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Original Article

Evaluation of Effect of Platelet Rich Plasma and Human Umbilical Cord Blood as Topical Application on Chronic Wound

Dr. Gourav Kanch[*1], Dr. Mukesh Singh Narwaria[2], Dr. Ankit Sahu[3], Dr. Achala Sahai Sharma[4]

[1] P.G. Student, Department of General Surgery, G.R. Medical College, Gwalior, MP, India
[2] Associate Professor, Department of General Surgery, G.R. Medical College, Gwalior, MP, India
[3] Assistant Professor, Department of Surgery, G.R. Medical College, Gwalior, MP, India
[4] Professor, Department of Obstetrics and Gynaecology, G.R. Medical College, Gwalior, MP, India

ABSTRACT

Background: Platelet rich plasma (PRP) and human umbilical cord blood (HUCB) are two cheap and easily accessible newer modalities used to improve wound healing. The aim of our study is to analyze the effect of these two new modalities and compare it with conventional dressings.
Method: Patients with chronic wounds were divided randomly into three different groups. Group A received a topical application of PRP to their wounds; group B received a topical application of HUCB, while group C were treated with conventional dressings. Wounds were observed weekly and results analyzed at the end of 6 weeks.
Results: Significantly better improvement in wound healing was observed in group A (PRP) and group B (HUCB) patients as compared to group C (Conventional dressing) with a reduction in surface area, improvement in the wound bed, reduction in exudates amount and healthy granulation.
Conclusion: Both PRP and HUCB are cost effective, easy to extract and prepare, and are better and convincing agents used in chronic wounds.

Key Words: *Conventional dressing, Healthy granulation, Human umbilical cord blood (HUCB), Platelet rich plasma (PRP)*

***Corresponding Author**
Dr. Gourav Kanch
P.G. Student, Department of General Surgery, G.R. Medical College, Gwalior, MP, India

INTRODUCTION

A chronic wound is a wound that does not heal in an expected way and in a predictable amount of time (4-6 weeks) as most wounds do [1]. A chronic wound can be recognized by a number of symptoms including the loss of skin and/or tissue surrounding the wound or by the amount of time it takes to heal.

The treatment of chronic wounds has undergone massive changes in the last few decades. With the better understanding of chronic wound pathology and the huge collection of newer wound dressing products and devices management of chronic wounds is no longer a simple scalpel debridement procedure [2, 3].

Apart from conventional methods to facilitate wound healing various new methods are emerging such as cellular therapies which include platelet-rich plasma (PRP) and human umbilical cord blood (HUCB) as local application. This can have an adjunctive role in a standardized, quality treatment plan. Platelets release certain growth factors from alpha granules which are located in thrombocyte cell membrane which include platelet derived growth factor (PDGF), epidermal growth factor (EGF), platelet derived angiogenesis factor and platelet factor [4]. These factors act locally on the wound and hasten the healing process. Platelet extract has been used in many studies and has shown impressive results in healing of chronic ulcers [5, 6]

Platelet rich plasma (PRP) is defined as a portion of the plasma fraction of autologous blood having a platelet concentration above baseline [7]. PRP has also been referred to as platelet-enriched plasma, platelet rich concentrate, autologous platelet gel, and platelet releasate. Platelet releasates have been used to treat wounds since 1985 [8]. It contains a high level of platelets and a full complement of clotting and growth factors.

In humans, PRP has been investigated and used as a clinical tool for several types of medical treatments, including nerve injury, chronic tendinitis, plantar fasciitis, osteoarthritis, cardiac muscle injury and androgenic alopecia for bone repair and regeneration, in plastic surgery, colorectal surgery and oral surgery.

Human umbilical cord and cord blood remains the most abundant, readily available and non-ethically controversial source of stem cells considering the global birth rate of about 133 million a year in 2011. The cord blood is a rich source of haemopoietic stem cells with naive immune status for clinical application [9].

Human umbilical cord blood contains mesenchymal progenitor cells that can be used to treat chronic wounds [10]. Stubendroff M et al [11] mention in their article that compared with mesenchymal stem cells from cord blood, placenta and Wharton's Jelly, cord lining mesenchymal stem cells showed the higher proliferation and migration potential. Furthermore, they expressed lower levels of HLA Class I and II, contributing to their lower immunogenicity. The major Histocompatibility Complex (MHC) was initially discovered as a genetic locus associated with the acceptance or rejection of transplanted organs in mice. In 1954, the same genetic system was described in humans by Jean Dausset and Jan van Rood and was called human leukocyte antigens (HLA) [12]. HLA class I antigens are expressed on all nucleated cells and platelets (except those of the central nervous system) while the HLA class II antigens are expressed on antigen presenting cells (APC) such as B lymphocytes, dendritic cells, macrophages, monocytes, Langerhans cells, endothelial cells, and thymic epithelial cells.

