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Comparing The Role of Mesenchymal Stem Cell Glue (MSCS) With Platelet Rich Fibrin (PRF) Gel in Treating Abrasions

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Abstract

Introduction: Abrasions are minor injuries to the body's skin and inner linings that can be seen on any part of the body, but are most commonly found on the forehead, nose tip, cheek, and chin region. Though, facial abrasions are superficial injuries, but it can also lead to unacceptable scars and appearances.

Hence, using the autologous medium as a dressing material over these abrasions can substantially reduce the tendency of scar and hyperpigmentation. A blood clot serves as the focal point for healing, with 95% red blood cells and 5% platelets making up a normal blood clot. PRF membranes prevent epithelial cells from migrating away from its surface, stimulate the development of micro vascularization, and protect open wounds. Natural stem cell therapy is the latest advancement in treatment of facial wounds and has shown to increase the level of collagen and elastin in skin and reduce scars. This study aims to compare and evaluate the outcomes of dressing materials over abrasive wounds and their role in soft tissue healing.

Purpose: The study aims to evaluate the healing potential of mesenchymal stem cells and platelet rich fibrin in treating skin abrasions.

Study Design: A total number of 32 patients requiring intervention in abrasive wounds were randomly divided into two groups: Group A-16 treated with PRF and Group B-16 treated with MSCs.

Results: Our study found that both PRF and PRFM induces a dense fibrous matrix and stimulates angiogenesis and epithelialization, leading to the conversion of soluble fibrinogen into insoluble fibrin that polymerizes with thrombin. The PRF membrane consists of a fibrin 3D mesh polymerized structure, platelets, leukocytes, growth factors, and circulating stem cells. Post-operative pain, clinical appearance of wound bed, size of the wound along with H_2O_2 epithelial test and Vancouver scar scale showed no significant difference ($p>0.05$).

Conclusion: PRF and MSCs have improved soft tissue healing, decreased discomfort, increased wound contraction and epithelization, and decreased scarring of healing wound sites. This is the first time that the efficacy of both dressing materials is compared, but additional clinical studies are needed to compare them. Future studies are needed to better understand the platelet concentrates' capacity for regeneration**.**

Keywords: Platelet Rich Fibrin (PRF), Mesenchymal Stem Cells (MSCs), Abrasive wounds, Platelet Rich Fibrin Matrix (PRFM)

Introduction

Abrasions are minor injuries to the body's skin and inner linings that break the continuity of the tissue. However, if the abrasions extend into the deep layer of the dermis, it results in scarring. These are the injuries limited to the epidermis that cause minimum bleeding and typically heal without scar. Friction against the epidermis causes abrasions, which lead to denudation. All types of blunt trauma result in abrasions, with friction and impact being the most frequent mechanisms.[1] Abrasions inflicted on by deliberate injury, such as sexual assaults, are more common in middle-aged people, particularly women while youngsters regularly sustain unintended abrasions through accidents and sportsrelated injuries. Abrasions can be seen on any part of the body, however they are most frequently found on the forehead, nose tip, cheek, and chin region.[2]

Any abrasive wound that develops after an accident is covered by a blood clot, which serves as the focal point for healing. 95% red blood cells and 5% platelets make up a normal blood clot. Platelets produce and release chemicals that aid in tissue healing and have an impact on immune response, angiogenesis, and inflammatory processes. They include significant pools of physiologically active proteins that, when bound to the extracellular matrix or a forming fibrin mesh, can produce chemotactic gradients that favour the recruitment of stem cells, encourage cell migration and differentiation, and facilitate repair.[3]

PRF is a platelet and immunological components of a blood specimen are all essential for immunity and healing; the components of blood sample is a concentrate that collects on a single fibrin membrane. Vasculature, defense, and epithelial coverage are the three elements of healing and soft tissue development.—are simultaneously supported by the PRF membranes. This membrane prevents epithelial cells from migrating away from its surface, stimulates the development of micro vascularization, and protects open wounds. Since the healing that results from employing this technique as "modified secondary intention healing" because it is neither pure primary intention healing nor pure secondary intention healing. This method's effectiveness is due to the different growth factors and proteins that are distributed locally on a fibrin mesh, simulating and promoting natural healing of wounds and leads to almost scarless cosmetic wound healing.[4]

