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Original Research Article

Micro needling vs micro needling combined with autologous topical platelet rich plasma in the treatment of melasma: a prospective randomized comparative study

Anil Kumar Panda, Ajaya Kumar Jena, Maitreyee Panda, Chinmoy Raj*, Ipsita Debata

Department of DVL, IMS and SUM hospital, Kalinga Nagar Bhubaneswar, Odisha, India

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***Correspondence:**
Dr. Chinmoy Raj,
E-mail: craj71285@gmail.com

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ABSTRACT

Background: Melasma is one of the most common pigmentary disorders worldwide with a still unresolved pathogenesis and treatment continues to be challenging. To assess the effect of micro-needling vs combination of micro-needling followed by application of topical platelet rich plasma (PRP) in the treatment of melasma.
Methods: Sixty patients having melasma were randomly grouped into A and B. Group A underwent micro-needling alone and group B was subjected to micro-needling followed by topical application of autologous PRP. The patients were subjected to 3 treatment sessions at monthly intervals. Melasma area and severity index (MASI) and patient satisfaction scores were recorded at each sitting and the final outcome was recorded one month after the last session.
Results: Twenty-four patients in group A and 27 patients from group B were selected for final analysis. There was significant improvement of MASI in both groups (Group A: p=0.001, group B: p=0.0001) however, the difference in improvement of MASI between the 2 groups was not significant (p=0.0457) Group B was highly satisfied with the treatment which was statistically significant (p=0.0001)
Conclusions: Combining micro-needling with topical PRP appears to be a promising therapeutic modality in the treatment of melasma.

Keywords: Platelet rich plasma, Dermato-surgery, Melasma, Micro-needling

INTRODUCTION

Melasma is a commonly occurring acquired pigmentary disorder worldwide, characterized by symmetrical distribution of brownish macules which coalesce to form patches mostly over the face with complex pathogenesis and challenging treatment.[1] The first-line treatment includes sunscreens and topical depigmenting agents. Although there are numerous choices in the therapeutic armamentarium for melasma, the majority of them are not very satisfactory and there is a lack of sustained therapeutic response, frequent relapse and associated impact on the quality of life.[2,3] Chemical peeling and laser therapy are beneficial as adjuncts but also expensive and associated with their own set of adverse effects. Newer treatment options like micro needling and platelet-rich plasma (PRP) in the management of melasma seems to be a promising option. Skin micro needling promotes proliferation of fibroblasts and upper dermal collagenosis, so it is believed to repair the upper dermis and basement membrane damage in patients of melasma which leads to reduced melanocytes contact with that of dermal delivered melanogenic stimuli such as endothelin, hepatocyte growth factor and stem cell factor. Micro needling also induces the expression of matrix metalloproteinases which is presumed to play a role in the reduction of hyperpigmentation.[4] The pigmentary improvement that occurs with PRP might be attributed to several elements including the repairing of the basement membrane by collagen IV, laminin as well as tenascin

which is triggered by transforming growth factor β (TGFβ) and due to suppression of melanin synthesis brought about by epidermal growth factor (EGF) and TGFβ, and also expansion of the skin volume by collagen synthesis, triggered by platelet derived growth factor (PDGF) and the extracellular components like hyaluronic acid, producing a seemingly glowing skin.[5] As micro needling causes microchannels and topical autologous PRP is then smeared over the area for easier penetration, combining the two procedures would probably result in better therapeutic response. A lack of similar studies in the Indian setting prompted us to undertake this study.

Aims and objectives

Aim and objectives of the study were to evaluate and compare the efficacy of micro needling alone vs micro needling plus topical PRP combination in the treatment of melasma and to determine the safety of the above two procedures and to determine the side effects if any.

METHODS

This is a prospective comparative study carried out in patients who presented with melasma to the dermatology outpatient department between November 2017-June 2019. Institutional ethical committee approval was taken and written informed consent was obtained from each patient after explaining the procedure and before recruitment.

