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Original Research Article

Efficacy of autologous platelet rich plasma over conventional mechanical fixation methods in split thickness skin grafting

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ABSTRACT

Background: Platelet-Rich Plasma (PRP) is an autologous product derived from whole blood through the process of gradient density centrifugation. After skin graft reconstruction, the healing process is longer and may be difficult, depending on the wound site, skin defect size, and patient comorbidities. The potential value of PRP lies in its ability to incorporate high concentrations of platelet-derived growth factors into the skin graft. Since not all patients afford commercially available recombinant platelet rich plasma for skin graft, platelet extract from patient's own blood is being used in this study to test and demonstrate the therapeutic role of PRP in skin graft. The aim of this randomized, prospective study is to compare the effectiveness of PRP in skin graft with conventional method like sutures, staplers or glue.
Methods: The source of data were the patients admitted as inpatients for the management of wounds to the department of general surgery, JSS Hospital, Mysore from September 2016 to September 2018. Total of 60 patients were studied; 30 cases were randomly chosen for study with autologous platelet rich plasma and 30 cases received conventional methods like staples/sutures used to anchor the skin grafts in a control group.
Results: Autologous PRP showed faster and better healing rates. With PRP study group instant graft adherence was seen in all cases. Hematoma, graft edema, discharge from graft site, frequency of dressings and duration of stay in hospital were significantly less in the PRP. There were no adverse effects or reactions seen with the use of autologous PRP among the study group.
Conclusions: The combination of PRP with Split Thickness Skin Graft (STSG) significantly improved clinical outcomes and shortened the wound healing time. Therefore, this treatment combination could provide a way to heal skin after skin graft reconstruction with minimal recovery time. It is found to be highly beneficial in many aspects both to the patient and surgeon based on our results.

Keywords: Growth factors, Platelet-rich plasma, Skin graft

INTRODUCTION

Platelet-rich plasma (PRP) is an autologous product that concentrates a large number of platelets in a small volume of plasma. PRP functions as a fibrin tissue adhesive with hemostatic and tissue sealing properties and provide a unique ability to promote wound healing.[1] PRP provides an immediate surgical hemostatic agent that is biocompatible, safe and effective. PRP accelerates endothelial, epithelial, and epidermal regeneration, stimulates angiogenesis, enhances collagen synthesis, promotes soft tissue healing, decreases dermal scarring and enhances the hemostatic response to injury.[1] Platelets are small discoid blood cells. The average platelet count

ranges from 1.5 to 3.0×10-5/mL of circulating blood and the in vivo half-life time of platelets is about 7days.[2] Split-thickness skin grafting (STSG) is commonly employed for soft-tissue coverage because of its broad application for use, ease of harvest, and universal equipment. STSG healing proceeds through 3 stages which are anchorage, inosculation and maturation. The success of the first two stages is critical to the overall success. The application of autologous Platelet-Rich Plasma (PRP) to STSG application sites has been recently described and theorized to provide immediate skin graft anchorage as well as inosculation of the STSG with nutrient-rich blood media.[3] The addition of PRP to STSG recipient sites seems to enhance primary healing and reduce healing time, likely as a result of shearing force reduction and enhancement of the wound environment with growth factors.[3] Chronic wounds may lack growth factors due to decreased production and release, trapping, excess degradation, or a combination of these mechanisms thus delaying wound healing, which is overcome by PRP. The purpose of this study was to compare two groups of patients with and without topical application of autologous PRP on wound beds prior to split skin grafts.

METHODS

This a prospective randomized controlled study, to test the efficacy of autologous platelet rich plasma in wound beds prior to resurfacing skin grafts instead of conventional methods like sutures, staplers or glue. The study was conducted in the department of surgery, JSS Medical College, Mysore for a period of two years from September 2016 to September 2018. The study was approved by the local ethical committee of our hospital. An informed written consent was obtained from all patients. They were divided into two groups of thirty each. Thirty cases were randomly chosen for study with autologous PRP and thirty cases received conventional methods like sutures, staplers or glue in wound bed for anchorage of skin grafts. Detailed history was taken in all cases regarding the duration, mode of onset, progression and associated symptoms. The etiological factor that might be responsible for chronicity was also elicited. Wound examination was done in all cases. All healing ulcer including traumatic, infective and post burn were included in study. Patients with co morbidities like DM, hypertension, and those on aspirin analogue were also included in this study.

