The Study of Effectiveness of Platelet-Rich Plasma (PRP) Treatment for Lichen Planus Pigmentosus (Pilot Study)

Pitcharat Pituvong[*, 1], Chanisa Kiatsurayanon[2], and Praneet Sajjachareonpong[1, 2]

[1]College of Medicine, Rangsit University, Pathum Thani, Thailand
[2]Institute of Dermatology, Bangkok, Thailand
[*]Corresponding author, E-mail: Picharat@gmail.com

Abstract

This study is the first pilot study utilizing PRP, and objectively measure the efficacy of intradermal platelet-rich plasma (PRP) in the treatment of ichen planus pigmentosus. The 5 participants with LPP by clinical and histological enrolled in this study. They received 3 sessions of intradermal PRP with 2 weeks apart and followed up to 2 weeks, 4 weeks, and 8 weeks. After the last session, we measured melanin index, improvement of pigment, patients' satisfaction score, and adverse effects.

Mean MI score of the subjects declined 12.8% from the baseline at the end of study. All patients demonstrated significant reduction of MI score since the first PRP injection. Clinical improvement as evidenced by escalation of mean QGS grading by 2 dermatologists was initially observed at week 6. The mean patient self-assessment score at week 12 was reported to be very satisfied. Adverse effects were minimal including swelling at injection sites and bruising which spontaneously resolved in a few days. Therefore, injection of PRP could be an effective alternative or complementary treatment option for treatment-resistance lichen planus pigmentosus or other hyperpigmentation conditions. The limitation of our study was the small sample size and short followed-up period.

Keywords**:** *Lichen Planus Pigmentosus, Platelet-Rich-Plasma, Macrophages, Melanin, Pigment*

1. Introduction

Lichen planus pigmentosus belongs to the group of acquires dermal macular hyperpigmentation (ADMH). Lichen planus pigmentosus presents as poorly defined, slate gray to brownish-black macules in sun-exposed areas, predominantly on the face and neck, in the flexural fold. The previous treatment study has found that none of the treatments is universally effective. This concern makes LPP a complex cosmetic problem.

Acquired dermal macular hyperpigmentation (ADMH) is a collective term for hyperpigmentation groups such as lichen planus pigmentosus (LPP), Riehl melanosis (RM), pigmented contact dermatitis (PCD), and erythema dyschromicum perstans (EPS) (Kumarasinghe et al., 2019). There is considerable overlap between the clinical and histopathologic features of these diseases.

In 1974, lichen planus pigmentosus (LPP) was first described by Bhutani et al. in 40 Indian patients with acquired macular pigmentation, and the term LPP was coined (Bhutani et al., 1974). LPP is widespread and occurs in young to middle-aged female adults with skin phototype (Rieder et al., 2013; Ingber et al., 1986) especially in patients of Indian, Latin American, or Middle Eastern origin. Clinically, it presents as irregularly shaped or oval brown to gray-brown blemishes and patches in sun-exposed areas (especially forehead, temples, and neck) or intertriginous areas with asymptomatic to mild pruritus or a burning sensation. Early lesions with an erythematous border in ash dermatosis help distinguish between these two conditions. The etiology of LPP is unknown. Photodistribution in some patients suggests that UV light may play a pathogenic role, and topical application of mustard oil, which contains allyl isothiocyanate and amla oil have been suggested as a possible trigger. For a definitive diagnosis, we must refer to clinical and histopathological findings: Basal vacuolar degeneration of the basal cell layer, a perivascular mononuclear cell infiltrate in the upper dermis, and increased epidermal melanin, dermal melanophages, lichenoid reaction, and colloid bodies. Histological staining within linear patterns has found the deposited IgM or C3 at the basement membrane

zone (Sehgal et al., 2011) indirect immunofluorescence (DIF). The patch test showed a negative result in most cases, ruling out other diseases.

Previous studies have used topical bleaching agents, vitamin A analogs, steroids, oral steroids, chemical peeling, and laser light-based therapy for treatment, the treatment of lichen planus pigmentosus is still questioned by physicians worldwide. The lesions significantly impact the appearance of patients, as purple, brown, or grayish spots gradually form on the body's surface. Treatment of lichen planus pigmentosus is limited due to its efficacy. Some studies were researched on topical therapies such as topical steroids, hydroquinone, tacrolimus ointment, and azelaic acid. Al Mutairi et al. conducted an open-label, nonrandomized, prospective study of 13 patients treated with topical tacrolimus ointment. The result was that seven patients showed improvement in pigmentation. Muthu et al. showed a low dose of isotretinoin in treating 27 patients, with 15 patients experiencing moderate improvements. In the study by Bhari et. al, nine patients were treated with a Q-switched Nd YAG laser. After six laser sessions, an average clinical improvement of 25.7% in lesions was noted by physician assessment. However, several of the studies had a small sample size and a relatively low level of evidence. but none of these are universally effective (Bhutani et al., 1979; Kim et al., 2012; Han & Goh, 2014), making LPP a complex cosmetic problem to treat.

Platelet-rich plasma (PRP) is autologous blood plasma with a concentration of platelets above baseline and reportedly releases high growth factors that may be valuable for numerous applications. PRP is recently used as an adjunct therapy for many medical conditions because of the numerous growth factors and very few adverse effects.