Natural stem cell therapy is the latest advancement in treatment of facial wounds and have shown to increase the level of collagen and elastin in skin and thereby

reducing the scars. MSCs are traditionally found in the bone marrow, but can also be isolated from tissues including core blood, peripheral blood, adipose tissues. MSCs differentiates into osteoblasts, adipocytes, and chondrocytes, increased epithelialization, cellularity, angiogenesis, and tensile strength were seen in wounds treated with bone marrow MSCs. MSCs have been demonstrated to promote angiogenesis by raising levels of vascular endothelial proliferation factor (VEGF), hepatocyte growth factor, and fibroblast and keratinocyte migration (HGF).

The purpose of this study is to compare and evaluate the outcomes of the dressing materials over the abrasive wounds and their role in soft tissue healing.

Material

This prospective randomized control study was conducted in the Department of Oral and Maxillofacial Surgery, Saraswati Dental College & Hospital. Lucknow. A total number of 32 patients requiring surgical intervention in the abrasive wounds all over the body will be recruited as per the inclusion/exclusion criteria and randomly divided into two groups of 16 patients each. Patients were divided into two groups: Group 1 - abrasive wounds treated with application of Platelet Rich Fibrin gel (PRF) and Group 2- abrasive wounds treated with applications of Mesenchymal Stem Cells (MSCs). All patients were explained about the procedure and written informed consent was obtained.

Methods

Preparation of Platelet Rich Fibrin (PRF) Gel:

10 ml venous blood withdrawn transferred into a test tube and centrifuged at 3200 rpm for 12 minutes. The resultant product consists of three layers, one of which contains the red cell corpuscular base and second layer contains the acellular platelet and third layer is poor plasma. The PRF gel was removed from the tube and stripped from the adjacent red blood cell layer. The wound was covered with a few thick pieces of gauze. All procedures took 15-30 mins and all evaluating parameters were noted.

Preparation of Stem Cells:

8ml of patient's own blood (whole blood) is drawn into a vacuum collection tube containing cell separator gel. The tube is then placed into a centrifuge and spun for 6 minutes at 3400RPM to separate the blood into a supernatant plasma/ stem cell suspension. The red blood cells are located below the cell separator gel. The stem cells in glue form 0.5-1ml just above the gel is kept aside for further use.

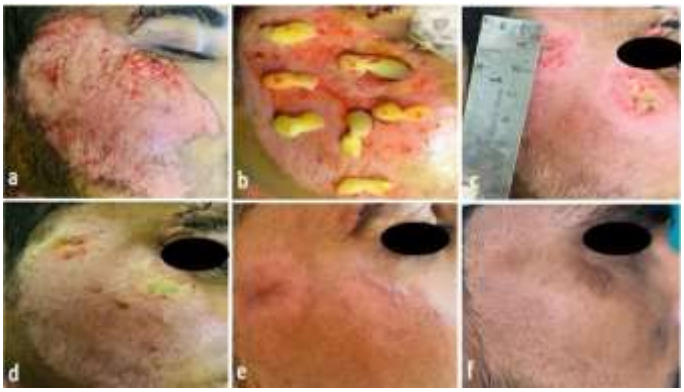


Figure 1: a) Pre Application of PRF over Abrasion in right cheek region b) Post Application c) 1st day post application d) 5th Day post application e) 15th Day post application f) 21st Day post application

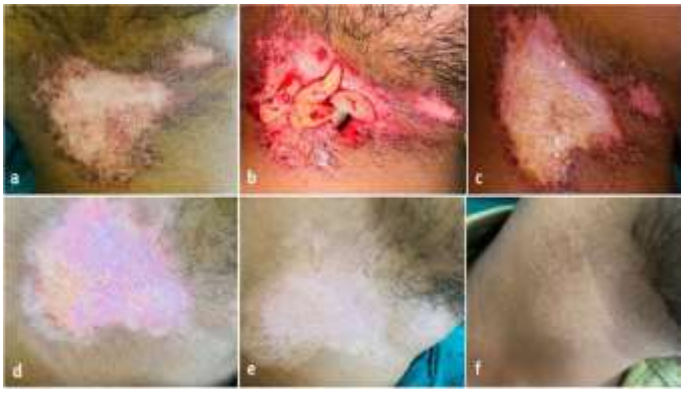


Figure 2: a) Pre Application of MSCs over abrasion in right supraclavicular region b) Post Application c) 1st day