Kamaloz et al [13], have indicated the potential of human umbilical cord blood stem cells to differentiate into keratinocytes under in vitro conditions. The potential of systemic infusion of ABO compatible human umbilical cord blood and the topical application of such blood to burns and other wounds opens up the possibility of providing cheap and accessible burns and wound care to more of the world's neediest patients.

Besides there is global wastage of cord blood in almost all parts of country which can be utilized to treat and cure chronic wounds.

METHOD

Sixty patients with chronic wounds with 20 in each group were included in this study after taking informed and a written consent and approval from institutional ethical committee.

The cases were divided equally into three groups (A, B & C) as mentioned earlier. The study group received standard care of treatment for chronic wound with dressings changed every 48 hours and weekly application of PRP, HUCB and conventional dressing in respective groups.

1) Group A ($n \geq 20$) received platelet rich plasma (PRP) as topical application on 50-200 cm^2 wound area.
2) Group B ($n \geq 20$) received human umbilical cord blood (HUCB) as topical application on 50-200 cm^2 wound area.
3) Group C ($n \geq 20$) received conventional dressings (normal saline) on 50-200 cm^2 wound area.

Procedure

- Group A and Group B received PRP and HUCB as a topical application weekly.
- Group C received conventional dressings on alternate days.
- Simple random sampling was done.
- Single blinding was used.
- Underlying etiology, management was as per guidelines.
- Changes in wound characteristics were followed weekly.
- Results were studied at the end of 6 weeks.
- Amount of blood collected in both groups according to wound size.
- Proper written and informed consent was taken from both groups.

Collection (Human umbilical cord blood)

Human umbilical cord blood was collected from the placenta of seronegative mother (HBsAg, HIV, HCV negative) from Dept. of Obstetrics and Gynecology. The HUCB was collected in heparinized container and stored in cold chain box for not more than 24 hours from the time of collection.

Collection (Platelet rich plasma)

Venous blood was collected from each patient and PRP was prepared with help of centrifuge.

1) Obtain Whole Blood by venepuncture in acid citrate dextrose (ACD) tubes
2) Centrifuge the blood using a 'soft' spin.
3) Transfer the supernatant plasma containing platelets into another sterile tube (without anticoagulant).
4) Centrifuge tube at a higher speed (a hard spin) to obtain a platelet concentrate.

5) The lower 1/3rd is PRP and upper 2/3rd is platelet-poor plasma (PPP). At the bottom of the tube, platelet pellets are formed.

Well informed and written Consent was taken from recipient and donor of HUCB as well as patient receiving PRP.

End point of study

1) Healed or healing wound.
2) Any deterioration of wound.

Observation

1. Measuring surface area before and after treatment
2. Quality of wound before and at the end of study.
3. Photographic documentation before, during and after completion of study.
4. Wound swab (culture and sensitivity) before and after treatment.

Statistical Analysis

Statistical analysis was done by SPSS software (Version V27).

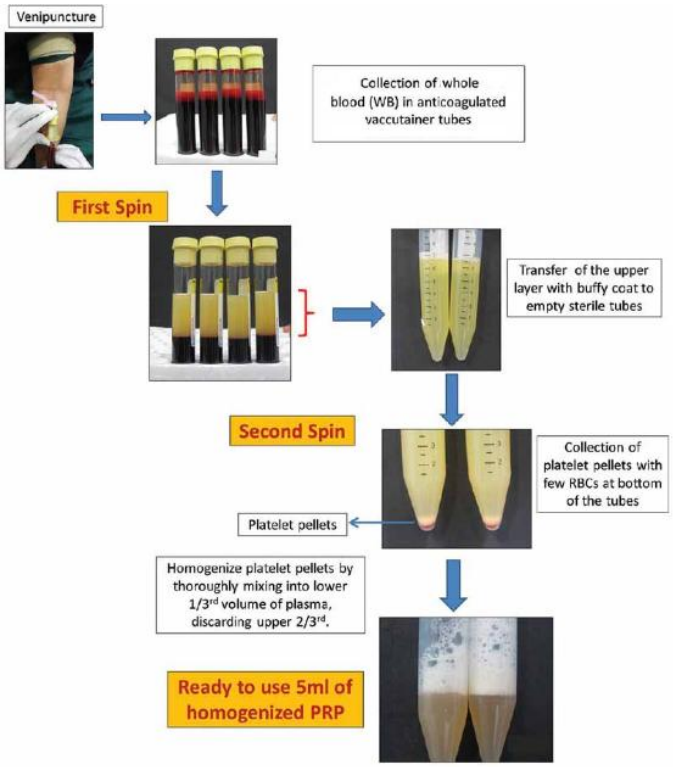

Figure1: Preparation Procedures (Dhurat R et al.)[14]