PRP is recently used as adjunctive therapy for several conditions, such as orthopedic indications (Wang & Avila, 2007; Xian et al., 2015), and various purposes in dermatologic treatments (Kim et al., 2011), such as wound healing, facial skin rejuvenation, scar revision, and hair restoration (Alam et al., 2018). The numerous growth factors in PRP (D'Mello et al., 2016; Lambert, Vancoillie, & Naeyaert, 1999; Yasumoto et al., 1997), such as platelet-derived growth factor (PDGF), which stimulates tissue and collagen healing, and transforming growth factor-beta (TGF-beta), which decreases melanogenesis and signal protein in melanogenesis. In addition, fibroblast growth factor (FGF) promotes fibroblasts in angiogenesis. In addition, epidermal growth factor (EGF) promotes mesenchymal and epithelial cell development. Keratinocyte growth factor promotes epithelial cell stimulation, while vascular endothelial growth factor (VEGF) stimulates collagen production.

According to the macromolecular activators of phagocytosis from platelets (MAPP: l-MAPP and s-MAPP), Ulk1, beclin in platelet-rich plasma induces phagocytosis in immune cells (Tachibana, 2000; Murakami, Matsuzaki, & Funaba, 2009). From the study of Czakai K. et al. (2017), PRP can promote phagocytosis activity of macrophages, and TGF-beta in PRP can increase chemotaxis, stimulate collagen matrix deposition, and decrease signaling response in melanogenesis through microphthalmia-associated transcription factor (MITF) in melanocytes. This effect may decrease the activity of tyrosine and tyrosine-releasing protein (TRP) in melanogenesis, which slows down signaling in the activation of the extracellular signal-regulated kinase (Sakamoto et al., 2011).

PRP has been used to treat pigmentary lesions such as periorbital hyperpigmentation (Al-Shami, 2014) and dermal melasma (Amini, Ramasamy, & Yew, 2015; Cayırlı et al., 2014; Amini et al., 2015). From the study of Hofny et al., platelet-rich plasma increases transforming growth factor-beta (TGF-beta) in patients with skin melasma and nearby skin, which decreases melanogenesis and signaling protein in melanogenesis (Hofny et al., 2019). This treatment effectively reduces melanin in the lesions to a significant extent, as evidenced by a study by Punyaphat S. et al., who studied melasma patients of mixed type by administering PRP intradermally on one side of the face compared to normal saline on the other side. After four sessions two weeks apart, there was a decrease in mMSI score and 3D-measured melanin on the side treated with intradermal PRP (Sirithanabadeekul, Dannarongchai, & Suwanchinda, 2020).

Therefore, our research hypothesized that LPP could be a promising effective treatment for Lichen planus pigmentosus.

2. Objectives

To investigate the efficacy of platelet-rich plasma (PRP) in treating lichen planus

3. Materials and Methods

This study is the first pilot clinical trial to noninvasively and objectively measure the efficacy of intradermal platelet-rich plasma (PRP) in the treatment of lichen planus and to study the safetiness in using platelet-rich-plasma.

3.1 Population and Samples

This research was an experimental pilot study. This study was reviewed and approved by the Ethics Committee (EC) at the Institute of Dermatology, Bangkok. After the study was submitted to the Ethics Committee, the research looked for five volunteers from the electronic outpatient department who fulfilled the criteria:

3.1.1 Inclusion Criteria:

1) Male or female, 18-60 years' old
2) The patient whose diagnostic was lichen planus pigmentosus, with an onset of six months or longer
3) There are lesions on the face
4) The biopsy showed relevant results for histological findings: perivascular infiltration, lichenoid reaction and melanin, melanophage in epidermis and dermis
5) The patch test was negative

3.1.2 Exclusion Criteria:

1) Pregnancy or breastfeeding
2) Individuals with a history of hypertrophic scar and/or keloid formation
3) Active infection at the location that is yet to be treated
4) Having a history of bleeding disorders
5) The use of anticoagulants
6) Having other hyperpigmentation conditions such as pigmented contact dermatitis, fixed drug eruption, lichenoid drug reaction, ochronosis, melasma, PIH, or endocrinopathies

Written informed consent was obtained from all participants. At the first meeting, all volunteers were informed about the information of the study, the steps of the study, and to make an appointment. The six appointment dates are comprised of three treatments, two weeks apart, with a follow-up at two weeks, one month, and two months. If a volunteer cannot participate on a previously stated appointment date, they can come the day after. If they cannot participate more than one day after the scheduled appointment with reason that is not relevant to the study, the research will not collect their data. However, if there are reasons presented that are relevant to adverse events from the study, the researcher will record the date, adverse events, and treat the complications accordingly.

The study took place at the bioengineering room at institute of dermatology, Bangkok

All the volunteers were advised to

Stop any treatments at least 3 months before the treatment

1) Not take NSAID before the treatment at least 14 days before the treatment
2) Not direct exposure to sunlight for 24 hours before the treatment
3) Not apply any make up 24 hours after the treatment
4) Not use any topical bleaching agents, such as vitamin analog, while in the study
5) Can only apply moisturizer and sunscreen that was given by the researcher

All of volunteer were advised to clean make up with soap before the study.

The lesions were marked by non-permanent marker.

All of the steps were performed under a sterile environment.

PRP preparation:

1) Prepared 2 cc. of anticoagulant agent (ACD-A) in a 20 ml. syringe

2) Collect 10 cc. of venous blood from the forearm with 20 ml. with a 21G disposable needle.

