Evaluation of the Effectiveness and Safety of Platelet-Rich Plasma in the Treatment of Melasma. A Clinical Trial Study

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Abstract

Background: Melasma is a human melanogenesis dysfunctic that result in localized chronic acquired hypermelanosis of skin, its symmetrically on sun exposed areas of body and affected especially women in menacme. **Aim:** To assess if there's improvement of melasma by using intradermal PRP. **Patient & Method:** A prospective clinical trial study for evaluated effect of PRP in treatment of melisma. The study was conducted in Al-Karh General Hospital in Baghdad city, carried period 6 months from First September 2021 to end of April 2022. Total sample of this study was forty patients (melasma) by non-random sampling method according to special criteria that included in the study as a convenience sample. **Result:** PRP using in treatment of melasma as adjuvant therapy with other lines of treatment better than using alone. **Conclusions:** Because PRP as a treatment option has become popular in treatment of melasma more studies are required to elucidate it's benefits and limitation. We advise to use PRP in treatment of melasma as adjuvant therapy with other lines of treatment not alone.

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Introduction:

Melasma is a human melanogenesis dysfunction that results in localized, chronic acquired hyper melanosis of the skin. It occurs symmetrically on sun exposed areas of the body, and affects especially women in menacme. [1] The word melasma originates from the Greek root “melas”, which means black, and refers to its brownish clinical presentation, although the term “chloasma” (derived from the

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Latin chlóos and the Greek cloazein: greenish) is still used in the medical literature. [2]

Melasma is a common, acquired, circumscribed hyper melanosis of the face and occasionally of the neck and forearms, which significantly impacts the quality of life. Although it may affect any race, melasma is much more common in darker-skinned individuals. [3]

Seminal reports on melasma in the Western medical literature date back to 1934 and 1961, respectively. In the first, the author describes the case of a 20- year-old woman from London (England), who presented with brownish, upper lip lesion with well-defined margins and history of worsening after sun exposure.[4] In the second, the authors described in detail the cases of 15 patients between 25 and 43 years of age, from the region of Los Angeles (USA), who presented with symmetrical hyperpigmentation of the face of unknown etiology. [5]

PATIENTS AND METHODS:

A prospective clinical trial study for evaluated the effect of platelet-rich plasma in treatment of melasma. The study was conducted in alkhark general hospital in Baghdad city. The study was carried out for a period of 6 months from the first of September 2021 to end of April 2022. Target population in this study were patients with melasma who lived in Baghdad (male and female). Selected according to specific criteria and that have approval to participate in study.

The total sample of this study was forty patients (melasma), we selected by non-random sampling method according to specific criteria that included in the study as a convenience sample.

Clinical diagnosis of melasma was approved with follow up was done. Pigmentation was assessed using melasma area and severity index (MASI) at baseline and after 2 weeks for 8 months and outcome measure included global improvement scale (grades 1-4).

A two-stage (separation and concentration) centrifuging process was employed in the preparation of platelet-rich plasma. PRP centrifuge machine was pre-cooled up to 20ºC for 10 minutes. 15ml of whole blood was drawn from the patient by venipuncture and transferred into vacutainer containing 1.5 ml of ACD-A (acid citrate dextrose-A) anticoagulant. The vacutainer 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 3/4 of platelet poor plasma the was discarded and the concentrated PRP at the lower 1/4 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. Whole procedure was carried out under aseptic conditions. Four sessions were done at 15 days interval along with photographic assessment. Only physical sunscreen lotion was given to every patient for photoprotection.

Patients were follow up once in 2 weeks to assess the improvement and to look for any adverse effects. (MASI) score was

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calculated at each visit, and the percentage of improvement was calculated by deducting MASI score from pretreatment MASI score and dividing it by pretreatment MASI score. Photographs were taken (with iPhone phone) in a standardized position at baseline and week 10. so that the clinical investigator can assess melasma improvement according to her experiences. In this case, melasma improvement was graded along four scales: 1 = >75% lightening (excellent), 2 = 51-75% (good), 3 = 26-50% (fair), and 4 = 0-25% (poor).