OBSERVATION AND RESULTS

Present study conducted on 60 patients at Department of Surgery, G.R. Medical College, Gwalior (M.P.). They were divided into three groups: Group A, B and C.Most of the patients in our study belongs to 21-30 years followed by 31-40 years age group (Table 1).

Table 1: Distribution of cases according to age

	Group A		Group B		Group C	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
0-10	1	5.0	1	5.0	2	10.0
11-20	1	5.0	3	15.0	3	15.0
21-30	6	30.0	5	25.0	5	25.0
31-40	5	25.0	5	25.0	3	15.0
41-50	2	10.0	2	10.0	3	15.0
51-60	1	5.0	2	10.0	2	10.0
>60	4	20.0	2	10.0	2	10.0
Total	20	100.0	20	100.0	20	100.0

Majority of patients in each group were male (Table 2).

Table 2: Distribution of cases according to gender

	Group A		Group B		Group C	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
Male	16	80.0	15	75.0	13	65.0
Female	4	20.0	5	25.0	7	35.0
Total	20	100.0	20	100.0	20	100.0

In group A half of the patients (50%) had a wound about 7-10 weeks duration while in group B fewer than half of the patients (40%) had duration of wound 15-18 weeks and group C majority of patients had wound of 15-18 weeks (25%) and 19-22 weeks (25%) duration (Table 3).

Table 3: Distribution of cases according to duration of wound

	Group A		Group B		Group C	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
4-6 weeks	3	15.0	0	0	1	5.0
7-10 weeks	10	50.0	0	0	2	10.0
11-14 weeks	2	10.0	5	25.0	4	20.0
15-18 weeks	1	5.0	8	40.0	5	25.0
19-22 weeks	1	5.0	3	15.0	5	25.0
22-25 weeks	2	10.0	2	10.0	2	10.0
>25 weeks	1	5.0	2	10.0	1	5.0
Total	20	100.0	20	100.0	20	100.0

In group A 70% of patients had > 50% reduction in surface area of the wound at the end of our study(6 weeks), in group B 75% of patients had > 50% reduction in surface area of the wound. In group C only 50% of patients had > 50% reduction in surface area of the wound, with p value of 0.042 while comparing group A and group C and p value of 0.029 while comparing group B and group C, 2 cases in group B and 2 cases in group C were lost to follow up (Table 4).

Table 4: Distribution of cases according to reduction in percentage of surface area

	Group A		Group B		Group C	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
<50% reduction	6	30.0	3	15.0	8	40.0
>50% reduction	14	70.0	15	75.0	10	50.0
Total	20	100.0	18	90.0	18	90.0
Missing	0	0	2	10.0	2	10.0
Total	20	100.00	20	100.0	20	100.0

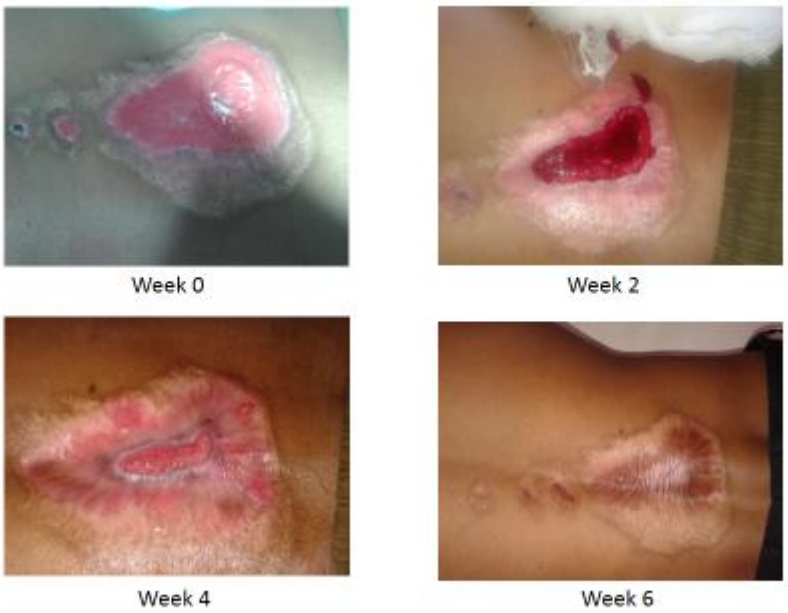

Figure 2: Chronic burn wound over back (HUCB Application)