3) Draw the blood in to e+PRP Kit (Minos, Gibthais.co.,LTD) and put the PRP tube with blood inside into a centrifuge device (L500 Tabletop Low Speed Centrifuge). The setting for the centrifugation was: 1 round at 2000G/5minutes.

4) Draw the 2-3cc. of Platelets rich plasma or buffy coat layer from the e+PRP Kit to a 1 ml. syringe The platelets rich plasma consists approximately 3,000,000 - 4,000,000 cell/micro-liters.

After having prepared the PRP of each individual, 0.05 cc. of PRP was injected intradermally with a 30-g needle at the marked lesion, 1 cm. apart and 1-2 mm. depth.

At baseline, after 1,2,3 treatment and two weeks, one month, and two months follow-up date

3.2 Research Instruments

Figure 1 Evaluation

On the first day and before injection, the investigators took 3 digital photographs of each participant ‘s face including front, right lateral, and left lateral views using Visia device to evaluate the hyperpigmented lesion. the melanin content of the 3 sites of lesion, which have the 3 darkest hyperpigmented all over the face were chosen, measured using the Mexameter. These measurements were exactly repeated for each participant 2-week, 4weeks and 8 weeks after treatment and compared with baseline.

3.2.1 Melanin index

To objectively measure the pigment outcome, the mexameter (Mexameter MX18, Courage & Khazaka (C&K) Electronic GmbH, Germany) is used to measure the melanin content with melanin index (MI).

3.2.2 Clinical improvement

Clinical photographs are taken by using A Canfield Visia-CR System®. Using the transparent paper to mark the lesion, and choosing both sites of the face on three points. To evaluate the improvements between the baseline picture and after each treatment by two physicians, the following quartile is used:

- 0, no improvement
- 1, < 25% improvement
- 2, 25–50% improvement
- 3, 51–75% improvement and
- 4, > 75% improvement

To judge final result, two independent blinded physicians rated the improvements based on before and after photograph using quartile grading scale 0= no improvement, 1 = mild improvement (0-24%), 2 = moderate improvement (25-49%), 3= good improvement (50–74%), 4= excellent improvement (75-100%), and an average was calculated.

3.2.3 Patient satisfaction

Figure 2 Analog scale

Overall satisfaction levels are scored with a visual analog scale (ranging from 0 = extremely unsatisfied, to 10= extremely satisfied). The ruler is used to provide a measurement in centimeters.

Participants were asked to rate their overall satisfaction every time after treatment on a 0-10 scale 0-1 = not satisfied, 2-4 = slightly satisfied, 5=neutral, 6-8= very satisfied, 9-10 = extremely satisfied.

3.2.4 Adverse effects

Any adverse effects that are observed are recorded (erythema, edema, bleeding, bruising, post inflammatory hyperpigmentation, other).

3.3 Data Collection

The data were recorded in Excel.

3.4 Data Analysis

Data is expressed as a mean +- standard deviation. The Wilcoxon signed-rank test was used to analyze difference in outcomes between each visit. The SPSS software version was used for all analyses. The P value <0.05 is considered statistically significant.

4. Results and Discussion

Four female and one male patients, with lesions on the face, were enrolled in this study. All completed the treatment protocol. Their average age was 47.6 (range,35-56 years). Among these 5 patients, 3 (60%) had skin phototype IV and 2 (40%) had skin phototype V. Their duration of illness ranges from 1 years – 6 years. All the patients have negative result in patch test and direct fluorescence test. Most of biopsy results show lichenoid reaction. Their past 6 months treatment are 2% hydroquinone and tacrolimus cream (Table 4.1).

Table 1 The demographic data and clinical featured of participating patients

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**	**Patient 5**
Sex	Female	Male	Female	Female	Female
Age	56	39	52	35	56
Skin phototype	V	IV	IV	IV	V
Location	Face, extremities	Face, neck, trunk	Face, neck, trunk	Face	Face, neck
Duration of illness	2 years	3 years	2 years	5 years	2 years
Patch test	Neg	Neg	Neg	Neg	Neg
DIF test	Neg	Neg	Neg	Neg	Neg
Biopsy	Lichenoid reaction	Infiltration of some melanopharge in papillary dermis, lichenoid reaction	Infiltration of some melanopharge in papillary dermis, lichenoid reaction	Lichenoid reaction	Infiltration of some melanopharge in papillary dermis, lichenoid reaction
Treatments	Hydroquinone	Hydroquinone	Hydroquinone	Hydroquinone	Hydroquinone, tacrolimus cream

4.1 Decrease of mean melanin index following PRP treatment

Mean melanin index values as meausured by the Mexameter fell from score of 450.33+-69.91 to 392.60+-73.88 at week 8 after 3rd PRP treatment, which this change was significant (P<0.05) (Table 4.2).