The total sample size was 60 which was calculated using Raosoft sample size calculator (confidence interval: 95% and estimated population size was 70) and the patients were randomized into two groups of 30 each-groups A and B using a sealed envelope enclosing a random number which was generated by computer.

Group A underwent micro needling and group B was subjected to micro needling followed by application of topical autologous PRP. Both groups were subjected to monthly treatment sessions for 3 months and follow up was done at one month (First follow up) and three months (Final follow up) after the final treatment sitting.

Inclusion criteria

All patients clinically diagnosed as having melasma, aged 18-50 years with skin types III, IV, V and patients who hadn't received any treatment except sunscreen for the last 30 days were included in the study.

Exclusion criteria

Patients having melasma with history of keloid, active inflammation, diabetes mellitus, collagen vascular disease, bleeding disorders, pregnant or lactating, anticoagulant therapy and unreasonably high expectations were excluded from this study.

Patient's clinical photographs were taken at every visit (baseline, before every subsequent session and one month after final treatment). Evaluation of the patients was done by the Melasma area and severity index (MASI) scoring using three parameters, (a) Percentage of total area involved (b) Darkness and (c) Homogeneity, at baseline, after one month and three months following the last treatment session which were calculated by an independent observer not related to the study.

The treatment responses of patient's were evaluated using a four-point grading system based on the percentage of improvement of the MASI scores: I. Excellent (>75-100%; near normal), II. Significant (>50-75%; marked lightening), III. Moderate (>25-50%; moderate lightening) and IV. Slight (0-25%; no change to slight lightening).

Patient's satisfaction score

The patients were advised to score their satisfaction in both groups on a scale of 1-10 with 1 being the worst and 10 being the best. The mean was calculated in both the groups and the results were analysed statistically (Figure 1).

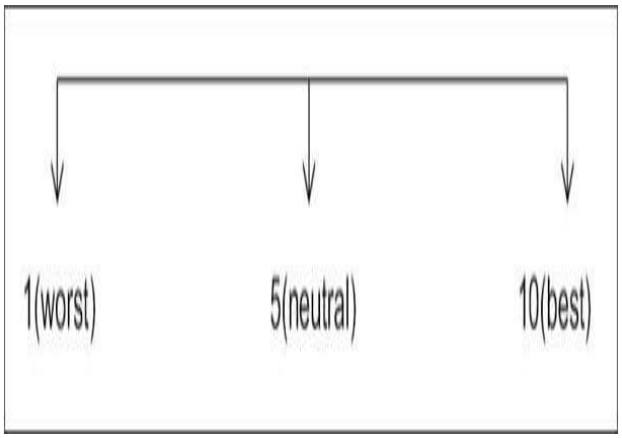

Figure 1: Patient visual analog score.

Dermaroller

Dermaroller with 192 needles and 1 mm depth was used for micro needling procedure.

PRP preparation

A two-stage centrifuging process was done using a Remi R8C centrifuge device to procure PRP. Under aseptic conditions, 5 ml of patient's whole blood was taken in a vial containing an anticoagulant.[6,7] It was centrifuged at 1500 rpm for 10 minutes. PRP, platelet-poor plasma (PPP) and few red blood cells (RBC) were taken in another tube and rotated at 3000 rpm for 20 minutes. The upper section containing PPP and PRP were aspirated and mixed in insulin syringes and were topically smeared after micro needling treatment.

Treatment protocol

Micro needling was done after achieving adequate anaesthesia after applying eutectic mixture of local anaesthetic. Uniform formation of small pinpoint bleeders marked the treatment endpoint. The bleeders were washed off with saline solution and topical autologous PRP preparation was then applied over the area. The patient remained in a supine position until the site of the PRP application dried up. This procedure was done monthly for three sittings.

Post-procedure care

Post procedure the patients were instructed to avoid washing of the face for one hour. The patients were counselled about the possibility of experiencing redness and swelling over treatment sites for 2-3 days post procedure and which could be minimized by applying icepacks. Post-treatment the patients were advised to apply only physical sunscreen and the patients were called up for final follow up at 3 months post-treatment.