Patients with ulcers with evidence of malignancy, active infection with pus discharge, slough, immune compromised patients, indexed ulcer has exposed tendons, ligaments or bone, evidence of gangrene in the ulcer or on any other part of limb, patient is currently receiving or has received radiation or chemotherapy within the last 3 months, patient with active cancer, decompensated liver disease, or on renal dialysis and patient on steroids for another illness were excluded in study. Under all aseptic precautions, 12ml of blood was drawn intravenously from the antecubital region into 2 bulbs containing CPDA (0.7ml) each. The bulbs were shaken thoroughly to ensure mixing of anticoagulant with drawn blood. The blood centrifuged at 3000rpm for 5mins. The supernatant formed is Platelet Poor Plasma (PPP) and buffy coat (Figure 1). PPP and buffy coat were aspirated and collected in another vacutainer and again centrifuged at 1000rpm for 5mins. The upper half is discarded and the lower half yields concentrated platelet rich plasma. Approximately 5ml of PRP was required for wound area of 100sq.cm. PRP was applied as a thin film over the raw area before application of the graft in case study group (Figure 2). The grafts were assessed for instant adhesion by moving graft with finger and then graft was covered by non-adhesive compressive dressing. In control group the edge was adequately secured with sutures or staples through the graft and surrounding skin.

Additional sutures were placed as needed in the central field of the graft to ensure good contact with the recipient bed and then graft was covered with non-adhesive compressive dressing. Graft success was quantified according to objective parameters used for assessment of efficacy of study like instant adhesion, graft edema, discharge from site, hematoma, graft loss, day of first graft inspection, frequency of dressing and duration of stay in hospital. Day of first graft inspection was done within one week and dressing was changed on basis of wetness present at site for both the group. Unpaired student's "t" test and chi-square test were used to find out the statistical significance. $P<0.05$ was taken as significant.

Figure 1: Platelet rich plasma.

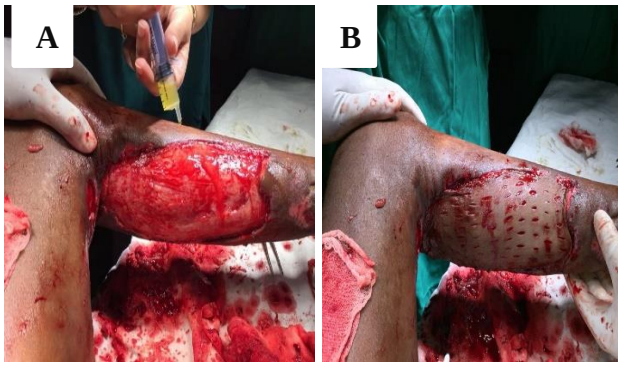

Figure 2: Putting platelet rich plasma during grafting.

RESULTS

Mean age, gender, etiology of wounds, location of wound, co-morbidities and patients on aspirin analogues were compared in both groups (Table 1). Subjects in both groups were compared with all objective assessment parameters. All PRP patient's grafts adhered well within seconds of application compared to 0% of control subjects. Graft edema with PRP group were present only in 2% of patients whereas in control group 18% of patients were observed with graft edema. 20% patients in control group showed discharge from STSGs site which was insignificant in PRP group. Only 3.3% patients from case group showed hematoma where as in control group 23.3% patients showed hematoma (Table 2). This shows effectiveness in achieving and maintaining hemostasis by PRP in STSGs. Only 2% patients from PRP group required secondary grafting compared to 33.3% patients in control group who were underwent secondary grafting due to graft loss. 90% patients from case group needed first graft inspection after 1week and 86.7% patients from control group needed first graft inspection within one week of procedure (Table 3). Total 90% patients from control group needed 3-5 times dressing whereas only 4% patients from case group needed 3-5 times dressing during their stay in hospital. About 90% of patients were discharged after 10 days in control group, whereas 83.3% of patients were discharged within 10days post graft days in the PRP group.

Diabetes, hypertension and intake of aspirin were significant factors detrimental to graft intake. PRP was beneficial in hypertensive patients and those who were on aspirin analogues in view of its hemostatic properties. Foot ulceration is a common complication of diabetes. The wounds are often multifactorial but arise in the setting of peripheral neuropathy or vascular complications. PRP use especially for patients with more severe wounds had shown promising result in early healing and graft intake compared to use of conventional methods without PRP.

