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Treatment of Vitiligo by PRP and Umbilical Cord Blood: A prospective study in 120 cases.

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Abstract
Introduction: *Vitiligo patients can be benefitted from the growth factors, cytokine and other anti-inflammatory mediators secreted from the alpha and beta granules of platelets, which helps in local immune regulation and thereby preventing damage of melanocytes and inhibition of melanin synthesis. Based upon this idea the present study was conducted to discern the actual application and benefit of platelet rich plasma (PRP) and umbilical cord blood (UCB) therapy in vitiligo patients.*
Materials and Methods: *A total number of 120 patients from all over India, suffering from Vitiligo were enrolled in this open prospective study. The study period was from July 2016 till June 2018. One unit Buffy coat platelet/ single donor platelet/Cord blood was utilized either as local application, intralesional injection or transfusion in every session. Approximately 400 treatments were given overall during the study period (Min 1 to max 6 in each patient) with treatment cycle every 30 days. Follow up was done every 15 days up to 3 months. All data of components prepared, issued and its adverse effect of transfusion to the patients and change in the vitiligo appearance was collected and analyzed.*
Results: *Good response i.e 2/3 rd re-pigmentation in affected area in cases of vitiligo was observed in 48.4% of patients out of which maximum response was observed in patients who received combines local PRP + UCB transfusion. No side effects of UCB transfusion and local application of PRP and micro-needling was observed.*
Conclusion: *Platelet products in form of PRP and UCB are beneficial in treatment of vitiligo. Local PRP with Micro needling gives good color match, and helps in initiation of Repigmentation on bony prominences, palms, soles, etc. Intravenous PRP and UCB Transfusions were beneficial in the initiation of re-pigmentation in old, chronic and non-responding patients.*
Keywords: *Platelet Rich Plasma, Umbilical cord blood, Vitiligo*

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I. Introduction

Vitiligo is known to be a recalcitrant skin disorder. Treatment remains a challenge, however, therapeutic options for vitiligo include: topical and systemic corticosteroids, topical calcineurin inhibitors, calcipotriol, phototherapy, excimer laser, and surgical methods such as skin/single-hair grafting, autologous cultured melanocyte or epidermal suspension transplantations and immunomodulators like tacrolimus.[1]. Encouraging results are recorded with advent of newer modalities in management of vitiligo [2] and research for better treatment options is still going on. Platelet rich plasma has emerged as a novel autologous therapeutic modality in various skin disorders and its role in wound healing, tissue remodeling and angiogenesis has led to its widespread use in dermatological practice [3]. It has been hypothesized that vitiligo patients can be benefitted from the growth factors, cytokine and other anti-inflammatory mediators secreted from the alpha and beta granules of platelets, which helps in local immune regulation and thereby preventing damage of melanocytes and inhibition of melanin synthesis. [4] Based upon this idea the present study was conducted to discern the actual application and benefit of platelet rich plasma (PRP) and (umbilical cord blood) UCB therapy in vitiligo patients. So far PRP and UCB therapy has not been utilized and studied in vitiligo on a larger scale, since there are only few clinical studies, and conference papers and poster presentations regarding utilization of PRP and UCB in vitiligo [4, 5,6,7]. Our aim to conduct this study was consolidate the application of PRP and UCB as an effective and safe treatment for vitiligo.

II. Materials And Methods

A total number of **120 patients** from all over India, suffering from Vitiligo were enrolled in this open prospective study. The study period was from July 2016 till June 2018. Patients were thoroughly evaluated for underlying disorders. Full informed, expressed, consent was obtained from the patients to be enrolled in the

study. Standard Medical Therapy (Topical steroids, Topical calcineurin inhibitors, Topical psoralens, UV therapy, Supplements) were given as per National and International Guidelines. Approximately 400 treatments were given overall during the study period (Min 1 to max 6 in each patient). Treatments were given every 30 days cycle. One unit Buffy coat platelet/ single donor platelet/Cord blood was utilized in every session and whenever it is thought to be beneficial local injections of platelet concentrate on white patches has applied.

Patient Selection:

1. New walk-in patients. Diagnosed with vitiligo for the first time.
2. Known patients of vitiligo already on medical and UV treatment.
3. Old chronic non-responsive patients.

Type of PRP and Cord Blood Preparation:

Various methods have been tested for clinical use of PRP in skin rejuvenation, but a clearly defined method is unavailable. We utilized the following PRP and cord blood preparations in our study.