Statistical analysis

A paired t test was adopted to compare the improvement in each group before and after treatment and also with the follow-up. An unpaired t test was applied to compare the improvement as well as satisfaction scores between the two groups. All the statistics were collected as a number, percentage, mean, median and standard deviation. The $p<0.05$, was considered statistically significant. All the calculations were done using Microsoft excel (version: Microsoft office professional plus 2016 for windows). The flowchart of patients in the study given in (Figure 2).

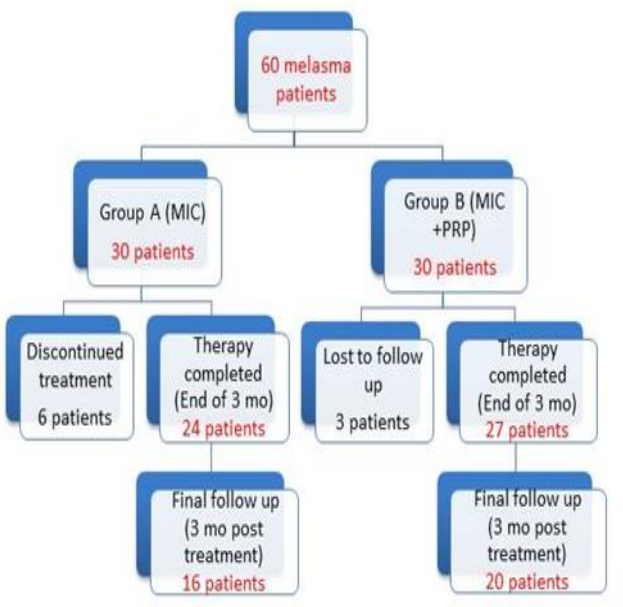

Figure 2: Flowchart of patients.

RESULTS

A total of 60 patients diagnosed with melasma were found to be eligible and enrolled in our study into two groups of 30 each. Out of which, 24 patients in group A and 27 patients in group B completed all the treatment sessions and were selected for analysis. Six patients withdrew from the study in between from group A due to dissatisfaction with the treatment. Three patients from group B were lost to follow up. There were 20 males and 31 females out of total 51 in the final analysis. The mean age of participants was 39.5±5.3 (years) in group A and 40±5.95 in group B. The mean duration of disease was 11.4±6.2 (months) in group A and 12.5±6.5 in group B. Out of 51 melasma patients, 29 patients were having the malar type and 22 were having centro-facial type of melasma. The demographic and clinical characteristics of patients are given in Table 1.

Table 1: Patient demographic.

Patient characteristics	Group A (micro-needling) n=24 (%)	Group B (micro needling + PRP), n=27 (%)	P value
Age (years) mean ± SD (Range)	39.5±5.3 (31-50)	40.0±5.95 (30-50)	0.7526
Sex			
Male	10 (42)	10 (37)	0.5029
Female	14 (58)	17 (63)	
Duration of illness (months)			
<6 months	5 (21)	6 (22)	
>6 months	19 (79)	21 (78)	0.5394
Mean±SD (Range)	11.4±6.2 (3-26)	12.5±6.5 (4-30)	
Distribution of melasma			
Malar	14 (58)	15 (56)	0.6965
Centro-facial	10 (42)	12 (44)	
Skin type			
Type III	11 (46)	11 (41)	0.4715
Type IV	13 (54)	16 (59)	
Sun exposure time			
<1 hr (in 24 hr)	9 (38)	10 (37)	0.9522
>1 hr (in 24 hr)	15 (62)	17 (63)	
Usage of sunscreen			
Yes	10 (42)	9 (33)	0.2218
No	14 (58)	18 (67)	

The mean baseline MASI score of group A was 10.19±6.2 and mean final score after one month of the last treatment session (First follow up) was 7.6±5.4. In group B the mean baseline MASI score was 10.63±5.9 and mean final score was 4.94±3.5. There was a statistically significant difference in MASI reduction when the baseline scores were compared with the final scores of both groups individually. While the before and after scores were extremely significant in group B

