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Determine the Effect of Platelet Rich Plasma (PRP) Injection on the Outcome of Narrow-Band-Ultraviolet B (NB-UVB)

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Key words: Narrow-Band-Ultraviolet B (NB-UVB), platelet rich plasma, vitiligo, saline injection, intradermal injection

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Abstract: Narrowband-Ultraviolet B is an efficient and secure vitiligo therapy, although, the course of care also needs a lengthy period of time that can present a possible danger of multiple side effects and non-compliance by patients. Study attempted to analyse whether the addition of PRP therapy has any advantage over the conventional NBUVB therapy in fastening the repigmentation rates in cases of Vitiligo. One injected with PRP and the other with control injections of normal saline. The study included a number of 32 patients and 64 lesions. Study found that addition of PRP has no statistically significant advantage in treating patients of stable vitiligo. The statistical tests do not show a significant advantage over the control group.

INTRODUCTION

In the past century and until now, the common usage of the words "vitiligo" up "leukoderma" has been a source of ambiguity in medical literature. Pearson, shortly after the end of the nineteenth century, identified as leukoderma, a condition that tends to be vitiligo. In the late twentieth century, the enigmatic existence of vitiligo contributed to cautious interpretations outside conditions of known aetiology (Manga *et al*., 2016). Vitiligo is categorized per the Picardo and Taieb into four types: non-segmental Vitiligo (NSV), segmental Vitiligo (SV), mixed NSV and SV and non-classifiable forms, e.g., focal, multifocal asymmetrical non-segmental and mucosal at one location. The aim of the present study is to compare between Platelet Rich Plasma (PRP) therapy and Narrowband Ultraviolet B photo-therapy (NBUVB) combination therapy vs normal saline and NB-UVB in the treatment of vitiligo.

Aim and objectives

Aim: To comparison of platelet rich plasma (PRP) and narrowband-ultraviolet B (NB-UVB) combination therapy vs normal saline injection and NB-UVB therapy in the treatment of vitiligo.

Objectives: To evaluate the efficacy of intralesional PRP injection along with NBUVB in the treatment of vitiligo. To assess whether addition of PRP to NBUVB therapy accelerates the repigmentation process. Study the side effect profile of PRP injection and NB-UVB therapy.

Literature review: The thorough review of literature was done by using appropriate MeSH (Medical Subject Headings) terms and operators. The skin is highly vascularized. Ruffini endings also detect deep pressure and extension of collagen fibers in the skin. Free ends of the nerves in the epidermis react to changes in pain, gentle contact and temperature. Merkel receptors associated with the Merkel cells respond to repeated infusion of light contact over the skin (Lopez-Ojeda and Oakley, 2015).

Vitiligo is the most extreme depigmentation condition in which aggressive melanocyte systemic

deterioration causes depigmentation of the face, hair and mucosa. Vitiligo commonly refers to localized patches of gray or white hair in the scalp, although there can be complete depigmentation of scalp blood. Depigmented body hair inside the macules of vitiligo are known as indicators of weak repigmentation prognosis. Vitiligo patches are easy to spot on darker photo-types, although, often depigmentation is hard to identify on people with very fair skin (Geel *et al*., 2001; Kanwar *et al*., 2005).

Thatte and Khopkar (2014) in their study observed Perivascular and dermoepidermal lymphocytic infiltrate among 42.3% and reduced melanocytes among 23.5% cases as the commonest histological findings.

PUVA and PUVASOL therapy are usually preferred for widespread vitiligo in adults which is not amenable to topical or other modalities of treatment. PUVA is known to induce repigmentation of lesions but has to be given for a prolonged duration with at least 100-200 sessions given at least a day apart, 2-3 times a week. Repigmentation of varying degrees has been achieved but sustained repigmentation is difficult to achieve (Kandaswamy *et al*., 2013). Shin *et al*. (2012) envisaged that different CO_2 lasers have improved NBUVB efficacy as various cytokines and growth factors that can induce melanocytes that are secreted as part of the wound healing process after laser surgery. Adverse effects like pain, burning sensation, erythema/edema and crusting were noticed after laser treatment, however, they subsided in few days. They, unlike Bayoumi *et al*. (2012) did not report scarring with prior laser treatment. These studies suggest a need to explore the synergistic role of lasers with NBUVB in the treatment of vitiligo, especially on traditionally UV resistant sites (Polakow *et al*., 2001; Bayoumi *et al*., 2012; Shin *et al*., 2012). Treatment of vitiligo, especially of wide-spread, recalcitrant disease is still prolonged and difficult and needs tenaciousness and patience on the part of the patient as well as the dermatologist. Photo-therapy is the cornerstone of treatment of widespread vitiligo. PUVA has been used widely for treatment of widespread recalcitrant vitiligo in adults, though, it is being increasingly surpassed by narrow band UVB (NB-UVB). PUVASOL (psoralens+natural sunlight) can be used in sunnier climates, utilizing the same principles as for PUVA. Less phototoxic oral psoralens such as 5-MOP are preferred in order to avoid phototoxic reactions (Kandaswamy *et al*., 2013; Henseler *et al*., 1981).

