The Efficacy of Platelet-Rich Plasma in the Treatment of Melasma: A Pilot Study

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Abstract

Melasma is a chronic acquired hyperpigmentation disorder that predominantly affects women and significantly impacts quality of life. Current evidence suggests that melasma involves not only epidermal melanogenesis but also dermal photoaging changes, which may contribute to disease persistence and recurrence. Conventional treatments primarily target epidermal pigment and are often limited by adverse effects and relapse after treatment was discontinued. Platelet-rich plasma, an autologous product rich in growth factors, has emerged as a potential therapeutic option; however, its efficacy as a monotherapy remains insufficiently explored. This prospective pilot study was conducted using a split-face randomized design, allowing direct intra-individual comparison. Ten participants with epidermal or mixed-type melasma received intradermal PRP injections on one randomly assigned side of the face for three monthly sessions. Clinical outcomes were assessed over a 12-week period using the modified Melasma Area and Severity Index (mMASI), melanin index, erythema index, patient satisfaction scores, and overall clinical improvement. Statistical analysis was performed using one-way repeated measures ANOVA, with statistical significance defined as $p < 0.05$. A significant reduction in mMASI scores was observed at Week 12 compared with baseline ($p = 0.038$). Patient satisfaction also increased significantly throughout the study period ($p < 0.001$). In contrast, reductions in melanin and erythema indices were observed but did not reach statistical significance. Reported adverse events were mild and transient. These findings suggest that intradermal PRP monotherapy is safe and may provide clinically meaningful improvement in melasma. Further investigation in larger controlled studies is warranted.

Keywords: *Melasma, Platelet-rich plasma, Hyperpigmentation, mMASI*

1. Introduction

Melasma is a common acquired hyperpigmentation disorder characterized by symmetrical brown to gray-brown macules on sun-exposed areas of the face (Ghasemiyeh et al., 2024; Kwon et al., 2019). Melasma primarily affects women of reproductive age and individuals with darker skin phototypes, particularly Fitzpatrick skin types III–V (Handel et al., 2014; Kwon et al., 2019). Although melasma is not physically symptomatic, its impact on appearance can lead to emotional distress and a reduced quality of life (Ghasemiyeh et al., 2024; Handel et al., 2014).

In the past, melasma was considered a disorder primarily driven by ultraviolet radiation and hormonal influences, leading to increased melanocyte activity and melanin production (Kwon et al., 2019; Parać & Bukvić Mokos, 2024). However, current studies suggest that this explanation is incomplete. Melasma is now recognized as a chronic photoaging-related condition rather than an epidermal pigment abnormality (Ghasemiyeh et al., 2024; Kwon et al., 2019). Histopathological studies have demonstrated that lesional skin commonly shows solar elastosis, disruption of the basement membrane, an increased vascularity, and increased number of mast cells (Kwon et al., 2019). These changes indicate that an altered dermal environment plays an important role in sustaining melanocyte stimulation and may contribute to the persistence and recurrence of the disease (Ghasemiyeh et al., 2024; Kwon et al., 2019).

Conventional management of melasma relies on strict photoprotection and topical depigmenting agents. Hydroquinone remains the standard first-line therapy, often prescribed as part of triple-combination regimens (Ghasemiyeh et al., 2024; Parać & Bukvić Mokos, 2024). Other treatment options include chemical peels, energy-based devices such as lasers, and systemic therapies including oral tranexamic acid (Ghasemiyeh et al., 2024; Jo et al., 2024; Kwon et al., 2019). However, these treatments have significant limitations. Long-term use of hydroquinone may cause irritation or exogenous ochronosis, while energy-

based treatments are associated with a risk of post-inflammatory hyperpigmentation, particularly in darker skin types (Ghasemiyeh et al., 2024; Kwon et al., 2019; Rodriguez & Mayrovitz, 2024). Many standard therapies focus only on epidermal pigment without correcting the underlying dermal photoaging. This limitation contributes to the high recurrence rates observed after treatment discontinuation (Boparai et al., 2020; Kwon et al., 2019).