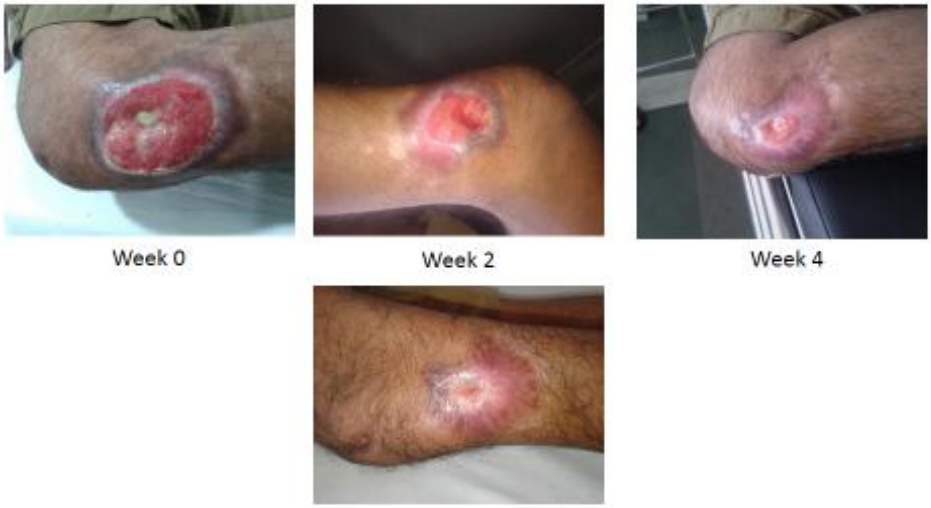

Figure 3: Chronic traumatic wound below knee (PRP application)

Significantly better improvement in wound healing was observed in group A (PRP) and group B (HUCB) patients as compared to group C (Conventional dressing) with a reduction in surface area, improvement in the wound bed, reduction in exudates amount and healthy granulation.

DISCUSSION

This study was carried out at Jayarogya hospital Gajra Raja Medical College Gwalior in the department of surgery from April 2021 to October 2022.

A randomized control trial study of patients (n=60) chosen from Out Patient Department (OPD) and wards of our hospital with chronic wounds was carried out. A total of 60 patients were taken and divided into 3 groups. In group A (n=20) patients received PRP as topical application on the wound of surface area 50-200 cm2 weekly. In group B patients received HUCB as topical application on wound of surface area of similar range. While in group C (n=20) patients received normal saline dressing daily.

Assessment was done by measuring wound size, wound swab, and clinical photographs on a weekly basis, all the parameters re-evaluated at after 6th week i.e. end point of our study.

The majority of patients in our study were in their 3rd and 4th decade of life, there were 30% in group A, 25% in group B and 25% in group C.

Most of the patients in our study were male i.e. 80% in group A, 75% in group B and 65% in group C. The majority of patients in our study had traumatic wounds that comprises 40% in group A, 40% in group B and 35% in group C.

The duration of each wound was varied among all the 3 groups half of the patients in group A majority(50%) of patients had wound of 7-10 week duration, in group B, 40% of the patients had wounds of 15-18 week duration, while in group C, half of the patients (50%) had wound of 15-22 weeks duration.

In group A (PRP group) we studied the effect of PRP on healing of chronic wounds, and a significant reduction in surface area of wound was observed. 70% of patients in group A had more than 50% reduction in surface area of wound was found at the end of 6^{th} week, while no patient showed deterioration of wound.

In group B (HUCB group) we studied the effect of HUCB on healing of chronic wounds and significant reduction in wound area was observed. 75% of patients with chronic wounds were observed to have reduction in more than 50% of surface area of wound at the end of 6^{th} week. While no patient reported to have deterioration of their wounds, two patients in group B out of 20 were lost to follow up.

In group C (Conventional dressing group) we studied the effect of conventional dressing (normal saline dressing) on chronic wounds, no significant reduction in surface area of wound observed. Only 50% of patients had greater than 50% reduction in surface area of wound at the end of our study.

CONCLUSION

Human umbilical cord blood and Platelet Rich Plasma were found to be more effective topical agents in the healing of chronic wounds in comparison to conventional dressing.

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