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CLINICAL EVALUATION TO OBSERVE THE EFFECT OF PRP IN IMPROVING ACCEPTANCE OF STSG (SPLIT-THICKNESS SKIN GRAFT)

Surgery

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ABSTRACT

Skin wounds are injury to healthy biological tissue including skin, mucus membrane and organ tissues. they are related to significant mortality and morbidity with the additional expenditures around 2% of the world wide patients have chronic wounds while older peoples are more prone to them due the age impaired healing process chronic wounds are caused due to various health conditions like diabetes mellitus, atherosclerosis, tuberculosis, leprosy, venous ulcers, pressure sores and trauma vasculitis. These wounds requires long period of time for healing. Resurfacing large skin wounds continue to be challenging in surgeries like reconstructive and plastic. Harvest techniques particularly split-thickness skin graft (STSG) is widely accepted for the resurfacing of large defects such as diabetic foot ulcer (DFU), venous leg ulcers (VLU), and burns. This technique involves 3 steps for wound healing (WH) including anchorage, inosculation, and maturation. Split-thickness skin graft Contain epidermis and a portion of dermis, this method can be utilized to shield large injuries and can survive in less vasculature grafted zone. The aim of the study was to observe the effect of PRP in improving the acceptance of STSG. The significant findings were the rate of WH was more in the PRP subjects (4.17±2.23) than the conventional group (3.53±2.03) The study was conducted "to observe the effect of PRP in improving acceptance of STSG". The rate of WH was more in the PRP patients compared to the conventional group and the time taken for percentage reduction of wound area was significantly less in the PRP group than the conventional group. PRP is biocompatible, effective, and safe which facilitates rapid surgical haemostasis and mimics the final steps of the coagulation process. It can cause rapid adhesion of graft to bed and prevent any deposition below the graft or undue shear.

KEYWORDS

INTRODUCTION:

Skin wounds are related to significant mortality and morbidity with additional expenditure. [1] Moreover, wounds, particularly chronic wounds (CW) are associated with compromised patients' quality of life. Globally, it is estimated that around 6 million people are suffering from chronic wounds. [2] Furthermore, among global wound patients, around 2% of them have chronic wounds while older adults are more vulnerable to wounds because of age-impaired healing process. Whereas, 70% of these wounds recur and 34% are exaggerated due to the infection. [3,4] The reported prevalence of wounds in India was 15.03/1000 population whereas, acute and chronic wounds prevalence were 10.55 and 4.48/1000 of the people respectively. [5] The causes of CW include diabetes mellitus, atherosclerosis, tuberculosis, and leprosy. The other significant causes are venous ulcers, pressure sores, and trauma vasculitis. [2]Resurfacing large skin wounds continue to be challenging in surgeries like reconstructive and plastic.[6] Harvest techniques particularly split-thickness skin graft (STSG) is widely accepted for the resurfacing of large defects such as diabetic foot ulcer (DFU), venous leg ulcers (VLU), and burns.[7,8] This technique involves 3 steps for wound healing (WH) including anchorage, inosculation, and maturation.[9] However, hematoma, shearing, and infection at the site of skin graft can cause its rejection or loss. This may lead to reopening of the wound, thus increasing the hospitalisation period, healthcare expenditure, and socioeconomic burden. Reduced hematoma formation, increasing sticking of skin graft, increasing revascularization, and inhibiting local infection can enhance skin graft acceptance.[10]

Autologous platelet-rich plasma (PRP) is a blood-derived product first introduced in the year 1984 by Assoian[11] . PRP is biocompatible, effective, and safe which facilitates rapid surgical haemostasis and mimics the final steps of the coagulation process. It can cause rapid adhesion of graft to bed and prevent any deposition below the graft or undue shear.[12-13] Moreover, various growth factors (GF) and bioactive proteins including platelet-derived GF, insulin GF-1, epidermal GF, vascular endothelial GF, and transforming GF are present in the α-granules of the platelets.[14] These GF can increase the regeneration of endothelium, epithelium, epidermis, and angiogenesis. Furthermore, it enhances collagen production, soft tissue curing, haemostatic against injury, and reduces dermal scarring. Also, it has antimicrobial action resulting from a high concentration of leukocytes.[15]It is described that the application of PRP to STSG has favourable effects on early surface regeneration. Despite this, there is a paucity of data regarding the application of PRP in STSG. Therefore, this study was carried out to observe the effect of PRP in improving the acceptance of STSG.