Platelet-rich plasma (PRP) has recently gained attention as a potential therapeutic option in dermatology. It is an autologous concentration of platelets containing multiple growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEG), and transforming growth factor-beta (TGF-β) (Asubiaro & Avajah, 2024; Platelet-Rich Plasma in Dermatologic Practice, 2021).

TGF-β has been shown to suppress melanogenesis through downregulation of microphthalmia-associated transcription factor and inhibition of tyrosinase activity (Boparai et al., 2020; Vladulescu et al., 2023). In addition, emerging evidence suggests that TGF-β may be involved in the modulation of the canonical Wnt/β-catenin signaling pathway, which plays a critical role in melanocyte proliferation and differentiation. Activation of this pathway promotes melanogenesis through β-catenin–mediated upregulation of microphthalmia-associated transcription factor and tyrosinase, whereas TGF-β has been shown to inhibit this signaling cascade, resulting in reduced melanogenic activity. Through this mechanism, PRP may contribute to the regulation of pigment production. Furthermore, PRP promotes collagen synthesis and extracellular matrix remodeling, which may help restore dermal integrity, including improvement of basement membrane disruption and solar elastosis observed in melasma (Ghasemiyeh et al., 2024; Vladulescu et al., 2023; Zhao et al., 2021).

Existing studies demonstrate diversity in platelet-rich plasma preparation protocols, including differences in centrifugation and delivery methods, leading to variable clinical outcomes (Parać & Bukvić Mokos, 2024; Zhao et al., 2021). While some studies report comparable or superior efficacy of platelet-rich plasma relative to established treatments, others have failed to demonstrate statistically significant results. Moreover, platelet-rich plasma has frequently been investigated as an adjunct to other procedures, such as microneedling or laser therapy, making it difficult to determine its independent therapeutic effect (Abd Elraouf et al., 2023) As a result, the clinical efficacy of platelet-rich plasma as a monotherapy remains unclear (Zhao et al., 2021).

In addition, most previous studies have primarily focused on pigmentary outcomes, with limited evaluation of patient-reported improvement and overall skin improvement. Given that melasma is increasingly recognized as a condition involving both epidermal and dermal pathology, this narrow focus may not fully capture the therapeutic effects of platelet-rich plasma. Therefore, there remains a need to clearly define the clinical efficacy and safety of intradermal platelet-rich plasma as a standalone treatment.

Accordingly, this pilot study was conducted to evaluate the clinical efficacy and safety of intradermal platelet-rich plasma monotherapy in patients with melasma.

2. Objectives

1. To evaluate the clinical efficacy of intradermal platelet-rich plasma in the treatment of melasma using both objective measures (modified Melasma Area and Severity Index [mMASI]and Mexameter readings) and subjective measures (patient satisfaction score and patient -reported improvement score).

2. To evaluate adverse events, including pain, erythema, edema, bruising, pruritus, and irritation, as reported by patients.

3. Materials and Methods

3.1 Study design and population

This study was designed as a prospective exploratory pilot study involving ten participants with clinically diagnosed melasma, recruited from the dermatology outpatient clinic. The small sample size was considered appropriate for a pilot study aimed at generating preliminary data on clinical efficacy, safety, and feasibility of intradermal platelet-rich plasma (PRP) monotherapy prior to larger controlled trials. The inclusion criteria were as follows:1.) Patients aged 18-65 years with Epidermal and Mixed type melasma. 2.) Fitzpatrick skin types III-V. The exclusion criteria were as follows: (1) use of oral contraceptives or hormone replacement therapy; (2) pregnancy or lactation; (3) disorders of hematopoiesis; (4) current or recent

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use of other melasma treatments, including chemical peels, skin-lightening agents, topical retinoids, topical hydroquinone within the past 3 months, or laser treatment within the past 6 months; (5) presence of active systemic disease; (6) local skin infection or inflammation in the treatment area; and (7) regular use of oral tranexamic acid.

Participants were assigned to treatment sides using an alternating allocation method based on enrollment order (odd/even numbering), whereby patients with even numbers received PRP on the right side of the face and those with odd numbers on the left side. This method represents quasi-randomization rather than true randomization and was selected due to the exploratory nature of this pilot study.