Any adverse effect was noted and treated accordingly. Subjected assessment was done by patients based on level of satisfaction with treatment .

Result:

The total study sample was 40 patients, out of them were 90% female and 10% were male. The mean age of study sample was (34.13±5.928) with most prevalent of occupation types were house wife (72.5%). while 20% were teacher and 7.5% driver. regarding to marital status of study sample, the result found 80% were married and 44% un married. as shown in table 1.

Table 1: distribution of study sample according to sociodemographic characteristic.

AGE	**Mean**	**Std. Deviation**
	34.13	5.928
sex	Frequency	Percent
female	36	90
male	4	10
Total	40	100
Occupation	Frequency	Percent
driver	3	7.5
house wife	29	72.5
teacher	8	20
Total	40	100
marital state	Frequency	Percent
married	32	80
unmarried	8	20
Total	40	100

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Regarding to past history of previous pregnancy among study sample were 62% have previous pregnancy and only 38% didn't have any past pregnancy hx.as shown in figure 1.

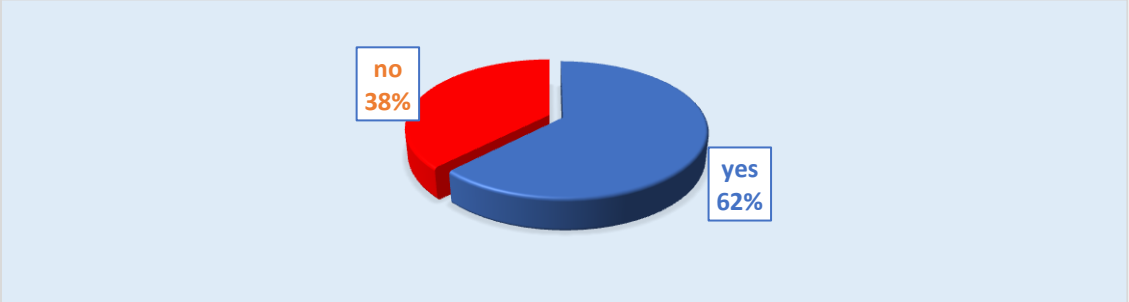

Figure 1: distribution of study sample according to pregnancy history.

Regarding to site of lesion the result of study showed the highest distribution were among malar (77.5%) and in chin (22.5%) with more than half of cases have duration of disease less than 5 years. also, the result found the most prevalent cases were skin type III and only 20% were skin type IV .as shown in table 2.

Table 2 : distribution of study sample according to skin lesion characteristic.

site of lesion	**Frequency**	**Percent**
malar	31	77.5
chin	9	22.5
Total	40	100
duration	**Frequency**	**Percent**
<5years	18	45
5years	22	55
Total	40	100
skin types	**Frequency**	**Percent**
III	32	80
IV	8	20
Total	40	100

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The result of current study showed the mean score of MASI before study were 10.3 and decrease after 2 weeks from beginning of study to become 9.8, after 4 weeks were 9.4, but after 8 weeks were 8,96 with statically significant association as shown in table 3,4 and figure 2.

Table 3: distribution of study sample according to MSAI score.

MASI SCORE	N	Mean	Std. Deviation
MASI before	40	10.3	3.227
MASIafter2weeks	40	9.8	2.788
MASIafter4weeks	40	9.4	2.649
MASIafter6w	40	9.06	2.621
MASIafter8weeks	40	8.96	2.622