(p<0.0001) but in group A it was highly significant (p<0.001). The baseline scores for both groups A and B when compared were not statistically significant (p=0.7960) which suggests that the severity of melasma was comparable at the start of treatment. The final mean scores after treatment for group A and B was found to be just significant (p=0.045) which suggests that though there was a significant improvement in both groups, addition of PRP in group B had a superior effect in the outcome as there was better reduction of MASI scores (Table 2). Out of 24 patients in group A, 15 patients had moderate improvement while 9 had slight improvement. Whereas out of 27 patients in group B, 1 patient had excellent improvement, 16 patients showed significant improvement while 10 patients had moderate improvement. So better outcomes can be seen in group B where PRP had an additional beneficial effect (Table 3) Group A patients experienced a mean satisfaction score of 4.7±1.1 while patients in group B showed a mean satisfaction score of 6.9±1.4. P value was found to be extremely significant (Table 4).

Table 2: Comparison of MASI scores.

Variables	Group A (micro needling)			Group-B (micro needling + PRP)			Group A vs group B		
	Before	After	P value	Before	After	P value	P value	Before	After
Mean ± SD	10.2±6.2	7.6±5.4	0.001	10.6±5.9	4.9±3.5	0.0001		0.796	0.0457

Table 3: Comparison of percentage of improvement of MASI scores.

Degree of improvement	Group A, (n=24) (%) (micro needling)	Group B, (n=27) (%) (micro needling + PRP)
Excellent improvement (>75-100%)	-	1 (3.7)
Significant improvement (>50-75%)	-	16 (59.2)
Moderate improvement (>25-50%)	15 (62.5)	10 (37.0)
Slight improvement (0-25%)	9 (37.5)	-

Table 4: Comparison of patient satisfaction score in both groups.

Patient Satisfaction score	Group A (Micro needling)	Group B (Micro needling + PRP)	P value
Mean score ± SD	4.7±1.1	6.9±1.4	0.0001

The mean MASI scores at 3 months post-treatment (final follow up) were also compared with that of the baseline and 1-month post-treatment (First follow up). The 16 patients from group A and 20 patients of group B visited for the final follow up at 3 months post-treatment. In group A the mean MASI scores at final follow up were found to be 8.9±5.1 while in group B it was found to be 5.6±4 which suggests that the mean MASI scores were maintained even after 3 months post-treatment. It was seen better maintained in group B as compared to group A which might be due to the addition of PRP in group B (Figure 3 to 6).

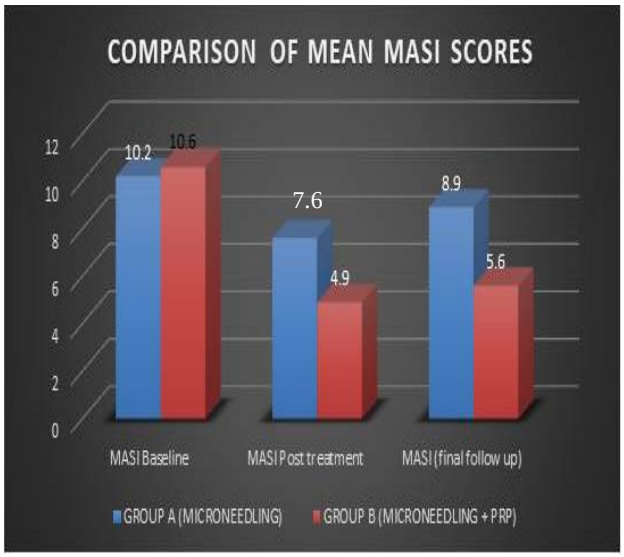

Figure 3: Pre and post treatment MASI comparison.