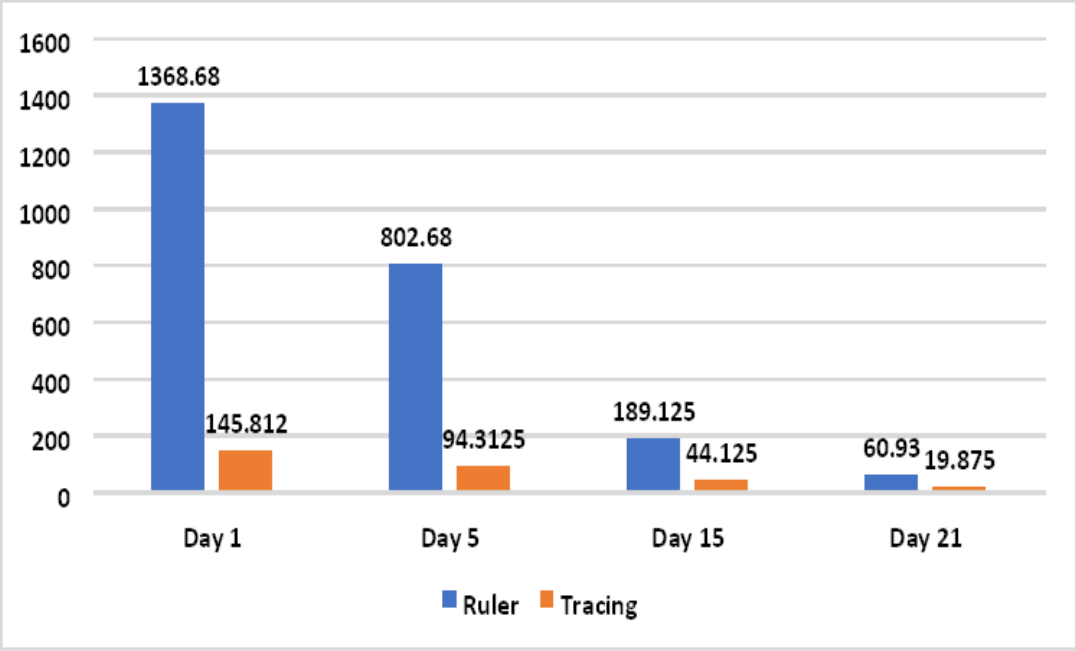
post application d) 5th Day post application e) 15th Day post application f) 21st Day post application

Data Analysis

The sample size was calculated using G power software, with an effect size of 0.53 and a confidence interval of 95% with 5% precision. Intergroup and intragroup comparisons were done using ANOVA, Tukey's Post Hoc analysis, Kruskal Wallis non parametric test, Mann Whitney U test. The p value was set at 0.05 to be significant, and value less than 0.01 was considered as highly significant.