In vitiligo involving >10% body surface area and patients with localized disease not responding to topical PUVA or other modalities of treatment.

Treatment protocols of PUVASOL in vitiligo (Kandaswamy *et al*., 2013; Handa *et al*., 2001; Pacifico and Leone). Vitiligo needs a larger number of treatments for clearance as compared with psoriasis, if therapy is continued till repigmentation is achieved which may last for months to years. Oral 8-MOP or TMP are commonly used. Dosage and frequency of administration is similar to that in psoriasis, the major difference being the need for prolonged treatment lasting for 150-200 sessions in vitiligo and the difficulty in achieving complete or near-to-complete response. A weekly increment of 0.25 J cm^{-1} 2 or by 20% of the previous dose is given till onset of erythema. Application of sunscreen to the surrounding uninvolved skin can prevent undue tanning. TMP and 5-MOP are more phototoxic topically. Though topical PUVASOL is generally avoided due to the greater phototoxic risk and frequent occurrence of painful blisters, it may be tried during rainy season. A total of 0.1% 8-MOP is applied carefully over the vitiliginous patches (one part of commercially available 8MOP lotion can be diluted with nine parts of eau-de-cologne and used). Propylene glycol can also be used as a diluent. After 30 min, the patches are exposed to sunlight starting with 0.5-1 min. Treatment is done 2-3 times/week and duration of sun exposure should be slowly increased by 0.5-1 min every week till slight erythema appears after which the time is kept constant.

PRP and its various forms such as platelet rich fibrin and platelet gel are being used in many branches of medicine including aesthetics, plastic surgery, orthopedic surgery, dentistry, trauma and wound healing, ocular surgery, gastroenterology, etc. as part of regenerative medicine. In aesthetic surgery, PRP is being used for rejuvenation of the skin, wrinkles, acne scars and regrowth of hair. This issue also carries articles on the use of PRP for and rogeneticalopecia, atrophic acne scars and chronic leg ulcer. PRP is also being used in combination with adipocyte stem cells derived from autologous fat for soft tissue augmentation. A major advantage of autologous PRP in the clinical setting is that it has no adverse effects to date (Khunger *et al*., 2009).

Ibrahim *et al*. (2016) in their study compared the effect of platelet-rich plasma in treating vitiligo on the outcome of short-term narrowband-ultraviolet B photo-therapy. They observed that repigmentation of the mixture population (PRP+NB UVB) had a statistically extremely important increase compared with NB UVB group.

Mahajan *et al*. (2018) in their study assessed the effect of PRP in management of vitiligo. They found that out of 40 patients enrolled in their study, 15 patients showed good response, 12 patients showed Average response and13 patients showed no-response to treatment. The average improvement in vitiligo area severity index ranged from 100-10. Visible signs of improvement were after the 3rd injection (6 weeks). Facial lesions responded very well with complete clearance of smaller lesions.

MATERIALS AND METHODS

The present study was a prospective, double blind, randomized controlled study. The study was conducted in the outpatient department of Dermatology in a tertiary care hospital in Karad, India. The total study duration was 24 months, from November, 2013 to October, 2015. Each patient was treated for 4 months which included bimonthly sessions of local injection of PRP or normal saline and biweekly sessions of NV-UVB exposure and the results analyzed. The sample size was calculated with the help of reference article which was a similar study by Ibrahim *et al*. (2016). The sample size of 32 patients with 64 vitiligo patches (32 patches each of control and experimental group) was calculated with the help of Open Epi, Version 3, open source calculator. A total of 32 patients were enrolled in the present study from the Outpatient Department of Dermatology of a tertiary care hospital in Karad, Maharashtra, India, during the period from November, 2013 to June, 2015 after obtaining the approval of the research ethics committee. A detailed informed written consent was taken from the patients before enrolling them into the present study.

For each patient, a lesion on one side of the body was treated with NB-UVB along with intradermal injection of PRP (case side) while the other side was treated with NB-UVB therapy along with intradermal injections of normal saline (control side). The NB-UVB therapy was given biweekly and intradermal injections of PRP and NS was given bimonthly. Each lesion of approximately palm size of the patient, along with a similar lesion on the opposite side was considered as two samples. Patients were photographed, at the first visit, at the end of 2nd month and at the end of 4th month.