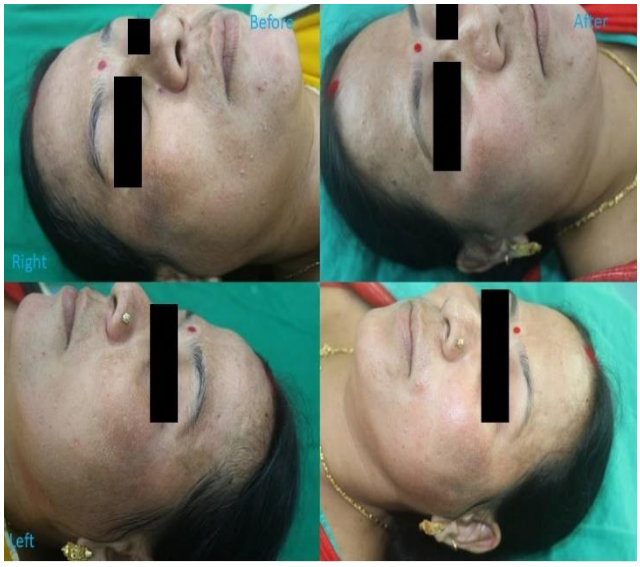

Figure 4: Before and after photographs of patient 1 (group B).

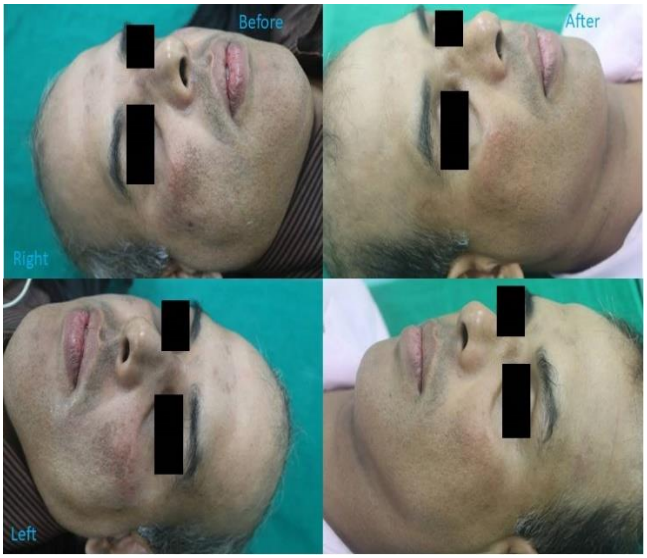

Figure 5: Before and after photographs of patient 2 (group A).

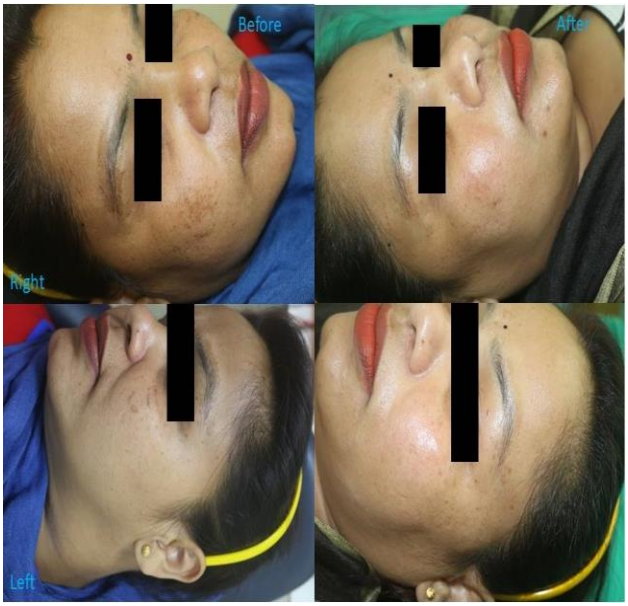

Figure 6: Before and after photographs of patient 3 (group B).