Wound- "Wound is an insult to the healthy biological tissue, including skin, mucous membranes, and organ tissues".[16]

There are 4 Types of wounds.
Class 1 (clean wounds): Example-Hernia repair, breast biopsy.
Class 2 (clean-contaminated): Example – Cholecystectomy, elective GI surgery.
Class 3 (Contaminated wound): Example – Enterotomy during bowel obstruction, penetrating abdominal trauma, large tissue injury.
Class 4 (Dirty wounds): Example - Perforated diverticulitis, necrotizing soft tissue infections.

Classification of wounds based on magnitude of severity
Acute Wound, Chronic Wounds, Wound healing[17]

The procedure of WH can be categorized into 4 phases (figure 1): Coagulation phase Inflammation phase, Granulation tissue formation phase, (proliferative phase), Remodelling or scar formation phase. Skin grafting is widely used procedure for resurfacing skin defects at various sites and is the gold standard for the care of thermal injuries. This strategy is utilized to cover the wound to defend from infections and to enhance the healing process.[18]

Skin grafting is distributed into three categories like:
Split-thickness skin graft:

Contain epidermis and a portion of dermis, this method can be utilized to shield large injuries and can survive in less vasculature grafted zone.

Though, it is related with graft contracture during the curative process.

Full-thickness skin graft: Graft comprises the skin and the whole dermis. It requires better vasculature in the grafted zone, but has less contraction at healing and can be consider to shelter exposed areas of the body including the face or neck. [19]

Epidermal skin grafts: They consist epidermis layer which chiefly contain keratinocytes responsible for discharge of GF, chemical mediators and prompt of WH process. [20]

Aim and objectives

Aim-To observe the effect of PRP in improving the acceptance of STSG.

OBJECTIVES -To observe the time taken for STSG uptake among the patients with and without the use of PRP before grafting and the incidence of graft oedema, wound discharge, hematoma, and graft loss in patients with STSG with and without the use of PRP prior to grafting.

MATERIALAND METHODS:

The present prospective interventional study was carried out at Dr. D. Y. Patil hospital and research center, Kolhapur from October 2019 to September 2021 after the institutional ethical approval. A sum of 92 subjects with healing ulcers including traumatic, infective, and post-burn and haemoglobin >10gm/dl were recruited after obtaining informed consent. Whereas, patients with malignant ulcers, active infection, compromised immunity, ulcer with exposed tendons, ligament or bone, on radiation or chemotherapy in last 3 months, liver disease, and renal dialysis were excluded from the study.

After thorough history of the subjects was taken and a thorough clinical investigation was completed. These participants were randomly categorized into two groups such as PRP group (n=67) and the conventional group (n=25).

To prepare PRP, under aseptic conditions blood was obtained alternatively from femoral vein and brachial vein using 10ml syringes than previously containing anticoagulants. The obtained blood was then transferred in to 10ml vacutainer which consisted of 1ml citrate phosphate, distrosadenine (CPD-A) anticoagulant. Further this blood was added in 5ml vacutainer tube without anticoagulants and again 4ml of CPD-A anticoagulant was added in each tube. These vacutainers were then subjected to initial hard spin using centrifuge at 3000 RPM for 20 minutes. This causes separation of blood into RBC layer (at bottom) and plasma layer (above RBC layer) which was extracted using wide bore needle. The extracted plasma from first spin was centrifuged by second soft spin at 1000RPM for 10min. This provided platelet pallets with few RBCs at the bottom of the vacutainer. The lower one-third of tube containing PRP and upper two-third containing platelet poor plasma (PPP) which was discarded to achieve PRP. In the tube containing PRP, calcium chloride was added as a clot activator. Considering its shelf life (2hrs), PRP was prepared when patient was transferred on operation table. This was put as a thin coat on the wound surface before grafting. The graft adhesion was assessed by moving it with finger and covered with a non-sticky compressive dressing. In conventional group patients, the edge was fixed with sutures or staples through the graft and surrounding skin. Graft success was quantified based on parameters such as rate of WH, time taken to decrease the wound area, and duration of stay in hospital. The post-surgery graft was assessed for oedema, discharge, hematoma, and graft loss. The dressing was done on 5th day and subsequently on every 3rd day till 15 days.