Table 2 The mean melanin index of each participant, the percentage of decrease in melanin index

visit		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Mean ±SD	P-value
before PRP	melanin index	420.33	437.67	402.00	418.33	573.33	450.33 ±69.91	ref
after 1st PRP (2 weeks)	melanin index	384.67	412.00	383.33	389.67	552.33	424.4 ±72.44	0.043
	Decrease (%)	35.66 (8.48)	25.67 (5.87)	18.67 (4.64)	28.66 (6.85)	21 (3.66)	25.93 (5.76)	
after 2nd PRP (2 weeks)	melanin index	359.33	418.00	368.00	378.33	538.00	412.33 ±73.75	0.043
	Decrease (%)	61 (14.51)	19.67 (4.49)	34 (8.46)	40 (9.56)	35.33 (6.16)	38 (8.44)	
after 3rd PRP (2 weeks)	melanin index	378.00	411.67	357.00	371.67	529.67	409.6 ±70.04	0.043
	Decrease (%)	42.33 (10.07)	26 (5.94)	45 (11.19)	46.66 (11.15)	43.66 (7.62)	40.73 (9.04)	
after 3rd PRP (4 weeks)	melanin index	356.33	403.00	350.00	366.33	522.67	399.67 ±71.76	0.042
	Decrease (%)	64 (15.23)	34.67 (7.92)	52 (12.94)	52 (12.43)	50.66 (8.84)	50.67 (11.25)	
after 3rd PRP (8 weeks)	melanin index	352.00	394.67	340.67	356.00	519.67	392.6 ±73.88	0.043
	Decrease (%)	68.33 (16.26)	43 (9.82)	61.33 (15.26)	62.33 (14.9)	53.66 (9.36)	57.73 (12.82)	

There was a trend toward gradual reduction of mean melanin index every visit. (Figure 4.1) In each participant, the mean melanin index showed in Figure 4.2.

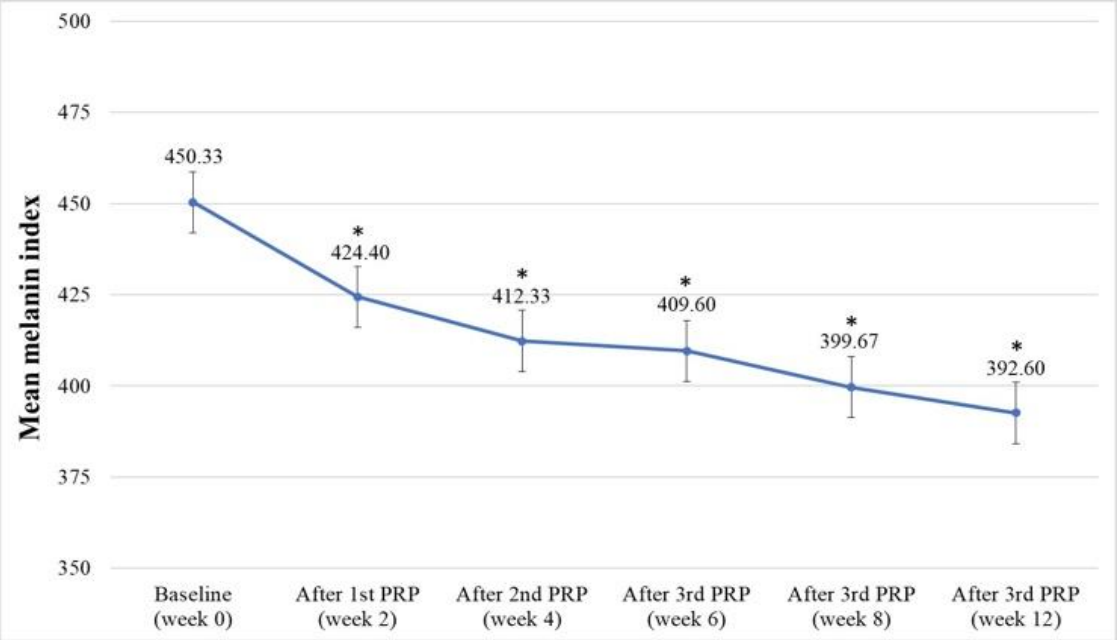

Figure 3 Decrease of mean MI in each visit. The line diagram demonstrates a trend of reduction of mean MI at different treatment sessions and follow-up visits. *P<0.05

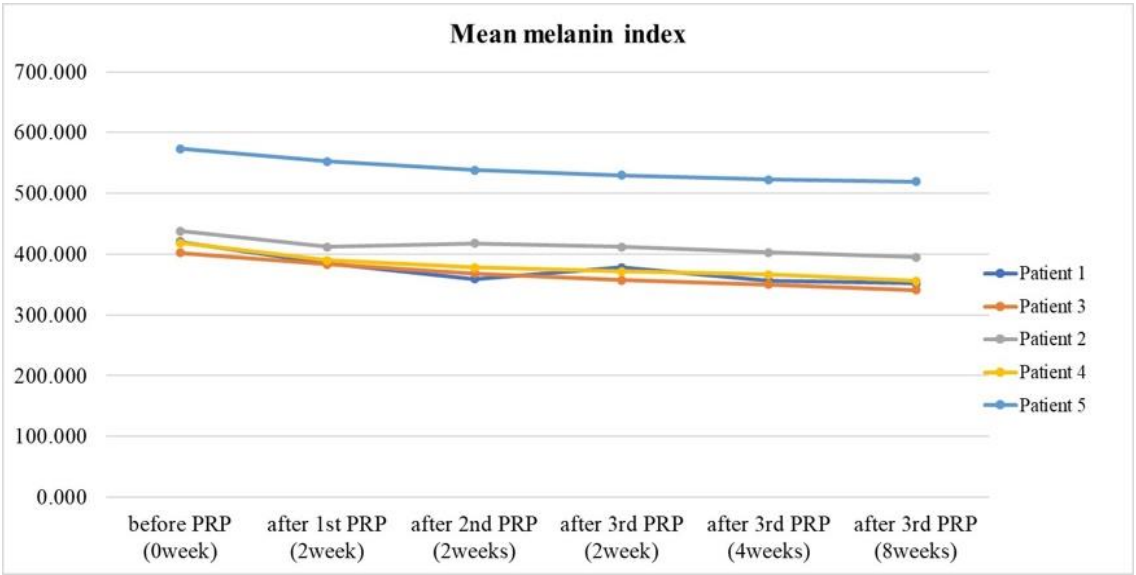

Figure 4 Mean melanin index in each patient at week 0, 2, 4, 6, 8, 12

The relative melanin index difference compared to baseline also shows significant difference with PRP after 2weeks of 1st PRP treatment ($p<0.05$) with 14.93% improvement.