The side effects were transient and well tolerated by all patients. Mild pain was experienced during the procedure. Mild erythema and localized edema were seen in almost all patients which typically resolved within 48 to 72 hours. But the patients observed less downtime in group B receiving PRP (in form of redness and swelling after the procedure) which might be attributed to the anti-inflammatory effects of PRP. No other significant adverse effects were seen in any patients.

DISCUSSION

Despite the available treatment options, effectively treating melasma remains a challenge since topical treatment shows varying results while laser therapy provides unpredictable results. So, we have conducted the present study using micro needling and PRP to see the response in melasma as few previous studies have shown promising results with no significant side effects. In group A, 42% were males and 58% were females. While the proportion of males and females in group B was 37% and 63% respectively. There was no significant difference between groups A and B (p=0.5029) in relation to gender distribution. However, females outnumbered males in both groups. This is also in accordance with Sarkar et al where 74% were females and 26% males.[8] Krupashankar et al observed 24.4% males and 75.6% females in his study.[9] Similar results were seen by Achar et al and Vazquez et al and other previous reports and literature where female preponderance was seen in melasma.[10,11] This can be linked to hormonal factors and also females are found to be more apprehensive about their skin problems which may have contributed to their higher percentage seeking medical attention in various studies. The mean age of the patients in group A was 39.5±5.3 years as compared to group B with 40±5.95 years, which showed no statistically significant difference in the age groups (p=0.7526). The age group in our study ranges from 30-50 years while majority belong to age group of 30-40 years (59%). This was in accordance to the study by Yalamanchili et al and Sarkar et al where the mean age of patients was 37.13 years and 38.02 years respectively.[8,12] Achar and Rathi found similar results in their study with mean age of 33.45 years.[10] However, in a study by Kalla et al, melasma was seen commonly in the younger age group where 87% of patients belong to age group of 20-40 years.[13] Majority of our patients (71% in group A and 72% in group B) had melasma for more than 6 months duration which is in accordance with the study by Yalamanchili et al and Kalla et al.[12,13]

The majority of the patients in our study group (58% in group A and 56% in group B) had a malar pattern of melasma. Rest had centro-facial type and there was no mandibular type in our study. These findings were similar with the study conducted by Sarkar et al and Hexsel et al were 42.8% and 90.1% of patients respectively were having a malar type of melasma.[8,14] However, Krupashankar et al reported a similar number of centro-facial and malar patterns of melasma-42% and 39% respectively in their study.[9] In our study, about 43% of patients belong to skin type III and 57% of patients belong to skin type IV. This is in accordance with Sarkar et al where the majority of patients (48.3%) were having skin type IV which suggests that melasma is more prevalent in darker skin types.[8]

Sun exposure was seen in almost all patients in our study population. The majority of our patients (63%) had a duration of exposure greater than one hour. These results are similar to the study by Yalamanchili et al suggesting the fact that melanogenesis stimulated by UV rays had a major role in melasma.[12] Overall, 37% of our patients

were using regular sunscreen which implies that most of the patients in our study group were not having regular sun protection.

Fabbrocini et al compared the efficacy of depigmenting serum monotherapy with that of combination of micro needling along with depigmenting serum in treatment of melasma and concluded that the combination treatment to be more effective than topical depigmenting serum monotherapy.[15] They also suggested the enhancement of transdermal drug delivery by the use of micro needling. Budamakuntla et al evaluated the therapeutic efficacy and safety of combination of micro needling and tranexamic acid application with that of tranexamic acid microinjections in patients of melasma and concluded that the combination to be more effective which could be the result of deeper and uniform delivery of drug through microchannels created by micro needling.[16] Lima et al studied the effectiveness of micro needling in patients with recalcitrant melasma followed by the application of triple combination cream daily and observed a very good response in almost all patients.[17] Lima et al in another pilot study observed both clinical and histological improvement by the use of micro needling followed by the application of triple combination cream daily in patients of refractory facial melasma.[18] Ismail et al in a first of its kind study, evaluated the efficacy and safety of a combination of micro needling and topical vitamin C in the treatment of melasma and found significant improvement from the baseline value.[19]