Statistical Analysis

Graph 1: Mean scores of size of wound in group A



Graph 2: Mean values of scores of size of wound for group B

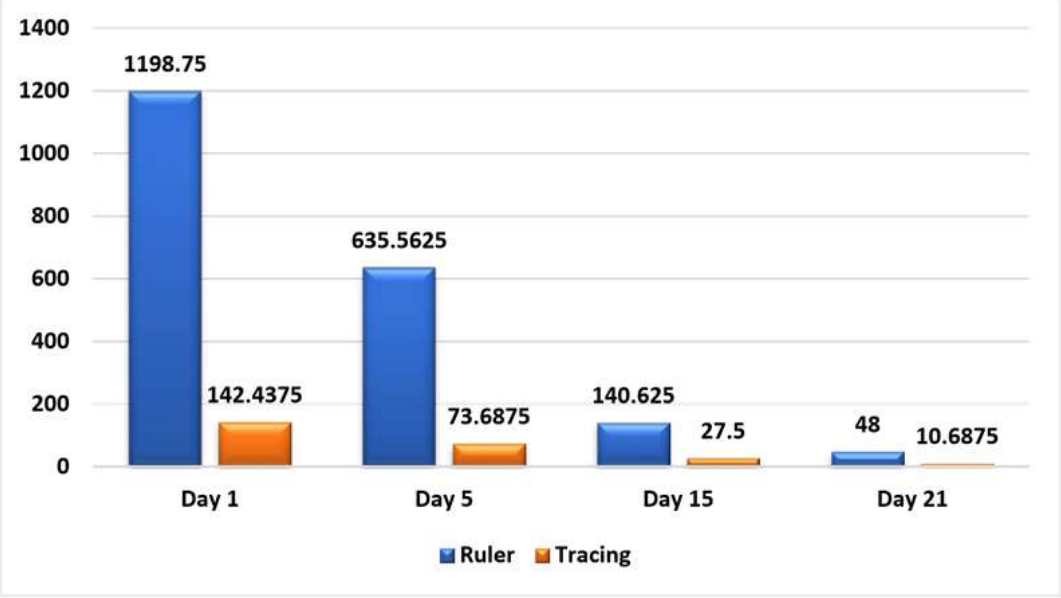


Table 1: Intergroup comparison of clinical appearance of the wound between group A and B at different time intervals

Clinical Appearance of wound bed	Group	N	Mean Rank	Sum of Ranks	P value
Day 1	Group A	16	18.16	290.50	0.221 (NS)
	Group B	16	14.84	237.50	
Day 5	Group A	16	14.94	239.00	0.287 (NS)
	Group B	16	18.06	289.00	
Day 15	Group A	16	14.97	239.50	0.281 (NS)
	Group B	16	18.03	288.50	
Day 21	Group A	16	14.88	238.00	0.250 (NS)
	Group B	16	18.13	290.00	

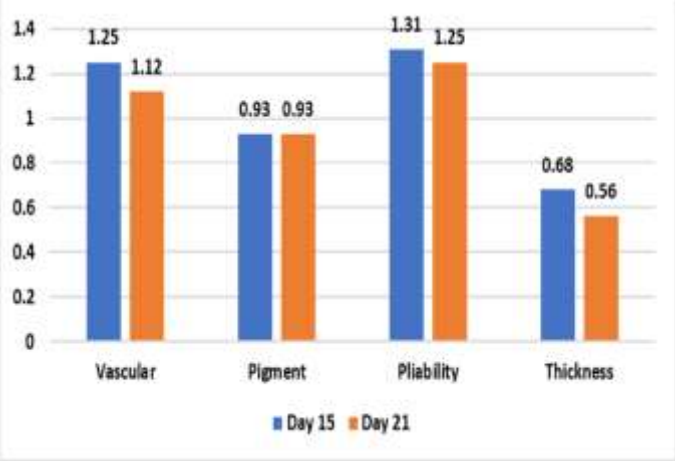
Table 2: Intergroup comparison of epithelization of the wound between group A and B at different time intervals

Epithelisation	Group	N	Mean Rank	Sum of Ranks	P value
Day 5	Group A	16	17.00	272.00	0.551 (NS)
	Group B	16	16.00	256.00	
Day 15	Group A	16	17.50	280.00	0.453 (NS)
	Group B	16	15.50	248.00	
Day 21	Group A	16	17.00	272.00	0.317 (NS)
	Group B	16	16.00	256.00	

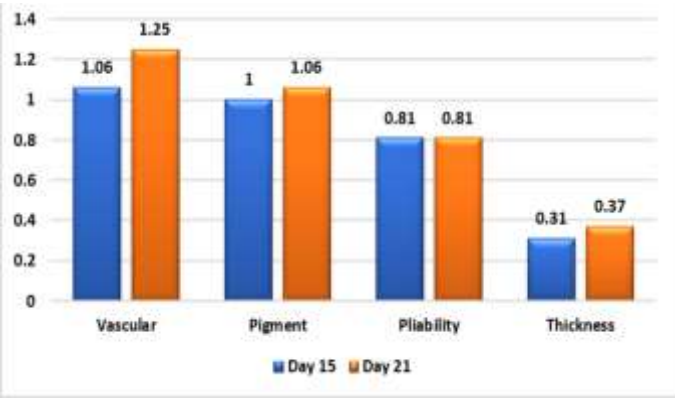
Table 3: Intergroup comparison of pain of the wound between group A and B at different time intervals