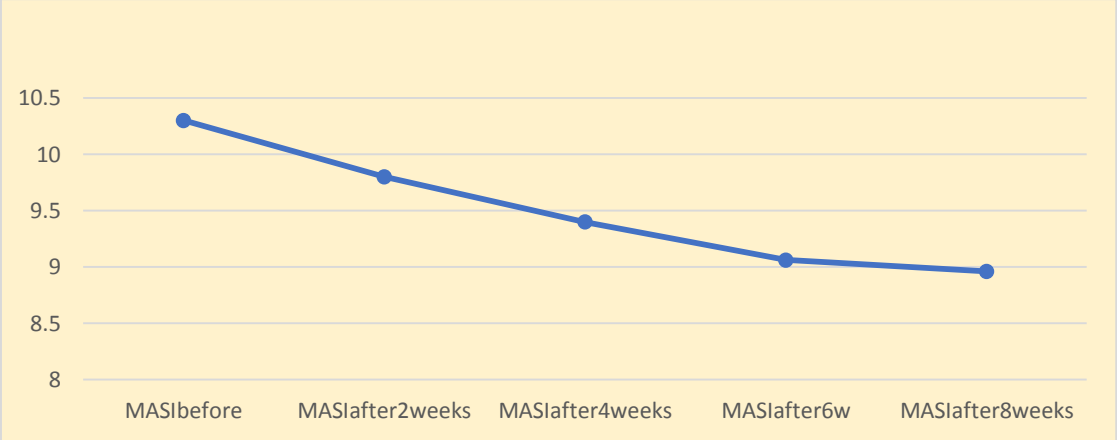

Figure 2: mean MSAI score of study sample.

Table 4: relation of mean MSAI score between deferent session

	Variables	N	Mean	Std. Deviation	P value
Pair 1	MASI before	40	10.3	3.227	0.001
	MASIafter2weeks	40	9.8	2.788	
Pair 2	MASIafter2weeks	40	9.8	2.788	0.001

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	MASIafter4weeks	40	9.41	2.649	
Pair 3	MASIafter4weeks	40	9.41	2.649	0.018
	MASIafter6weeks	40	9.06	2.621	
Pair 4	MASIafter6weeks	40	9.06	2.621	0.044
	MASIafter8weeks	40	8.96	2.622	

Table 5. score for assess melasma improvement

Grading	NO	Percent
Grade 1 (>75% excellent	0	0
Grade 2 (51-75 good)	6	15%
Grade 3 (26-50 fair)	8	20%
Grade 4 (0-25 poor)	26	65%
Total	40	100

DISCUSSION

Melasma is an acquired hyperpigmented skin disorder commonly found in iraq. its dermatological condition, which has a considerable psychological impact on the individual. It adversely affects the individual's quality of life as appearances play a significant role in self-perception as well as social interactions.[1]

Melasma remains therapeutically challenging, despite various treatment options available with multimodality. Treatment efficacy can vary due to several factors, including variability in clinical presentation and response to treatment amongst different genders, skin phototypes, and ethnicities. The effect of treatment also depends on the treatment time, the usage concentration, and the

addition of other components. A detailed history should be taken for each patient to exclude individuals at risk for untoward complications.[2]

In recent times, PRP is becoming to get attention in aesthetic medicine. PRP is blood plasma that has been enriched with platelets. As a concentrated source of autologous platelets, PRP contains several different growth factors and other cytokines that can stimulate various effects of soft tissue. Interestedly, we aimed to assess the effectiveness of PRP injection in melasma treatment. [3]

The 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, 2, epidermal growth factor, and mitogenic growth factors such as platelet-derived angiogenesis factor and fibrinogen . To our knowledge, only TGF-β1 has been investigated about its relation with melanogenesis.[4]

Kim et al.4 investigated the effects of TGF-β1 on melanogenesis by using a spontaneously immortalized mouse melanocyte cell line, and asserted that TGF-β1 significantly inhibits melanin synthesis in a concentrationdependent manner. They declared that TGF-β1 decreases melanogenesis via delayed extracellular signal-regulated kinase activation .[5]

In our therapeutic trial, 40 patients with melasma treated with intradermal PRP injection every 2weeks for 4 sessions. Results were assessed on the basis of percentage of reduction in baseline mMASIscore which showed

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21(52.5%) fair improvement, 32.5% had fair improvement and 15% good and 10% , with overall efficacy 15% so we can say that PRP have a role in melanogenesis but the efficacy is limited in our people. The improvement of pigmentation may be due to release of TGF-β1and EGF which are known to decrease melanogenesis. The TGF delayed extracellular signal related kinase activation which leads to inhibit melanin synthesis, while EGF lowers melanin production by inhibiting PGE2 expression and tyrosinase enzyme activity[11][14].