3.2 Study protocol

1. All participants provided written informed consent prior to enrollment. The study protocol was reviewed and approved by the institutional ethics committee, and subject confidentiality was maintained through the use of coded identification numbers. Before each treatment and assessment session, participants were instructed to remove facial makeup and cleanse their face with a facial cleanser and water.
2. Standardized clinical photographs were obtained at baseline and at each follow-up visit prior to objective assessment.
3. Prior to treatment, a topical anesthetic cream was applied to the treatment area under occlusion for 30–45 minutes and removed before injection. Participants received monthly platelet-rich plasma treatments for a total of three sessions. Subjects were assigned numbers according to enrollment order; those with even numbers received platelet-rich plasma on the right side of the face, and those with odd numbers on the left side. Platelet-rich plasma was injected intradermally under strict aseptic conditions using a 32-gauge needle and a 1-mL syringe, with approximately 0.1 mL administered at 1-cm intervals over the lesional area, for a total volume of 2 mL per half-face.
4. For platelet-rich plasma preparation, 10 mL of venous blood was collected via venipuncture using a 21-gauge catheter and transferred into tubes containing 3.2% sodium citrate as an anticoagulant under sterile technique. Samples were centrifuged using a tabletop centrifuge (UGAIYA L500 Low -Speed Centrifuge) at 3,500 rpm for 5 minutes. Following centrifugation, approximately 2–3 mL of platelet-rich plasma was carefully aspirated using a 3-mL syringe. The platelet concentration of the prepared platelet-rich plasma was not quantitatively measured in this pilot study, which represents a limitation. However, based on the standardized centrifugation protocol used, the platelet-rich plasma obtained was expected to have a platelet concentration higher than that of baseline whole blood.
5. Post-procedure, participants were instructed to avoid washing the face for 4 hours, refrain from applying makeup for 24 hours, and use broad-spectrum sunscreen with SPF 50 while minimizing sun exposure throughout the study period.

3.3 Outcomes assessment

Clinical improvement of melasma was evaluated using the modified Melasma Area and Severity Index (mMASI), and was assessed by a single dermatologist. To reduce assessment bias, the evaluating dermatologist was blinded to the side of the face receiving PRP treatment. Objective pigmentary changes were assessed using melanin index and erythema index measurements obtained with a Mexameter device. Patient satisfaction was evaluated using a visual analog scale ranging from 0 (very dissatisfied) to 10 (very satisfied). In addition, participants assessed their overall clinical improvement using a 4-point scale, categorized as excellent (>75% improvement), good (50–75% improvement), fair (25–50% improvement), or poor (<25% improvement or worsening).

Adverse events were assessed at each visit. After each session of PRP injection, participants were specifically questioned regarding the occurrence of common dermatologic adverse events, including pain, erythema, edema, bruising, eczema, and skin irritation. Participants were also encouraged to report any additional symptoms not listed. The onset, duration, and any interventions required for adverse events were documented. All reported events were recorded by the investigator and reviewed for clinical relevance. Any

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significant or unexpected adverse reactions were monitored until resolution, and appropriate medical management was provided when necessary.

3.4 Statistic analysis

Descriptive analysis was used to summarize the demographic data. One-way repeated ANOVA was used to analyze changes across different time points in the same condition for mMASI score, Melanin index and Erythema index. A P value <0.05 was considered statistically significant. Data were analyzed using SPSS software. Descriptive statistics were used to summarize adverse effects, patients' satisfaction scores and overall clinical improvement score.

4. Results and Discussion

4.1 Result

The pilot study included a total of 10 participants clinically diagnosed with melasma who were screened for eligibility.

Baseline Characteristics

Baseline patient characteristics are shown in Table 1. All 10 participants were female with a mean age of 50 years. The majority of subjects had no underlying diseases, while 20% had dyslipidemia and 10% had chronic hepatitis B. Regarding medication and allergy history, 90% of participants were not on any medication, and 80% had no known drug allergies.