STATISTICALANALYSIS

Data were evaluated using SPSS V 1.2.5001 software. Continuous variables were shown in mean±SD whereas, categorical variables were presented in percentage and frequency. The significant mean difference between the two groups was observed by the Two samples independent T-Test. The p-value is less than or equal to 5% considered as significant.

RESULTS

Among the included patients most were male (67.39%, n=62). The detailed distribution of the participants according to gender is illustrated in table 1.

Table 1: Frequency Distribution of Gender.

Gender	Frequency	Percentage (%)
Female	30	32.61%
Male	62	67.39%
Total	92	100.00%

In PRP and the conventional group, most of the participants were male (n=43 and n=19). Detailed group-wise distribution of gender is shown in table 2.

Table 2. Frequency distribution of gender according to groups

Groups	Female (n)	Percentage (%)	Male (n)	Percentage (%)	Total	Percentage (%)
PRP	24	26.09%	43	46.74%	67	72.83%
Conventional	6	6.52%	19	20.65%	25	27.17%
Total	30	32.61%	62	67.39%	92	100.00%

Majority of the subjects (n=30, 32.61%) were from 60-75 years age group including n=23 males (Table 2). The average age of the PRP and conventional group patients was 49.6418 ± 17.39 and 64.00 ± 13.98 years respectively.

Table 3. Frequency distribution age with gender

Age	Female (n)	Percentage (%)	Male (n)	Percentage (%)	Total (n)	Percentage (%)
15-30	5	45.45%	6	54.55%	11	11.96%
30-45	6	30.00%	14	70.00%	20	21.74%
45-60	9	37.50%	15	62.50%	24	26.09%
60-75	7	23.33%	23	76.67%	30	32.61%
75-90	3	42.86%	4	57.14%	7	7.61%
Total	30	32.61%	62	67.39%	92	100.00%

The average duration of the wound in all participants was 14.70 weeks. According to groups, the mean duration of the ulcer was 14.28 ± 15.28 and 15.84 ± 12.68 weeks in the PRP and conventional group respectively. Distribution of duration of the wound showed that 53.26% (n=49) of patients had 1-10-week duration of the wound. Detailed distribution of the duration of the wound is illustrated in table 3.

Table 4. Frequency distribution of duration of wound

Duration (Weeks)	Frequency (n)	Percentage (%)
1-10	49	53.26%
11-20	20	21.74%
21-30	16	17.39%
31-40	3	7.61%
Total	92	100.00%

In study subjects infection (54.35%, n=50), diabetes (18.48%, n=17), and trauma (14.13%, n=13) were the commonly found precipitating cause of ulcer (table 4).

Table 5. Frequency distribution of precipitating cause of ulcer

Precipitating cause of ulcer	Frequency (n)	Percentage (%)
Diabetes	17	18.48%
Infection	50	54.35%
Pressure	6	6.52%
PVD	1	1.09%
Trauma	13	14.13%
Varicose Vein	5	5.43%
Total	92	100.00%

DISCUSSION:

The aim of the study was to observe the effect of PRP in improving the acceptance of STSG.

studies suggested that the existence of fibrin matrix, leukocytes, cytokines, and GF cause reduction of oedema by enhancing angiogenesis. PRP also increases the rate of WH and reduces infection risk. Moreover, PRP could significantly reduce operation duration, post-operative dressing, and medical expenditure. The topical usage of PRP could decrease the chances of hematoma development, graft edema, and occurance of weeping at recipient sites.hence it improves the acceptance of STSG in PRP group than conventional group.

Age and sex incidence- Here, majority of the participants were male (67.39%) followed by female (32.61%), similarly out of 67 PRP group

participants 43 were male whereas, 19 out of 25 were male in conventional group. Various other studies shown male predominance in either groups (Table 9). This is because men are at increased risk of diabetes, vascular diseases, and accidental injury. [21]However, current as well as previous studies showed insignificant difference among the gender.

Table 6. Comparison of gender predominance among studies

Studies	Male (%)		Female (%)	
	PRP group	Conventional group	PRP group	Conventional group
Thimmanahalli GU. et. al.[91]	80	90	20	10
Hersant B. et. al.[92]	57.14	61.53	42.86	38.47
Waiker VP et. al.[93]	76	64	24	36
Present study	70.14	76	29.86	24

Majority of the subjects (32.61%) were from 60-70 years of group followed by 26.09%, 21.74%, 11.96%, and 7.61% belongs to 45-60, 30-44, 15-30, and 75-90 years of age group respectively. Among these age categories, male were predominantly present. The average age of the conventional and PRP patients was 64.00 ± 13.98 and 49.6418 ± 17.39 years respectively. In the studies conducted to assess the effect of PRP on chronic wound the mean age of patients were ranging from 45-56 years in both groups (table 6).