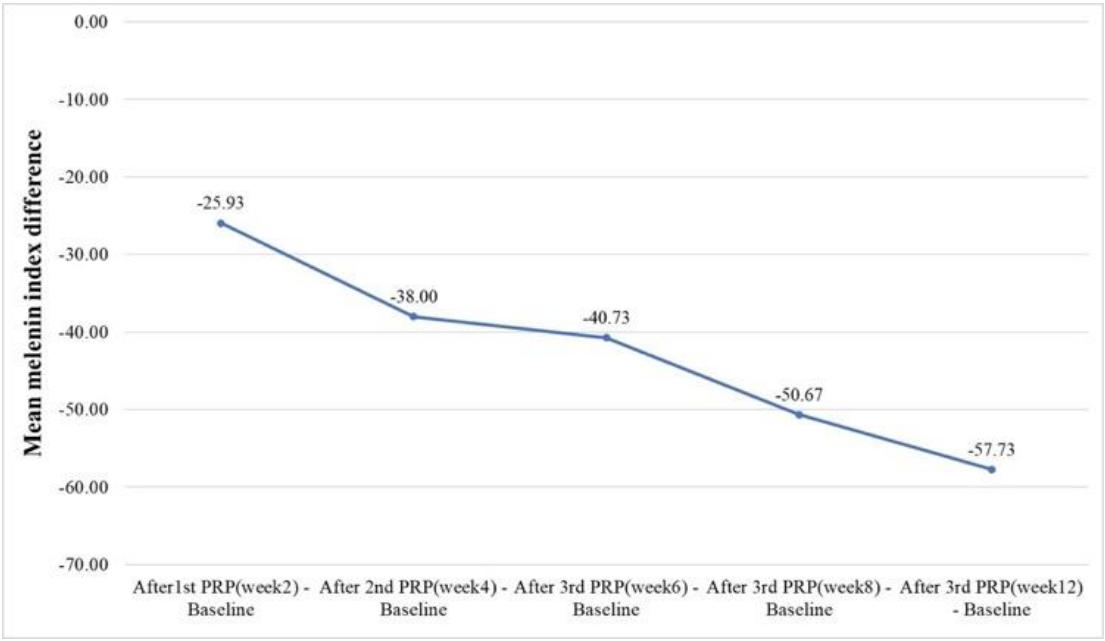

Figure 5 Mean melanin index difference from baseline and each visit

4.2 Improvement of lesion by two physicians

To judge the final result, two independent blinded physicians rated the improvements based on before and after photograph using quartile grading scale 0= no improvement (less than 1%),1 = mild improvement (1-25%), 2 = moderate improvement (26-50%), 3= good improvement (51–75%), 4= excellent improvement (>75%). Their result show in Figure 4.4, and an average was calculated.

After 1st PRP and 2nd PRP, the mean improvement was 1.4 and 1.9, which is fair improvement, after 3rd PRP and after 1 month, the mean improvement was mild. There was excellent improvement after 8weeks after 3rd PRP.