The mean duration of melasma was 9.10 ± 6.19 years. Half of the participants reported a family history of melasma. Sunscreen use was reported by 80% of participants, with daily use (7 days per week). The Fitzpatrick skin type distribution showed that 50% were type IV, 30% were type V, and 20% were type III. The majority of participants presented with mixed-type melasma, while 20% had the epidermal type.

Table 1 Baseline patient characteristics

Characteristics	n (%)	Mean ± SD
Sex		
Female	10 (100)	
Age		50±5.12
Underlying disease		
No	7 (70)	
DLP	2 (20)	
Chronic hepatitis B	1 (10)	
Medication		
No	9 (90)	
Atorvastatin 20mg/d	1(10)	
Allergy		
No	8 (80)	
Avelox	1 (10)	
Dicloxacillin metoclopramide	1 (10)	
Melasma duration (year)		9.10±6.19
Melasma duration (month)		0
Family history of melasma		
No	5 (50)	
Yes	5 (50)	
Occupation		
Nurse	5 (50)	
Practical nurse	1 (10)	
State enterprise employee	2 (20)	
Salesman	1 (10)	

Table 1 Cont.

Characteristics	n (%)	Mean ± SD
Freelance	1 (10)	
Sunscreen use		
5-6 days per week	2 (20)	
7 days per week	8 (80)	
Fitzpatrick scale		
grade III	2 (20)	
grade IV	5 (50)	
grade V	3 (30)	
Melasma type		
Epidermal	2 (20)	
Mixed	8 (80)	

Abbreviations: SD, standard deviation; DLP, dyslipidemia

Patient Satisfaction and Clinical Improvement

Patient satisfaction scores increased throughout the treatment course. The mean satisfaction score at Week 4 was 4.90 (SD = 1.45), increasing to 6.30 (SD = 1.42) at Week 8, and 7.70 (SD = 2.00) at Week 12. Statistical analysis using One-Way Repeated -measures ANOVA confirmed a significant difference in satisfaction scores across the time points ($F = 17.523$, $p < 0.001$). Figure 1 illustrates the upward trend in estimated marginal means of satisfaction scores from Week 4 to Week 12.

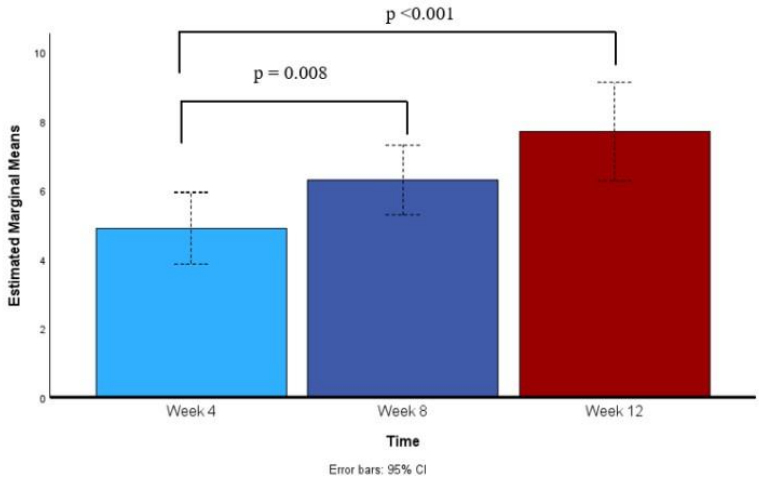

Figure 1 Comparison of Mean Satisfaction Scores at Week 4, Week 8, and Week 12

Overall clinical improvement was assessed at the end of the study 40% of patients reported "Excellent" improvement (>75% improvement), 40% reported "Good" improvement (50–75% improvement), and 20% reported "Fair" improvement (25–50% improvement). No patients reported poor results. These findings were shown in Table 2.