A. Local PRP application :-
1. Topical PRP Application with Micro-needling by Derma-roller (1 mm, 2 mm).
2. Direct intradermal injection of PRP with insulin syringe in the lesions.
B. Systemic PRP/ SDP (Single Donor Platelets) – Intravenous infusion.
C. Umbilical cord blood- Intravenous transfusion.

Platelet Rich Plasma:

Platelet concentrates was obtained from blood bank, J.A. Hospital, Gwalior prepared from whole blood collected as per slandered protocol of Flood and Drug Administration, Government of India.

Umbilical Cord Blood: UCB was collected in CPD bags of 100 ml capacity (HLL Life- care Limited) with all aseptic precautions from normal healthy deliveries conducted in Labor Room, Obstetrics and Gynecology Department and transported to blood bank, J. A. Hospital Gwalior. From Blood Bank it is issued to the respective patient's following the same protocol implies to adult human blood.

Patients were registered either on request of clinicians who had an opinion that their patients will be benefited by the transfusion of UCB or to those patients who were willing to have UCB transfusion as a prospective treatment for their illness.

Inclusion criteria:

- UCB was collected only from patients who gave legal consent for the procedure.
- UCB was collected from normal deliveries with a visibly healthy placenta and fulfilling all aseptic criteria.

Exclusion criteria:

- UCB from diseased or anemic placenta was not collected.
- Collected Units positive for HIV I &II, HbsAg, HCV, VDRL and MP were discarded.
- Unit's positive for ICT and DCT were also discarded.
- Quantity of blood collected less than 60 ml was unfit for transfusion.

Cord blood was transfused at Apollo Hospital and K.S. Nursing Home Gwalior under medical supervision with proper documentation. After completion of transfusion, follow-up of patients were done in accordance with the treating doctor every 15 days up to 3 months.

All data of components prepared, issued and its adverse effect of transfusion to the patients had been collected and tabulated. Data is summarized and compared statistically by frequency distribution and percentage proportion. Chi square (X2) test was applied to know the significant *(p value)* ratio of difference statistically by using software **EpiCalc 2000,** a statistical calculator.

III. Results

Total number of patients registered for the study is 120. Male to female ratio of the patients in the study was Male 59 and female 61 (*p=0.855132),* differentiation is statistically insignificant**.** Average age of the patients was 31.96 **± SD 11.60.** Age group distribution of the patients showed in the Table no. 1.

Table no 1: Age group distribution of Patients in the study

Age group	**No of Patients**	
11-20	**21**	
21-30	**39**	
31-40	**32**	*p-value: 0.000001*
41-50	**17**	
51-60	**10**	
>60	**1**	

Out of 120 patients registered for the study, 20 patients given I PRP I/V and local treatment, 30 patients given I/V Cord blood only, 50 patients given I/V CB + PRP and in 20 cases only local PRP was applied, statistically significant *(p-value : 0.000170)*, Table no. 2.

Table no. 2: Type of therapy and number of patients

Type of therapy	**No of Patients**	
PRP I/V & Local	**20**	*p-value:0.000170*
Cord Blood	**30**	
I/V CB + Local PRP	**50**	
PRP Local	**20**	
Total	**120**	

Outcome of the study i.e. response of the treatment on vitiligo patch is summarized in the Table no 3.

Table no. 3 Outcome of response in the study

Type of therapy	**No of Patients**	**Type of response**	**Response**
PRP I/V & Local	**20**	Local & Systemic	Good response* - 30% Average response# - 50% No response- 20%
Umbilical Cord Blood (UCB)	**30**	Systemic	Good response* - 40% Average response# - 40% No response- 20%
I/V UCB + Local PRP	**50**	Systemic	Good response* - 60% Average response# - 30% No response- 10%
PRP Local	**20**	Local	Good response* - 50% Average response# - 30% No response- 20%
Total	**120**		Good response* - 48.4% Average response# - 35.8% No response- 15.8%

**** 2/3 rd re-pigmentation in affected area, # half re-pigmentation in affected area***

Different Picture of the 4 patients is there in Figure no. 1, initial picture before the therapy on the left side and after the therapy on the right side in the diagram.

Figure No. 1: Case no. 1 to 4; Response of treatment

Adverse event encountered in the study period

Side effects:

Basically we encountered two types of side effects of intravenous transfusion of PRP in our study.

- Allergic reaction.
- Febrile Non-Hemolytic Transfusion Reaction (FNHTR).