This result agrees with study conducted by Suhad J. et al. [6] that found 30 patients with melasma treated with intradermal PRP injection every 2weeks for 5 sessions. Results were assessed on the basis of percentage of reduction in baseline mMASIscore which showed high rate of fair response19(63.3%) patients and low rate of good response 5(16.7%) patients, with overall efficacy 16.7% .

In 2014,Turkish case reported by Mutlu Çayırlı et al, observed more than 80% reduction in hyperpigmentation after PRP injection for melasma every 2weeks for 3 sessions[7].

Another case from Malaysia reported by Yew Chet al showed variable results in reduction of mean mMASI score in two cases (33.5% and 20%) after monthly intradermal injection of PRP for two sessions in combination of QS ND:YAG laser and topical α-arbutin therapy[8].

In 2016 a controlled clinical trial conducted in Thailand by A. Dannarongchaiet alon ten patients with melasma injected by PRP to one side of the face and intradermal injection of normal saline to another side as control

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group every 2weeks for 4 sessions, the notable finding was that the mean mMASI score was reduced by 28.9%, but that study was based on small sample size[9].

In 2017, a therapeutic trial study conducted in Pakistan by Faiz et al on 20 patients with melasma injected by PRP intradermally for 5 sessions 2weeks apart, showed decrease in MASI score in majority of patients but the efficacy of treatment was low (13.3%)[10].

In our study inspite of decrease in mMASI score in majority of patients but not reached to the point of effective value.

in study conducted by Dannarongchai A et al.[3] that enrolled, ten volunteers with melasma were randomly treated with ID PRP injection at one side of the face every two weeks for four times and then follow up one month after the last treatment. The study was conducted during 10 weeks to evaluate melasma patients in both the objective assessment inclucing mexameter and Antera 3D camera analysis and the subjective assessment including mMASI score. Moreover, The most notable finding of this study was that the mean mMASI score was significantly reduced from 4.92 ± 0.96 to 3.5 ± 0.67, showing 28.9 % improvement after four sessions of treatment in PRP group.

In present study we showed reduction in mean MASI score after each treatment by PRP. Like see in meta-analysis of ten studies that involved 395 adults in clinical trials on PRP therapy, either in combination with other therapy or alone, showed a significant reduction in mMASI score from pre-treatment to post-treatment. The overall efficacy evaluation of PRP showed that patients or doctors had a high degree of

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satisfaction with the treatment of melasma by PRP. [11]

Another recent study [12] showed that PRP significantly outperformed tranexamic acid in treatment for melasma from week 4 through week 24, suggesting that PRP therapy may be superior to other procedures; however, more randomized controlled studies are needed to confirm this. In addition to regaining a more balanced and stable complexion, many patients with PRP also have improved skin quality, including wrinkle levels, elasticity and skin hydration [13]. Therefore, it would be valuable to offer a more personalized combination therapy to patients who want to treat melasma and improve skin quality simultaneously. In terms of mechanism study, it is meaningful to study the upstream and downstream molecules interacting with TGF-b in melasma, such as transcription of activating protein-1, PAX3, p53, MITF, tyrosinase-related protein 1 and tyrosinase [14].

Eman R. M. et al. observed a statistically significant decrease in mean mMASI score after three monthly PRP sessions. However, the reduction was only 28% in patients who had mixed type of melasma. The authors also noted statistically significant improvement among those with epidermal type than those with mixed type.[15] Another, trial of 20 melasma patients treated with five fortnightly sessions of activated PRP injections reported 31.7% mean reduction in MASI scores. Authors reasoned lower percentage of improvement in MASI to irregular use of sunscreen lotions, higher Fitzpatrick skin phototype and mixed type of melasma which is generally resistant to all kind of therapies. [16] Latest split-face pilot study conducted in Thailand, injected

PRP and normal saline intradermally in 10 patients every two week for four sessions. Study showed significant improvement in mean mMASI score by 1.03 ± 0.44 at the end of study compared to baseline.[17]

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