Pain	Group	N	Mean Rank	Sum of Ranks	P Value
Day 1	Group A	16	14.88	238.00	0.312 (NS)
	Group B	16	18.13	290.00	
Day 5	Group A	16	16.94	271.00	0.777 (NS)
	Group B	16	16.06	257.00	
Day 15	Group A	16	16.03	256.50	0.770 (NS)
	Group B	16	16.97	271.50	
Day 21	Group A	16	17.00	272.00	0.551 (NS)
	Group B	16	16.00	256.00	

Graph 3: Mean values of scores of Vancouver scar scale for patients of group A



Graph 4: Mean scores of Vancouver scar scale for group B



Result

Analysis of size of wound by **RULER** method, It was found that after 15th day, significant decrease in the size of wound was seen in both the groups with mean value of group A at day 1 was 1368.68 and 60.93 respectively and group B at day 1 32.8 and 22.32 respectively. Statistically significant difference (P> 0.001) in mean values of wound size from day 1 to 21st in both groups was noted. (Fig 3)

Analysis of size of wound by **TRACING** method, It was found that after 15th day, significant decrease in the size of wound was seen in both the groups with mean value of group A at day 1 was 145.8 and 19.8 respectively and group B at day 1 was 142.4 and 10.68 respectively. Statistically significant difference (P> 0.001) in mean values of wound size from day 1 to 21st in both groups was noted. (Fig 4).

The order of the size of the wound seen here as: Day 21=< Day 15 =< Day 5< Day 0.

Evaluation of clinical appearance of wound bed in group A on the day 1st , 5th, 15th, 21st showed mean values of 18.16, 14.94, 14.97, and 14.88 respectively whereas group B on the day 1, 5th, 15th, 21st showed mean values 14.84, 18.06, 18.03, 18.13 respectively. Mean values shows that there is a significant difference ($p<0.05$) in the clinical appearance of the wound between the time intervals of both the groups day 5 and 15, the higher mean rank at day 15 implies that the score for clinical appearance on day 15 was significantly higher than at day 5. A highly significant difference ($p<0.01$) in the clinical appearance of the wound between the time intervals of day 5 and 21, the higher mean rank at day 21 implies that the score for clinical appearance on day 21 was significantly higher than at day 5. There is no statistical significant difference ($p>0.05$) in the appearance of the wound between the two groups A & B when compared at different time intervals (Table 1).

Evaluation of mean values of VAS score of patients in group A on day 1st, 5th, 15th, 21st showed 6.93, 4.62, 2.62, 1.12 respectively whereas group B on same days showed mean values of 7.43, 4.62, 2.75, 1.06 respectively. There is a highly significant difference ($p<0.01$) in the pain score of the patients when compared mean score indicates the following order (reducing pain score with increasing time interval): Day 0> Day 5 >Day 15> Day 21 (Table 4).

Assessment of mean values of epithelization of patients in group A on day 5 (1.12), day 15 (1.75) and day 21 (2.06) and group B day 5 (1.06), day 15 (1.62), day 21 (2). There is a highly significant difference ($p<0.01$) in

the epithelization of both the groups. The mean score indicates the following order (increase in epithelization with increasing time): Day 21>Day 15> Day 5.(Table 2)

Mean values of Vancouver scar scale for group A based on four factors of evaluation that is vascularity, pigmentation, pliability, thickness on 15th day are- 1.15, 0.93, 1.31, 0.68 respectively and on 21st day are- 1.12, 0.93, 1.25, 0.56 respectively and for group B based on above mentioned factors mean values on 15th day are- 1.06, 1, 0.81, 0.31 respectively and on 21st day are- 1.25, 1.06, 0.81, 0.37 respectively. Based on the mean values, it suggests that there is no significant difference ($p>0.05$) in the various components of Vancouver scale as seen at day 15 and at day 21.