In our study it is observed that applying PRP is an effective therapeutic approach for graft healing, and faster graft healing as expected. PRP is able to improve graft integration in the recipient bed and reduce hematoma after the surgical procedure was observed. The difference in all the objective assessment parameters between controls and PRP groups were found to be statistically significant. (P value <0.05) (Figure 3).

Table 1: Percentage distribution of age, gender, comorbidities, medication, location and etiology

Demographic	PRP	Control
Age, years	49.10±15.36	55.87±11.16
Male, %	24, 80%	27, 90%
Female, %	6, 20%	3, 10%
Co-morbidities		
Diabetic, %	15, 50%	13, 43.3%
Hypertension, %	10, 33.3%	8, 26.7%
Aspirin analogue, %	4, 13.3%	3, 10%
Location of wound, %		
Forearm	2, 6.7%	0, 0%
Hand	1, 3.3%	0, 0%
Thigh	0, 0%	4, 13.3%
Leg	20, 66.7%	12, 40%
Foot	7, 23.3%	13, 43.3%
Sole	0, 0%	4, 13.3%
Etiology of wound, %		
Abscess	1, 3.3%	0, 0%
Amputation	1, 3.3%	0, 0%
Burn	1, 3.3%	1, 3.3%
Cellulites	9, 30%	9, 30%
Compartment syndrome	1, 3.3%	0, 0%
Diabetic	3, 10%	7, 23.3%
Fournier's gangrene	0, 0%	1, 3.3%
Necrotizing fasciitis	7, 23.3%	3, 10%
Trauma	7, 23.3%	7, 23.3%
Varicose ulcer	0, 0%	2, 6.7%

Table 2: Outcome variables

	Instant adhesion, %	Graft edema, %	Discharge from graft site,%	Hematoma, %	Graft loss, %
Case	30, 100%	2, 6.7%	1, 3.3%	1, 3.3%	2, 6.7%
Controls	0,0%	18, 60%	6, 20%	7, 23.3%	10, 33.3%
p value	0.0001	0.0001	0.044	0.022	0.009

Table 3: Outcome variables

	Case, %	Control, %	p value
Day of 1st graft inspection			
<1 week	3,10%	26,86.7%	0.00001
>1 week	27,90%	4, 13.3%	
Frequency of dressings			
1-2 times	26,86.7%	3,10%	0.00001
3-5 times	4,13.3%	27,90%	
Stay in hospital			
10 days	25,83.3%	3,10%	0.00001
>10 days	5,16.7%	27,90%	

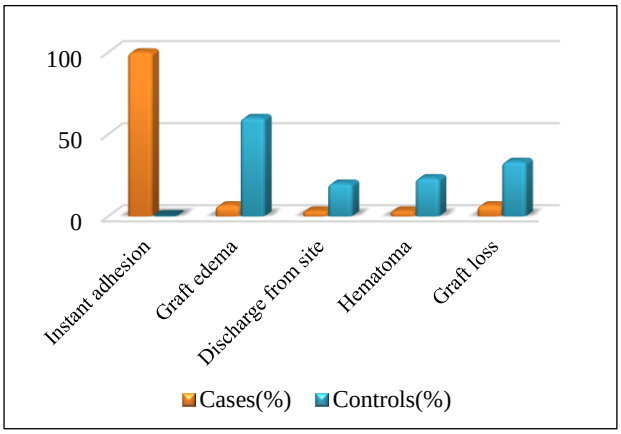

Figure 3: Results of assessment parameters.

DISCUSSION

PRP is a biological product defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline. It is obtained from the blood of patients collected before centrifugation.[4]