Table 7. Comparison of age predominance among studies

Studies	Average age (years)	
	PRP group (mean±SD)	Conventional group (mean±SD)
Thimmanahalli GU. et. al.[91]	49.10± 15.36	55.87± 11.15
Gupta S et. al.[89]	45.1	48.2
Anil K. et. al.[96]	47.93±15.86	47.20±14.45

Predisposing factors-The most predominant precipitating causes of ulcer in all subject were infection (54.35%), diabetes (18.48%), and trauma (14.13%), followed by pressure (6.52%) varicose vein (5.43%), and PVD (1.09%). Whereas, in the research of Thimma nahalli GU. et. al. diabetes (33.3%), cellulitis (30%), and trauma (23.3%) were the reason of ulcers. [22]In the series of Zarchi K. et al. the common causative factor of wound was arterial, venous ulcers, diabetes and vasculitis in 58% of subjects followed by surgery (28.7%) and pressure ulcer (7.4) (table 8)[23]. The difference in precipitating factors may be because of differences in geography, socioeconomic status, and occupation of the subjects.

Table 8. Comparison of precipitating factors among studies

Precipitating factors	Studies		
	Thimmanahalli GU. et. al.	Zarchi K. et al.	Present study
Diabetes	33.3%	58%	18.48%
Infection	-	-	54.35%
Pressure	-	7.4%	6.52%
PVD	-	-	1.09%
Trauma	23.3%	-	14.13%
Varicose Vein	6.7%	-	5.43%
Cellulitis	30%	-	-
Surgery	-	26.8%	-

Rate of WH

In the current study, the avearge rate of WH was more in the PRP patients (4.17 ± 2.23) than conventional group (3.53 ± 2.03), but the difference was not statistically significant (P=0.19). Similarly, Hasibuan L. et al. suggested no variation in the WH rate. [24]However, Adly OA. et. al. and Hersant B et. al. showed a significantly augmented rate of WH in PRP than the conventional group. [25, 26] This may be because of the process of preparation of PRP, blood drawing; speed, time, the temperature of centrifuge, and anticoagulant used. [27] Different guidelines may produce a varying concentration of PRP, which may cause altered effectiveness of treatment. [29] Furthermore, studies suggested that the existence of fibrin matrix, leukocytes, cytokines, and GF cause reduction of oedema by enhancing angiogenesis. PRP also increases the rate of WH and reduces infection risk.[28-29]Moreover, PRP could significantly reduce operation duration, post-operative dressing, and medical expenditure. The topical usage of PRP could decrease the chances of hematoma development, graft edema, and occurance of weeping at recipient sites. Waiker VP et. al. suggested that autologous PRP has higher efficacy and practical advantages facilitating enhanced chances of graft acceptance on wounds despite the etiology.[30]Considering its cost-effectiveness, ease of preparation, haemostatic, adhesive, and healing properties it should be considered as an additive in the treatment of wounds in developing nations.

The study indicated an increased WH rate, less time taken for WH, and duration of hospital stay in the PRP group. Depend upon the present study findings we assume that the autologous PRP can be routinely used in all patients irrespective of their age and wounds before grafting to assure better and faster healing. The drawbacks of the study including the investigator was not blinded, and being single centred, all together could have led to some bias. The other important limitations like adverse effects such as instant adhesion and rate of dressing were not assessed in either group. Moreover, follow-up for the evaluation WH process, patient satisfaction, quality of life, number of debridement required, and expenditure of management were not assessed. Further, a study with a sufficient sample size in each etiological group with extrapolation of results and long-term follow-ups would provide the character of wound during autologous PRP treatment

CONCLUSION:

The study was conducted "to observe the effect of PRP in improving acceptance of STSG". The rate of WH was more in the PRP patients compared to the conventional group and the time taken for percentage reduction of wound area was significantly less in the PRP group than the conventional group. Period of stay in the hospital was less in the PRP group than the conventional group. Further, large multicentre studies to evaluate the long term effects of PRP such as scar assessment and quality of life are required.

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