RESULTS AND DISCUSSION

In this study, 32 patients were admitted to a tertiary care hospital in Karad from the outpatient department of Dermatology, Maharashtra, India, during the period November, 2013 to June, 2015. We enrolled patients with overall symmetrical stable vitiligo lesions fulfilling inclusion criteria.

Out of total 32 cases, Number of female cases-19 (59.37%) outnumbered male cases-13 (40.62%) (Table 1). We assessed demographic profiles of the study participants (Cases of vitiligo).

In the present study, we included cases of generalized vitiligo, above the age of 18 years. Further, we studied their age-wise distribution, we found that the majority of the study participants belonged to the age group of 36-45 years (9 cases (28.12%)) followed by 26-35 years (8 cases (25%)) and then 46-55 years (5 cases (15.62%)). Cases were less in number above the age of 65 years (2 cases (6.25%)) (Table 2).

Table 1: Distribution of study population according to their gender

Gender	Number	Percentage
Male	13	40.62
Female	19	59.37
Total	32	100.00

Table 2: Distribution of study population according to their age

Age distribution	Number	Percentage
18-25	4	11.47
26-35	8	25.00
36-45	9	28.12
46-55	5	15.62
56-65	4	12.50
>66 years	2	6.25
Total	32	100.00

Qualitative response to the treatment: In this study, we used various ratings to score the outcome of both the treatments from the side of physician as well as patients. In the present study, we rated the outcome response (repigmentation) on Likart scale which ranged from 1-4. Response 1 belonged to qualitative response (re-pigmentation) of 0-25%, scale 2 belonged to qualitative response (re-pigmentation) of 26-50%, scale 3 belonged to qualitative response (re-pigmentation) of 51-75% whereas scale 4 belonged to qualitative response (re-pigmentation) of 76-100%. In PRP group, we reported 10 (31.25%), 13 (40.62%), 7 (21.87%) and 2 (6.25%) cases with percentage of re-pigmentation rate in the ranges of 0-25, 26-50, 51-75 and 76-100%, respectively.

Side effects associated with the treatment: In the present study, we studied side effects that were experienced during the treatment. In the PRP group, we injected PRP in the lesion. In order to eliminate the bias, we injected normal saline in the control group. Pain during injection of normal saline was observed to be the most frequently experienced side effect during the treatment. The 15 (46.87%) cases in PRP group complained of pain while injecting the PRP while the number of participants complaining of pain in control group was slightly more, i.e., 17 (53.12%). Ecchymosis was observed among 3 cases (9.37%) treated with PRP and 2 cases (6.25%) treated with NB-UVB alone (control group).

The NB-UVB therapy was given twice a week and dermal injections of NS and PRP were given twice a month. Each lesion of approximately palm size of the patient, with a similar lesion on the other side was considered as two samples. Patients were photographed, at the first visit, after 2 months and at end of 4 months of treatment. In the control side, in order to avoid bias and to be as a control for the micro-needling effect of PRP, blinding method was used. In this the lesions of control side not receiving PRP injections, 0.1 cc of normal saline was injected intradermally per point with a space of 2 cm between different points of injections. We assessed

demographical characteristics of study participants. Majority of the cases were females (59.37%) as compared to male cases. Majid (2014) in their study, also found female sex as preponderant (14 males in comparison with 26 females). Kumar *et al*. (2009) in their study among 150 cases of vitiligo, observed 69 males, 81 females, aged 3-70 years. Mahajan *et al*. (2018) in their study included 40 patients with localized stable vitiligo attending the outpatient clinic of dermatology and venereology department with depigmented patches involving less than 1% body surface area with inadequate response to conventional line of treatment for over one year in the study. They observed 18 males (45%) and 22 females (55%). Their ages were from 12-40 years. The NB-UVB therapy was given twice a week and dermal injections of NS and PRP will be given bimonthly. Each lesion of approximately palm size, along with a similar patch on the other side was considered as two samples. Patients were photographed, at the first visit, after 2 months and at end of 4 months of treatment, in order to observe the pigmentation occurred among cases enrolled in this study. At the end of 2 months of PRP therapy, pigmentation was seen only among 4 cases (12.5%) which is significantly not different than control group (i.e., NB-UVB only) where only 3 (9.37%) cases shown pigmentation. At the end of therapy, i.e., after 4 months almost all the cases showed pigmentation in both the groups. However, the difference was not found statistically significant when we compared the results between two groups.

CONCLUSION

From the present study, we conclude that though PRP may have some role to play in the faster repigmentation seen in some patients, the statistical tests do not show a significant advantage over the control group.

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