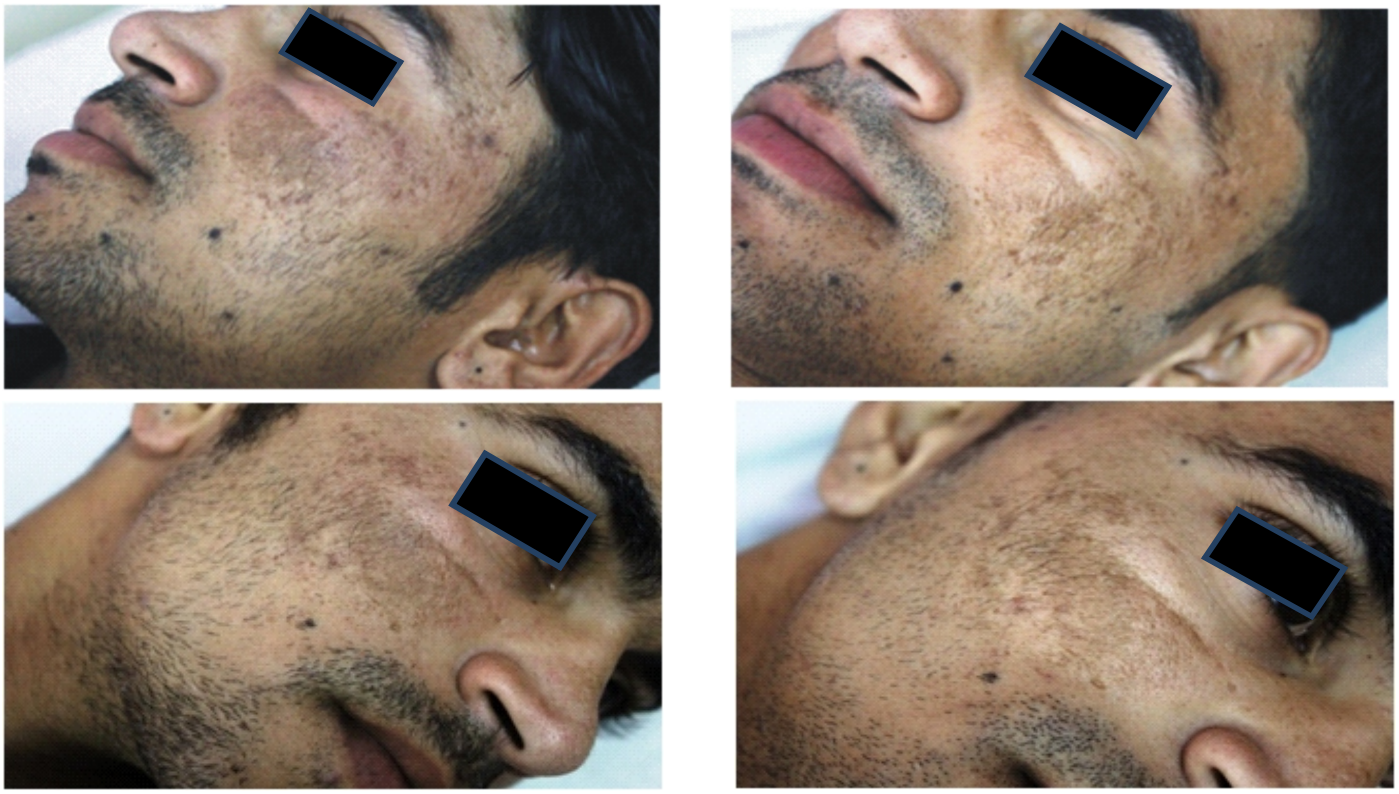
who delivered the therapy) to assess the visual analogue scale (Table1).

A five point likert type grading scale was used by one blinded dermatologist (other than who deliver the therapy) to assess the clinical improvement (Table 2, Figure 2 and 3). Patient satisfaction follow up is given in Table 3.

DISCUSSION

In Tawfic et al[7] study fractional CO_2 alone group, fractional CO_2 laser + topical TXA group, and fractional CO_2 + intradermal injection of TXA in melasma, MASI score and EI were better on the fractional CO_2 laser alone group, followed by fractional CO_2 laser + topical TXA group, then fractional CO_2 laser + intradermal TXA group which is similar to present study. Trelles et al[8] compared the effect of topical bleaching agents alone (Group A), pulsed CO_2 laser alone (Group B), and combination of both (Group C). They noted 100 percent efficacy in all three groups in first month, but declined subsequently in groups A and B. Group C maintained their clinical efficacy at the 12-month follow-up which is similar to our CO_2 laser alone group study in which complete remission of melasma in initial months and repigmentation occurs after 2-3 months follow up.

Angsuwarangsee et al[9] conducted a study on six Thai females who were treated with combined Ultrapulse CO_2 laser (Lumenis) + QSAL on one side of the face and QSAL alone on the other side. These patients were suffering with refractory melasma. The rationale was to use an ablative laser to remove the excess epidermal melanin and abnormal melanocytes and then follow with a Q-switched laser to target the deeper melanocytes in the dermis without causing side effects. The patients were evaluated for upto six months. Their results indicated that the combined treatment had a statistically significant reduction of both the indices, whereas the side treated with just QSAL did not show significant results. It depicts that CO_2 laser is more effective as in our study. In this present study, CO_2 laser alone group study at follow up of 2.5 month, there were fair improvement in 46.7% patients, good improvement in 23.3% patients and excellent improvement in 13.3% patients while 10% patient (3 out of 30) having poor result or not satisfied because of more



Baseline **Follow up**

Figure 2: Effect of CO_2 laser.

Table 3: Patients satisfaction follow up at 2nd session and at 2.5 months

Patients Satisfaction	2nd session				2.5 months			
	CO_2 Laser		PRP		CO_2 Laser		PRP	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Not Satisfied	0	0	0	0	3	10	0	0
Neutral	8	26.7	27	90	5	16.7	27	90
Satisfied	17	56.7	3	10	9	30	3	10
Very Satisfied	5	16.7	0	0	8	26.7	0	0
Strongly Satisfied	0	0	0	0	5	16.7	0	0

(PRP) Platelet Rich Plasma

Baseline **Follow up**

Figure 3: Effect of platelet rich plasma (PRP) laser.

hyperpigmentation from baseline which is similar to this study. A case reported by Yew CH et al[10] showed that the reduction of mean MASI score in two cases (33.5% and 20%) after administered intradermal PRP within QSNd:YAG monthly for two sessions and applied topical alpha arbutin every day. Dannarongchai A et al[11] published a study on melasma they treated with intradermal PRP injection at one side of the face and intradermal normal saline injection at another side as control group every two weeks for four times and then follow up one month after the last treatment. In this study, there was not statistically significant difference between PRP and control in the melanin index, erythema index, Antera 3D levels (melanin, hemoglobin, and texture) during 10 weeks of the study. Results were similar with present study in which group B (intradermal injection of PRP) dermatologists assessed clinical improvement at 2.5 months found no change and fair improvement were seen in 83.3% and 16.7% patients, respectively which was statistically significant. Group B 90% patients were neutral and only 10% of patients were satisfied. The MASI score of PRP showed very little variability due to ineffective or less effective treatment results.

Limitation of study: These procedures are recent advances in cosmetic dermatology. National and International literature is lacking for comparison on such type of study.

CONCLUSION

CO_2 laser was found to be superior to PRP for treatment of melasma. However, rebound pigmentation was seen more in cases treated with CO_2 laser. Side effect noted were erythema and burning sensation after CO_2 laser while with PRP, pain at the time of intradermal injection was noted.

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