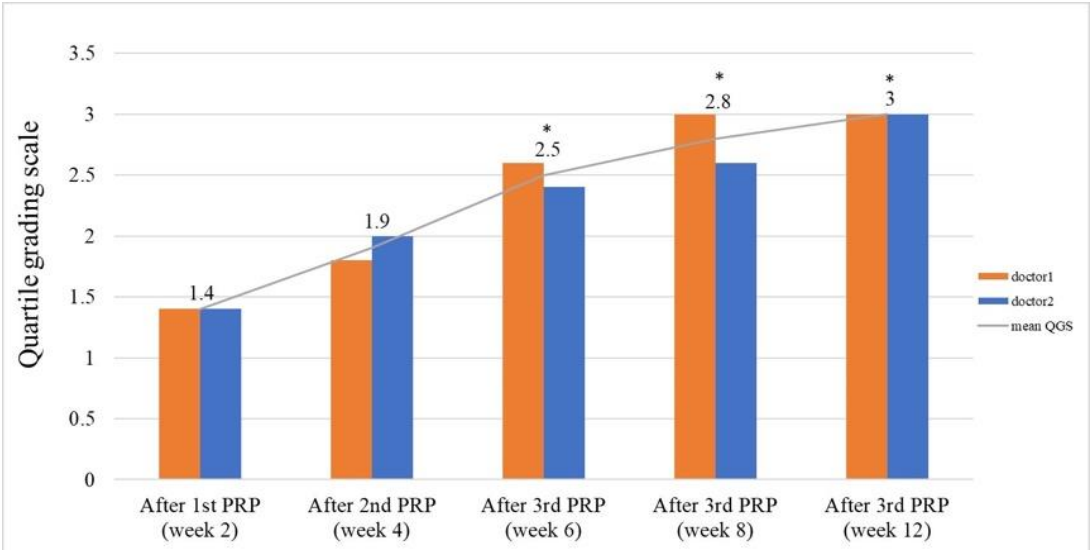

Figure 6 Improvement of mean QGS from week 2 to week 12. *P<0.05

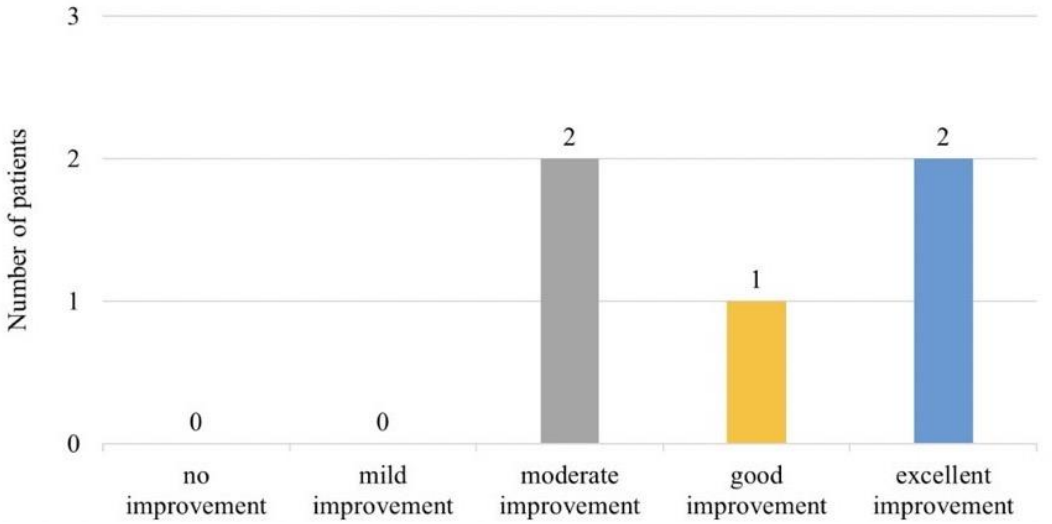

Figure 7 Mean improvement score from two physicians at 8 weeks after 3rd PRP (week 12)

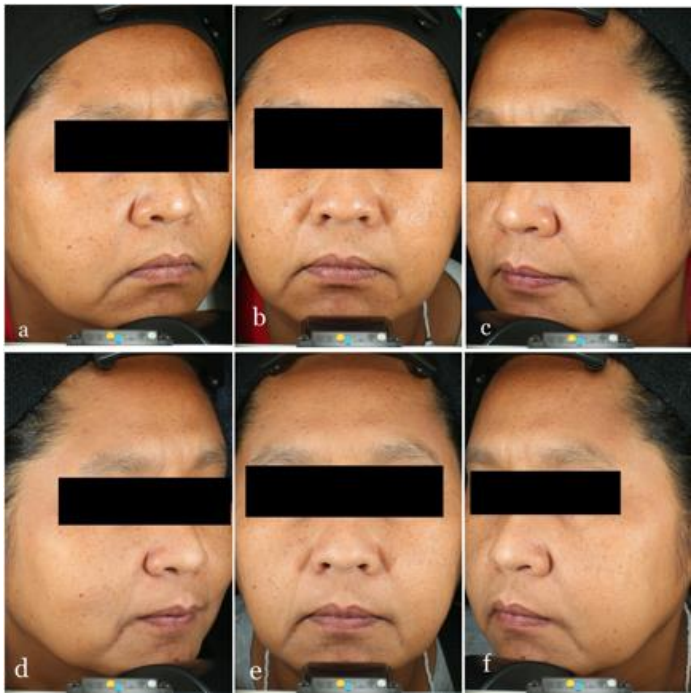

Figure 8 Clinical photograph of a patient at baseline (a-c) and after 3 sessions of PRP treatment at week 12 (d-f). There is a decrease of hyperpigmentation in the frontal and malar regions

4.3 Participants' overall satisfaction assessment

Participants were asked to rate their overall satisfaction every time after treatment on a 0-10 scale 0-1 = not satisfied, 2-4 = slightly satisfied, 5=neutral, 6-8= very satisfied, 9-10 = extremely satisfied.

In term of the degrees of patient's satisfaction, After the first PRP treatment, mean of overall satisfaction score was slightly satisfied but since after 2nd PRP of, mean of overall satisfaction score was were very satisfied (Figure 4.7).