Discussion

The natural healing process of a wound involves a cascade of biological reactions, including platelet aggregation and blood vessel constriction. Neutrophils are the first to swarm in and release mediators and cytokines that encourage angiogenesis, thrombosis, and epithelialization. Scaffolding is provided by extracellular components that the fibroblasts will lay down. The inflammatory phase usually lasts a few days, while the proliferative phase may continue for a few weeks. Addition of PRF or MSCs has been shown to increase satellite cells proliferation and differentiation. Wound dressings play a vital role in the treatment.

Our study found a statistically significant difference (P0.001) between day 1 and 21 and a similar reduction in wound size in both groups beyond that point. Kulkarni et al[5] and Arvindaksha et al[6] found that all PRF affected sites had completed uneventful full healing and wound contraction by the 18th post-operative day. Rupa S et al[7] conducted a prospective randomized comparative study, where the two treatment groups for patients with chronic non-healing ulcers were Platelet-rich fibrin matrix (PRFM) group and Autologous Non Cultured Epidermal cell Suspension (NCES). The growth factor release was seen to be increasing steadily and gradually as a result of the PRF membrane results. Our study found a significant difference in the clinical appearance of the wound bed between two groups, with the mean score changing from sloughy and necrotic to granulating and epithelizing from day 1 to day 21. Choukroun J and Diss A et al[8] explained that the fibrin matrix of both PRF and MSCs is responsible for the healing of the wound edges. Khawabata H et al[9] and Ozcan M[10] hypothesized that platelet concentrates consists of thinner fibrin fibers that are more easily degraded and may release growth hormones more quickly, leading to faster healing mechanisms and approximation of wound edges. Our study found no significant difference in pain scores between day 1 and 21 post-surgical. This can be attributed to the release of mediators from platelets, which have been reported to have a role in postoperative pain modulation. Shanmugam M[11] and Rastogi S et al[12] compared wound healing parameters with Platelet-rich fibrin (PRF) membrane and collagen dressing (CollaCote®). Femminella B et al[13] discovered lower patient morbidity in the PRF and MSCs group. Our study found no significant difference in epithelization of the wound between group A and B. Zhu G et al[14] suggested that H_2O_2 promotes oxidative stress and resolves inflammation, while Reddy S et al[15] found an uneventful comprehensive healing at the site with PRF by 18 days. The PRF membrane features all the essential parameters permitting optimal healing, and the H_2O_2 test measures the quality of epithelial barrier. Our study found that scar formation is the third phase of healing, involving progressive remodeling of the granulation tissue. Scar scaling was done every 15th and 21st day for both groups, and almost all patients showed a return to normal

vascularity. However, MSCs group showed tendency to develop hypertrophic scars, with 75% of cases being scarless. The use of both PRF and MSCs as dressing materials has been documented in literature, but the efficacy of both has not been compared together. Azad AK et al[16] study compared chitosan membrane and collagen membrane as wound-dressing materials and found that chitosan had superior pigmentation and firm scars.

Healing with both dressings usually resulted in a return to normal height and contour in 80% patients.

Future studies evaluating the effects of each platelet formulation on cell behavior and in vivo study are needed.

Conclusion

PRF and MSCs are a new generation of platelet concentrates that have a significant biologic activity. The gradual polymerization of PRF membrane has a favorable physiologic architecture to promote the healing process. PRF and PRFM improved soft tissue healing, decreased discomfort, increased wound contraction and epithelization, and decreased scarring. Compared to PRF, scarring and contracture of the wounds are more commonly associated with MSCs.

Both PRF and MSCs demonstrated clinically excellent soft tissue recovery. PRF enables local administration of fibrin matrix, cells, growth factors, and proteins, which can accelerate wound healing and tissue regeneration. However, there is heterogeneity in the quality and quantity of platelets and blood components, making it difficult to compare efficacy. Independent, comprehensive, randomized controlled clinical trials are needed to standardize PRF preparation techniques.

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