Allergic reactions are due to foreign proteins and we encountered 4 instances of a reactive episode of generalized itching, erythema, urticaria which subsided with antihistamines and stat dexamethasone injection on the same day and two patients encountered Febrile Non-Hemolytic Transfusion Reaction (FNHTR). This is because of platelets and leucocytes (antibodies and leucotoxins). This reaction also subsided with paracetamol and supportive treatment within 24 hours.

We did not encounter any side effects of cord blood transfusion and local application of PRP and micro-needling.

IV. Discussion

Vitiligo refers to an acquired, idiopathic, and common de-pigmentation disorder of the skin [8]. Vitiligo affects approximately 0.5% to 2% of the population worldwide [9, 10]. The incidence of vitiligo is found to be 0.25-2.5% in India [11, 12]. Gujarat and Rajasthan states have highest prevalence ~8.8 % [13] . In our study, we could not drown any conclusion about the prevalence of Vitiligo because our patients are from different states of India. The prevalence appears to be equal between men and women [9, 10]. In our study male to female ratio is also insignificant (p=0.855132) while Shajil E M et al [14] reported female to male ratio is 1.6:1.

Although neither life-threatening nor symptomatic, the effect of vitiligo can be cosmetically and psychologically devastating, resulting in low self esteem, poor body image and other negative effects [15-17] and in our study, we also reported higher percentage (70-80%) of patients suffering from such type of conditions.

Patterns of vitiligo are classified into following categories [18]:

1. Generalized vitiligo - the lesions are symmetrical and bilateral.
2. Segmental vitiligo - one or more areas of de-pigmentation on only one side of the body.
3. Universal vitiligo - severe form of vitiligo in which more than 80 percent of the body loses pigment.
4. Lip-tip vitiligo - unusual form of vitiligo which only occurs on the lips, fingers, and toes.
5. Focal vitiligo - uncommon form of vitiligo in which just one or a few isolated lesions appear on the skin in no consistent pattern.

However, in our study the proposed treatment regimen with blood and components was not customized according to the type of vitiligo.

Standard Medical Therapy including Topical steroids, Topical calcineurin inhibitors, Topical psoralens, UV therapy, and Supplements are available for treatment of vitiligo. However, the results are not satisfactory. Many cases show progressive lesions and recurrence after resolution.

Search for newer treatment modalities is underway for effective management of vitiligo. Blood components, mostly platelet rich plasma has emerged as possible contenders. PRP is the simplest and cheapest regenerative medicine intervention that is rapidly extending to multiple medical fields mainly due to the easy use and bio-safety that facilitates translation in humans.[19] It is hypothesized that PRP which is a concentration of multiple growth factors and plasma proteins, namely fibrin, fibronectin and vitronectin plays a pivotal role modulation of tissue repair and regeneration.[3, 20] These growth factors stimulate keratinocytes and fibroblasts proliferation with subsequent improvement of their interaction with melanocytes leading to the stabilization of melanocytes.[5]

Another hypothesis is that vitiligo patients can be benefitted from the growth factors and cytokine mediated local immune regulation which prevents damage to melanocytes and promotes melanin synthesis. [18] Studies conducted till now using PRP have shown promising results. [5, 21, 22]

Introduction of UCB as a potential treatment modality in cases of advanced, refractory and unresponsive vitiligo is unique to our study. In our institute the benefits of UCB has been evaluated in two large scale studies. [23,24]. In the study by Khatoon M et al, out of 61 patients, 30% showed re-pigmentation in more than $2/3^{rd}$ of affected area (good response) with an average of 2.60 transfusions/patient of UCB. [24] Encouraged by results of this study in vitiligo patients, it was hypothesized that growth factors, cytokines and some unknown factor/ proteins in the UCB work for regeneration of melanocytes or transfused stem cells richly present in UCB implant at vitiligo sites and get converted in melanocytes. In the present study, intravenous PRP and UCB transfusions were beneficial in the initiation of re-pigmentation in old, chronic and non-responding patients. Patient group in which transfusions were combined with local application of PRP, showed maximum

response. Repigmentation in more than 2/3rd of affected area was observed in 60% of the patients receiving combined I/V UCB transfusion and local PRP injection.

V. Conclusion

From the present study we conclude that

1. Platelet products are beneficial in treatment of vitiligo.
2. Local PRP with Micro needling gives good color match, and helps in initiation of Repigmentation on bony prominences, palms, soles, etc.
3. Intravenous PRP and Cord Blood Transfusions were beneficial in the initiation of re-pigmentation in old, chronic and non-responding patients.
4. It's a cost effective procedure and has minimal side effects.
5. It has a great potentiality in the treatment of idiopathic disorders in the form of Stem cell reserve.

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