Table 2 Overall clinical improvement result

Overall improvement result	n (%)
Fair (25–50% improvement)	2 (20)
Good (50–75% improvement)	4 (40)
Excellent (>75% improvement),	4 (40)

Modified MASI score

To compare mean modified Melasma Area and Severity Index (mMASI) scores at baseline (week 0) and at weeks 4, 8, and 12, a one-way repeated measures ANOVA was performed. Prior to the analysis, the assumption of sphericity was tested and was not violated (p = 0.100). The mean mMASI scores showed a decreasing trend from week 0 to week 12. The mean mMASI scores was 7.50 (SD=4.12) at week 0, 7.10 (SD=3.81) at week 4, 5.40 (SD=3.37) at week 8, and 5.20 (SD=2.66) at week 12, as presented in Table 3. Pairwise comparisons of mean mMASI scores across time points revealed that at least one pair of weeks differed significantly at the 0.05 significance level (F = 6.474, p = 0.002). Detailed results are shown in Table 3.

Table 3 Comparison of mean mMASI scores at weeks 0, 4, 8, and 12 using one-way repeated measures ANOVA

Source	Sum of Squares	df	Mean Square	F	p-value
Time	41	3	13.667	6.474	0.002
Error	57	27	2.111		

Based on Table 3, the results indicate that at least one pair of weeks showed a statistically significant difference in mean mMASI scores. Therefore, pairwise comparisons were performed using the Bonferroni correction. The analysis demonstrated that a statistically significant difference in mean mMASI scores at the 0.05 level required a 12-week duration, with the mean mMASI at week 12 being significantly lower than that at week 0 by 2.30 points (mean difference = 2.30, p = 0.038). Detailed results are presented in Table 4 and Figure 2.

Table 4 Pairwise comparisons of mean mMASI scores at each time point using the Bonferroni correction

Time	Mean±SD	Mean difference (p-value)		
		Week 4	Week 8	Week 12
Week 0	7.50±4.12	0.40 (1)	2.10 (0.174)	2.30 (0.038)
Week 4	7.10±3.81	-	1.70 (0.070)	1.90 (0.107)
Week 8	5.40±3.37	-	-	0.20 (1)
Week 12	5.20±2.66	-	-	-

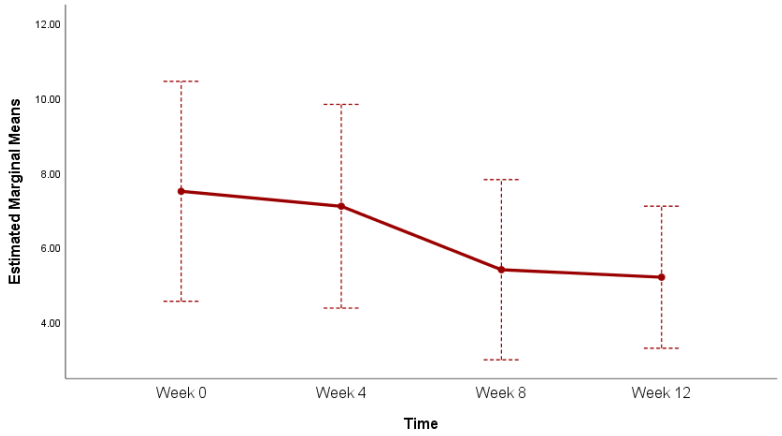

Figure 2 Modified MASI Score

Melanin Index and Erythema Index

The Melanin Index at baseline (week 0) and at weeks 4, 8, and 12 was compared using One-way repeated -measures ANOVA. Prior to the analysis, the assumption of sphericity was tested and found to be violated (p = 0.03). Therefore, the Greenhouse–Geisser correction was applied. The Melanin Index showed a downward trend over time, as illustrated in Figure 3. The reduction was not statistically significant (F = 0.542, *p* = 0.539), as shown in Table 5,6.