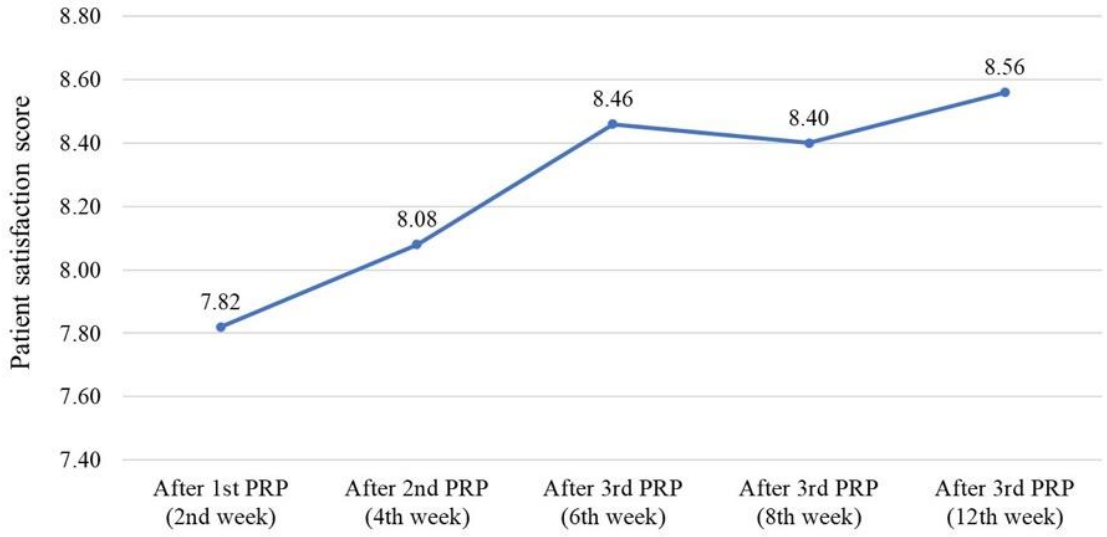

Figure 9 Patient satisfaction score from patients in each visit

4.4 Adverse effects

Most patients experienced swelling on the sites of injection ranging from 1-3 hours after treatment, and spontaneously resolved without any treatments. One of participant experience bruising for 2 day and resolved in day 3. None of the participants report infection, altered in pigment after PRP treatment.

5. Conclusion

In our study, after eight weeks of a third PRP intradermal injection at the site of hyperpigmentation lesion in five patients, the mean melanin index values measured by Mexameter decreased from a value of 450.33+-69.91 to 392.60+-73.88, and this change was significant ($P < 0.05$). There was a trend toward a gradual decrease in the mean melanin index at each visit. The difference in relative melanin index compared to baseline also showed a significant difference with PRP after two weeks of 1st PRP treatment ($p < 0.05$) with an improvement of 14.93%. According to the global assessment of the investor by two physicians, the mean improvement is moderate. After the 1st PRP and 2nd PRP, injections after the third PRP, and after one month, the mean improvement was slight. After the 3rd PRP, there was a remarkable improvement after eight weeks.

As for the degree of patient satisfaction, after the first PRP treatment, the mean of overall satisfaction was slightly satisfied, but after the second PRP, the overall satisfaction was very satisfactory. Finally, all side effects of treatment included edema and bruising, but these were mild and resolved spontaneously within a few days. Limitations of this study design include the small sample size and the lack of a double-blind or placebo-controlled study.

In summary, this is the first PRP trial to treat hyperpigmentation in lichen planus pigmentosus. We found that PRP intradermal injection significantly improved lesions within 3 treatments of PRP, as reported by two physicians, and increased patient satisfaction. We also observed a trend toward a gradual decrease in pigmentation in terms of melanin index. Due to numerous growth factors in PRP, which can stimulate melanophage to phagocyted the melanin in the lesion. Ultimately, we hereby propose PRP as a noval therapy for LPP which could be an effectiveness in treatment of LPP compare to prior any treatments.

Recommendations: Further well-designed studies with larger sample size are necessary to confirm this preliminary observation.

6. References

Al-Shami, S. H. (2014). Treatment of periorbital hyperpigmentation using platelet-rich plasma injections. *American Journal of Dermatology and Venereology, 3*(5), 87-94. doi:10.5923/j.ajdv.20140305.03

Alam, M., Hughart, R., Champlain, A., Geisler, A., Paghdal, K., Whiting, D., Hammel, J. A., Maisel, A., Rapcan, M. J., West, D. P., & Poon, E. (2018). Effect of Platelet-Rich Plasma Injection for Rejuvenation of Photoaged Facial Skin: A Randomized Clinical Trial. *JAMA dermatology, 154*(12), 1447–1452. doi:10.1001/jamadermatol.2018.3977

Amini, F., Ramasamy, T. S., & Yew, C. H. (2015). Response to intradermal autologous platelet-rich plasma injection in refractory dermal melasma: Report of two cases. Journal of Health and Translational Medicine, 18(2), 1-6. doi:10.22452/jummec.vol18no2.1

Bhutani, L. K., Bedi, T. R., Pandhi, R. K., & Nayak, N. C. (1974). Lichen planus pigmentosus. *Dermatologica, 149*(1), 43–50. doi:10.1159/000251470

Bhutani, L. K., George, M., & Bhate, S. M. (1979). Vitamin A in the treatment of lichen planus pigmentosus. *The British journal of dermatology, 100*(4), 473–474. doi:10.1111/j.1365-2133.1979.tb01653.x

Cayırlı, M., Calışkan, E., Açıkgöz, G., Erbil, A. H., & Ertürk, G. (2014). Regression of melasma with platelet-rich plasma treatment. *Annals of dermatology, 26*(3), 401–402. doi:10.5021/ad.2014.26.3.401

Czakai, K., Dittrich, M., Kaltdorf, M., Müller, T., Krappmann, S., Schedler, A., Bonin, M., Dühring, S., Schuster, S., Speth, C., Rambach, G., Einsele, H., Dandekar, T., & Löffler, J. (2017). Influence of Platelet-rich Plasma on the immune response of human monocyte-derived dendritic cells and macrophages stimulated with Aspergillus fumigatus. *International journal of medical microbiology, 307*(2), 95–107. doi: 10.1016/j.ijmm.2016.11.010