Very few studies are present in literature regarding the use of PRP in the treatment of melasma. Cayirli et al successfully treated one patient with centro-facial melasma with autologous PRP injections and observed 80% improvement in epidermal pigmentation at the end of the third session.[20] Ch et al treated two patients of melasma with autologous PRP injections along with a monthly Q-switched Nd YAG laser and topical alpha-arbutin application which showed improvement in mean MASI score from baseline values.[21] However, recurrence was noticed in one patient at six months follow up. In our study, there was no statistically significant difference in the mean MASI score in group A (10.19±6.2) and group B (10.6±5.9) at the baseline. However, at the first follow up visit (one month after last treatment session) a significantly greater reduction was seen in the mean MASI score in group B as compared to group A ($p=0.045$) implying better pigment reduction in micro needling and PRP combination group than in micro needling group alone.

These findings were in accordance to a study by Hofny et al where PRP was used in two delivery methods i.e., micro needling using dermapen and microinjections with meso needles and there was a statistically significant reduction of mean MASI scores before and after treatment ($p<0.000$).[22] There are no other documented studies in literature combining the above two procedures in the treatment of melasma.

We also evaluated the degree of improvement based on the percentage reduction of MASI scores before and after treatment. Out of 24 patients in group A, 15 (62.5%) patients had moderate improvement and 9 (37.5%) patients had slight improvement. Whereas out of 27 patients in group B, 1 (3.7%) patient had excellent improvement, 16 (59.2%) patients had significant improvement and 10 (37%) patients had moderate improvement. These findings clearly revealed that better improvement was seen in group B where PRP had an additional beneficial effect and similar results were seen when compared to a study by Hofny et al where higher percentage of patients were having significant (21.7%) and moderate improvement (43.5%) in patients receiving PRP treatment with dermapen.[22]

The patient's mean satisfaction score after the final treatment session in group B (6.9±1.4) was found to be better than group A (4.7±1.1) and the values were statistically significant ($p=0.0001$). The patients have also followed up three months post-treatment in our study and the mean MASI scores were calculated. We observed a better-sustained reduction of MASI scores in group B (5.6±4) as compared to group A (8.9±5.1) even after three months post-treatment. This finding can be related to a randomized controlled study by Trink et al where they have got sustained response even at 1 year follow up after giving monthly PRP treatment for 3 months for androgenetic alopecia.[23] This leads to a hypothesis of the sustained response of PRP even after treatment and is a significant finding in relation to therapy in melasma which might be due to the persistence of growth factors in melasma lesions. But longer follow up duration is required for the justification of this finding in our study.

The secondary objective of our study was to evaluate the side effects of the procedure in the two groups. Transient adverse events were experienced but were of no bother to the patients. Mild pain was experienced during the procedure. Mild erythema and localized edema were seen in almost all patients which typically resolved within 48 to 72 hours. But the patients observed less downtime in group B as compared to Group A which might be attributed to the anti-inflammatory effects of growth factors like hepatocyte growth factor (HGF) of PRP.[24] Which was in accordance to the findings in a study by Kar et al where fractional CO_2 was combined with topical autologous PRP in the treatment of acne scars.[7] No other significant side effects were observed in any patients.

Limitations

Considering that all patients had facial melasma, we were not able to do a histopathological evaluation to assess the depth of involvement. Long term follow-up of patients could not be done due to the time-bound nature of the study. Lack of a third arm containing PRP alone to compare with the two treatment arms in our study. No comparison with established treatment such as hydroquinone was done in our study.

CONCLUSION

We can conclude that the treatment arm comprising of a combination of micro-needling with application of topical autologous PRP was found to be more efficacious in terms of higher mean MASI score reduction and better patient satisfaction as compared to treatment with micro needling alone. Both the procedures are relatively safe and had no significant side effects except for mild pain due to micro needling, post-procedure erythema and edema. But the downtime is relatively less in combination group as compared to micro needling alone.

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Ethical approval: The study was approved by the institutional ethics committee

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