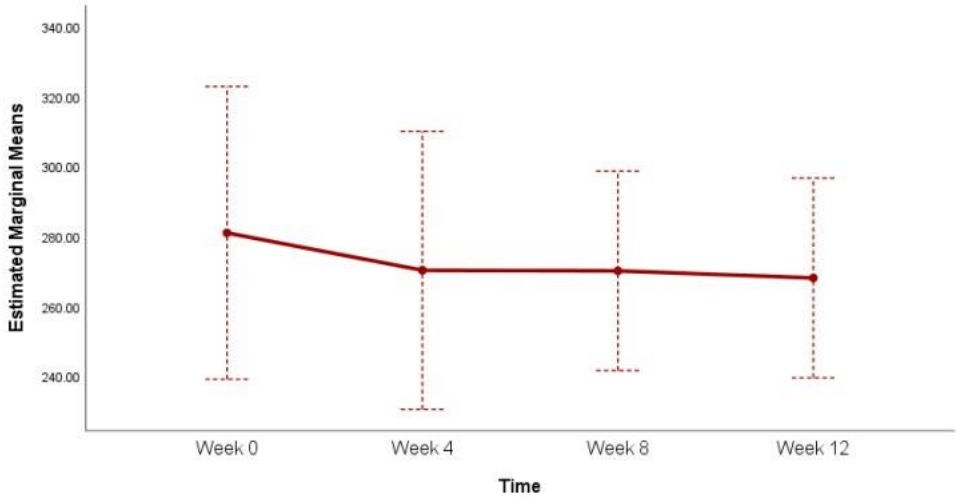

Figure 3 Melanin Index

Table 5 Comparison of mean Melanin Index at weeks 0, 4, 8, and 12 using one-way repeated-measures ANOVA

Source	Sum of Squares	df	Mean Square	F	p-value
Time	1019.967	1.450	703.547	0.542	0.539
Error	16947.533	13.048	1298.886		

Table 6 Comparison of mean Melanin Index at each time point using the Bonferroni correction

Time	Mean±SD	Mean difference (p-value)		
		Week 4	Week 8	Week 12
Week 0	280.93±58.53	10.70(0.476)	10.87 (1)	12.90 (1)
Week 4	270.23±55.59	-	0.17 (1)	2.20 (1)
Week 8	270.07±39.86	-	-	2.03 (1)
Week 12	268.03±39.93	-	-	-

The Erythema Index at baseline (week 0) and at weeks 4, 8, and 12 was compared using one-way repeated -measures ANOVA. Prior to the analysis, the assumption of sphericity was tested and not violated ($p = 0.405$).

The results demonstrated that the mean Erythema Index varied across the four time points. The mean Erythema Index was 362.00 (SD =54.38) at week 0, 374.67 (SD = 54.58) at week 4, 368.70 (SD =56.25) at week 8, and 370.40 (SD = 76.56) at week 12. However, these differences were not statistically significant at the 0.05 level ($F = 0.213$, $p = 0.887$). Detailed results are presented in Tables 7, and 8 and Figure 4.

Table 7 Comparison of mean Erythema Index at weeks 0, 4, 8, and 12 using one-way repeated-measures ANOVA

Source	Sum of Squares	df	Mean Square	F	p-value
Time	831.475	3	277.158	0.213	0.887
Error	35147.108	27	1301.745		

Table 8 Comparison of mean Erythema Index at each time point using the Bonferroni correction

Time	Mean±SD	Mean difference (p-value)		
		Week 4	Week 8	Week 12
Week 0	362±54.38	-12.67 (1)	-6.70 (1)	-8.40 (1)
Week 4	374.67±54.58	-	5.97 (1)	4.27 (1)
Week 8	368.70±56.25	-	-	-1.70 (1)
Week 12	370.40±76.56	-	-	-