D'Mello, S. A., Finlay, G. J., Baguley, B. C., & Askarian-Amiri, M. E. (2016). Signaling Pathways in Melanogenesis. *International journal of molecular sciences, 17*(7), 1144. doi:10.3390/ijms17071144

Han, X. D., & Goh, C. L. (2014). A case of lichen planus pigmentosus that was recalcitrant to topical treatment responding to pigment laser treatment. *Dermatologic therapy, 27*(5), 264–267. doi:10.1111/dth.12134

Hofny, E. R. M., Abdel-Motaleb, A. A., Ghazally, A., Ahmed, A. M., & Hussein, M. R. A. (2019). Platelet-rich plasma is a useful therapeutic option in melasma. *The Journal of dermatological treatment, 30*(4), 396–401. doi: 10.1080/09546634.2018.1524821

Ingber, A., Weissmann-Katzenelson, V., David, M., Bialowons, M., & Feuerman, E. J. (1986). Lichen planus und Lichen planus pigmentosus nach Goldtherapie--Fallberichte und Literaturübersicht [Lichen planus and lichen planus pigmentosus following gold therapy-case reports and review of the literature]. *Zeitschrift fur Hautkrankheiten, 61*(5), 315–319.

Kim, D. H., Je, Y. J., Kim, C. D., Lee, Y. H., Seo, Y. J., Lee, J. H., & Lee, Y. (2011). Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast. *Annals of dermatology, 23*(4), 424–431. doi:10.5021/ad.2011.23.4.424

Kim, J. E., Won, C. H., Chang, S., Lee, M. W., Choi, J. H., & Moon, K. C. (2012). Linear lichen planus pigmentosus of the forehead treated by neodymium:yttrium-aluminum-garnet laser and topical tacrolimus. *The Journal of dermatology, 39*(2), 189–191. doi:10.1111/j.1346-8138.2011.01233.x

Kumarasinghe, S. P. W., Pandya, A., Chandran, V., Rodrigues, M., Dlova, N. C., Kang, H. Y., Ramam, M., Dayrit, J. F., Goh, B. K., & Parsad, D. (2019). A global consensus statement on ashy dermatosis, erythema dyschromicum perstans, lichen planus pigmentosus, idiopathic eruptive macular pigmentation, and Riehl's melanosis. *International journal of dermatology, 58*(3), 263–272. doi:10.1111/ijd.14189

Lambert, J., Vancoillie, G., & Naeyaert, J. M. (1999). Molecular motors and their role in pigmentation. *Cellular and molecular biology (Noisy-le-Grand, France), 45*(7), 905–918.

Murakami, M., Matsuzaki, F., & Funaba, M. (2009). Regulation of melanin synthesis by the TGF-beta family in B16 melanoma cells. *Molecular biology reports, 36*(6), 1247–1250. doi: 10.1007/s11033-008-9304-6

Ogawa, Y., Sakamoto, H., Oryu, M., Shinnou, M., Sakamoto, N., Yanghong, W., Khatun, R., & Nishioka, M. (2000). Production of macromolecular activators of phagocytosis by lysed platelets. *Thrombosis research, 97*(5), 297–306. doi:10.1016/s0049-3848(99)00178-4

Rieder, E., Kaplan, J., Kamino, H., Sanchez, M., & Pomeranz, M. K. (2013). Lichen planus pigmentosus. *Dermatology online journal, 19*(12), 20713.

Sakamoto, H., Wu, B., Nagai, Y., Tanaka, S., Onodera, M., Ogawa, T., & Ueno, M. (2011). Platelet high-density lipoprotein activates transferrin-derived phagocytosis activators, MAPPs, following thrombin digestion. *Platelets, 22*(5), 371–379. doi:10.3109/09537104.2010.533797

Sehgal, V. N., Srivastava, G., Sharma, S., Sehgal, S., & Verma, P. (2011). Lichenoid tissue reaction/interface dermatitis: recognition, classification, etiology, and clinicopathological overtones. *Indian journal of dermatology, venereology and leprology, 77*(4), 418–430. doi:10.4103/0378-6323.82389

Sil, P., Wong, S. W., & Martinez, J. (2018). More Than Skin Deep: Autophagy Is Vital for Skin Barrier Function. *Frontiers in immunology, 9*, 1376. doi:10.3389/fimmu.2018.01376

Sirithanabadeekul, P., Dannarongchai, A., & Suwanchinda, A. (2020). Platelet-rich plasma treatment for melasma: A pilot study. *Journal of cosmetic dermatology, 19*(6), 1321–1327. doi:10.1111/jocd.13157

Tachibana M. (2000). MITF: a stream flowing for pigment cells. *Pigment cell research, 13*(4), 230–240. doi:10.1034/j.1600-0749.2000.130404.x

Wang, H. L., & Avila, G. (2007). Platelet rich plasma: myth or reality?. *European journal of dentistry, 1*(4), 192–194.

Xian, L. J., Chowdhury, S. R., Bin Saim, A., & Idrus, R. B. (2015). Concentration-dependent effect of platelet-rich plasma on keratinocyte and fibroblast wound healing. *Cytotherapy, 17*(3), 293–300. doi:10.1016/j.jcyt.2014.10.005

Yasumoto, K., Yokoyama, K., Takahashi, K., Tomita, Y., & Shibahara, S. (1997). Functional analysis of microphthalmia-associated transcription factor in pigment cell-specific transcription of the human tyrosinase family genes. *The Journal of biological chemistry, 272*(1), 503–509. doi: 10.1074/jbc.272.1.503