Platelet-Rich Plasma (PRP) is also known as Platelet-rich Growth Factors (GFs), Platelet-Rich Fibrin (PRF) matrix, PRF, and platelet concentrate. The concept and description of PRP started in the field of hematology. Hematologists created the term PRP in the 1970s in order to describe the plasma with a platelet count above that of peripheral blood, which was initially used as a transfusion product to treat patients with thrombocytopenia.[4] Subsequently, PRP has been used predominantly in the musculoskeletal field in sports injuries. Other medical fields that also use PRP are cardiac surgery, pediatric surgery, gynecology, urology, plastic surgery, and ophthalmology. More recently, the interest in the application of PRP in dermatology i.e., in tissue regeneration, wound healing, scar revision, skin rejuvenating effects, and alopecia, has increased.[4] Our primary aim of application of PRP prior to resurfacing with skin graft is to facilitate its instant stable adhesion as result of its cohesive and adhesive nature to the wound bed without mechanical fixation. It also facilitated more rapid soft-tissue wound healing and faster vascularization of the healing tissue by delivering growth factors. We have achieved other benefits like hemostasis, reduction in operating time and frequency of post-operative dressings. PRP exerts its beneficial effects via the degranulation of the alpha granules in platelets that contain growth factors. The active secretion of these growth factors begins within minutes of the start of the coagulation sequence, and more than 90% are secreted during the first hour. Growth factors serve to accelerate the wound-healing process by increasing cellular proliferation, matrix formation, connective tissue healing, angiogenesis, and collagen synthesis.[1]

PRP functions as a tissue sealant and drug delivery system, with the platelets initiating wound repair by releasing locally acting growth factors via α-granules degranulation.

The secretory proteins contained in the α-granules of platelets include Platelet-Derived Growth Factor (PDGF-AA, BB, and AB isomers), Transforming Growth Factor-β (TGF-β), Platelet Factor 4 (PF4), Interleukin-1 (IL-1), Platelet-Derived Angiogenesis Factor (PDAF) , Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF) Platelet-Derived Endothelial Growth Factor (PDEGF) , Epithelial Cell Growth Factor (ECGF), Insulin-like Growth Factor (IGF) , Fibrinogen (Ff), Vitronectin (Vn), Fibronectin (Fn), and Thrombospondin-1 (TSP-1) .

These growth factors aid healing by attracting un-differentiated cells in the newly formed matrix and triggering cell division. PRP may suppress cytokine release and limit inflammation, interacting with macrophages to improve tissue healing and regeneration, promote new capillary growth, and accelerate epithelialization in chronic wounds.[5]

Studies showed the use of PRP in particular etiological groups whereas in our study, PRP has been used in all types of wounds irrespective of the etiology and has been found to yield favorable results.[6-10] The application of autologous (PRP) to STSG application sites has been recently described and theorized to provide immediate skin graft anchorage as well as inosculation of the STSG with nutrient-rich blood media.[3]

In our study there was instant adherence of skin graft to wound bed in all 30 patients in the PRP test group as compared to control group in whom it did not happened. Studies showed instant adherence of split skin graft on burn wounds following application of fibrin sealant.[11]

According to Gibran et al, study done on forty post burn patients state that PRP is safe and effective for fixation of skin grafts due to its adhesive nature and outcomes are better than securing skin graft to wound margins or bed with sutures, staples or glue.[12] This not only saves the operative time but also the surgeon's time and effort of removing sutures/staplers in the post-operative period.

In the PRP treated group, we observed only 2% with graft edema, compared to 18% of patients in control group who had graft edema within a week. Angiogenic capacity of PRP because of present of fibrin matrix, leukocytes and a plethora of cytokines and growth factors.[13] Hence application of PRP accelerates the stage of capillary inosculation and early circulation thereby reducing graft edema much earlier.[14] In our study 27 patients from control group needed dressing for 3-5 times in 15days whereas frequency of dressing was less in PRP group including diabetic patients. PRP enables healing and reduces infection rates and exudates and also very promising for diabetic wounds.[15] The study concluded the effectiveness PRP in the management of chronic non-healing ulcers and reduces the overall hospital stay.[16] In our study 90% of patients in PRP group were discharged within 10days post graft. The mean hospital stay was ten days compared to the control group which was 16days. Sixty patients ranging from 18 to 70years were enrolled in the study. There was a statistically significant result (<0.005) between controls and PRP groups in all the objective parameters.

Autologous PRP has large potential and practical benefits which improved the outcome of graft take on wounds irrespective of the etiology. There were no adverse effects or reactions seen when autologous PRP were applied over the wound.

CONCLUSION

The use PRP is safe and effective in the management of acute wounds. It is a cost-effective procedure, helps in early skin grafting and reduced hospital stay. It is found to be highly beneficial in many aspects both to the patient and surgeon based on our results. We recommend the use of autologous PRP routinely in all age groups and all types of wounds prior to resurfacing to ensure better and faster healing as suggested by our results.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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