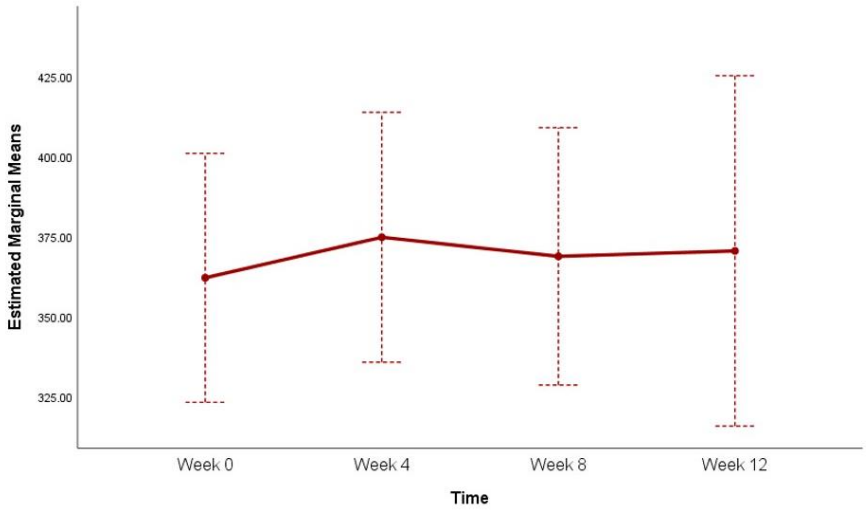

Figure 4 Erythema Index

Safety Evaluation: Pain Scores and Adverse Events

Pain scores were evaluated at Week 0, Week 4, and Week 8. The mean pain score was 3.30 (SD = 1.95) at baseline (Week 0), decreasing slightly to 2.90 (SD = 1.20) at Week 4, and 3.10 (SD = 1.37) at Week 8. A one-way repeated-measures ANOVA with Greenhouse–Geisser correction was performed. The test of sphericity was significant ($p = 0.007$), indicating a violation of the sphericity assumption. However, no statistically significant difference in pain scores was observed across visits ($F = 0.783$, $p = 0.416$).

Adverse events were minimal. At Week 0, bruising was observed in 20% of participants. At Week 4, no adverse events were reported. At Week 8, bruising was noted in 10% of participants. No serious adverse events, such as infection or skin irritation were reported.

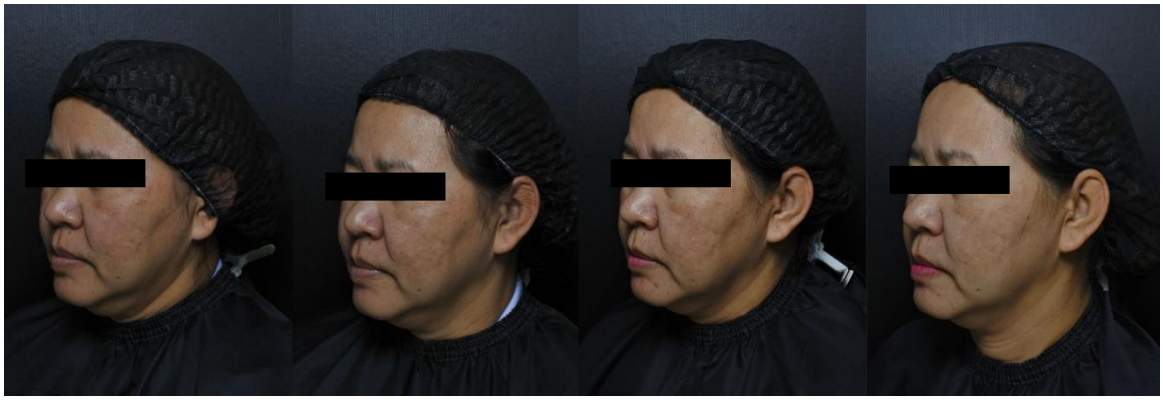

Figure 5 Digital photography from baseline and at Weeks 4, 8 and 12

4.2 Discussion

This pilot study evaluated the efficacy and safety of intradermal platelet-rich plasma as a monotherapy for the treatment of melasma. The results demonstrated a significant improvement in patient-reported satisfaction and modified MASI (mMASI) scores over a 12-week period, while objective measurements using the Melanin Index and Erythema Index did not show statistically significant changes. Importantly, intradermal platelet-rich plasma was well tolerated, with minimal and transient adverse events observed throughout the study.

The significant reduction in mMASI scores observed at Week 12 suggests that intradermal platelet-rich plasma may contribute to clinical improvement in melasma. These findings are consistent with previous studies evaluating PRP in melasma. For example, Hofny et al. (2019) and Tuknayat et al. (2021) reported significant clinical improvement in MASI scores following intradermal PRP treatment. Transforming growth factor-beta (TGF-β) has been shown to suppress melanocyte activity by downregulating the microphthalmia-associated transcription factor and reducing tyrosinase activity, thereby decreasing melanin production (Boparai et al., 2020; Vladulescu et al., 2023). In addition, PRP promotes collagen synthesis and the restoration of the extracellular matrix, which may improve the disrupted basement membrane and dermal photoaging changes commonly observed in melasma lesions (Ghasemiyeh et al., 2024; Zhao et al., 2021). These mechanisms may explain the gradual improvement in clinical severity reflected by mMASI scores, which include both lesion extent and pigmentation intensity.

Despite the clinical improvement, objective pigmentary assessment using the Melanin Index did not demonstrate a statistically significant reduction. This discrepancy between clinical scoring and instrumental measurements has been reported in previous studies and highlights the complex nature of melasma (Abd Elraouf et al., 2023). The lack of statistical significance despite a downward trend in the Melanin Index may be explained by several factors. First, the small sample size limits the statistical power of the study, reducing the ability to detect subtle changes. Second, the Mexameter primarily reflects epidermal melanin content and may not adequately capture improvements occurring in the dermal compartment. This is particularly relevant given that platelet-rich plasma is thought to exert its effects through dermal remodeling and the improvement of overall skin quality (Kwon et al., 2019; Vladulescu et al., 2023). Furthermore, melasma is increasingly recognized as a chronic photoaging-related disorder involving both epidermal and dermal pathology. Improvements in dermal structure can lead to visible clinical benefits that are not immediately detected by pigment-specific devices (Ghasemiyeh et al., 2024).This may also explain the significant increase in patient satisfaction observed in this study, as patients often perceive improvements in skin texture, brightness, and overall appearance beyond pigment reduction alone. In addition, variability in instrumental measurements should be considered. The Melanin Index may be influenced by factors such as probe pressure, skin hydration, and measurement site variability. These factors can reduce the sensitivity in detecting subtle changes over time. This measurement variability may further contribute to the lack of statistically significant findings despite observable clinical improvement.

A key strength of this study is the use of platelet-rich plasma as a standalone treatment. Many previous investigations have evaluated platelet-rich plasma in combination with other modalities, making it difficult to isolate the independent effect of PRP (Abd Elraouf et al., 2023; Zhao et al., 2021). In contrast, the present study focused on intradermal platelet-rich plasma monotherapy, thereby providing clear insight into its intrinsic clinical contribution. The observed improvement in mMASI scores and patient satisfaction suggests that platelet-rich plasma alone may offer therapeutic benefits, especially for patients who cannot tolerate conventional treatments.

As a pilot study, these findings should be interpreted as preliminary rather than definitive evidence of efficacy. The limitations of this study include a small sample size and the absence of a control group, preventing direct comparison with placebo or standard treatments. Although a split-face design was used for treatment allocation, the study did not perform direct comparisons between treated and untreated sides. Therefore, the findings should be interpreted as within-subject improvements rather than controlled side-to-side effects. Furthermore, the 12-week follow-up period may not be sufficient to assess long-term effectiveness and recurrence. Objective measurement tools for the Melanin Index may also have a limited ability to detect improvements at the dermal level following platelet-rich plasma treatment. Future studies with larger sample sizes, longer follow-up periods, and standardized platelet-rich plasma preparation protocols are needed to further clarify and better define the role of intradermal platelet-rich plasma as a standalone or adjunctive treatment for melasma.

5. Conclusion

This pilot study demonstrated that intradermal platelet-rich plasma is a safe and well-tolerated treatment for melasma with high patient satisfaction reported. Although objective melanin reduction did not achieve statistical significance in this study, the notable clinical improvement supports the role of platelet-rich plasma in improving overall skin quality in melasma. Platelet-rich plasma emerges as a promising therapeutic option, particularly for managing the dermal and photoaging aspects of this recalcitrant disease. Future research should involve a larger sample size and standardized protocol for platelet-rich plasma administration.

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