Comparison of gelatin sponge (GS) and platelet rich fibrin (PRF) in assisting palatal healing following the harvesting of an epithelialized free gingival graft (FGG) – A randomized clinical trial

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Comparison of gelatin sponge (GS) and platelet rich fibrin (PRF) in assisting palatal healing following the harvesting of an epithelialized free gingival graft (FGG) – A randomized clinical trial

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Abstract:

Background: Procurement of FGG from the palate presents with bleeding, pain, discomfort and delayed healing at the recipient sites. In this study platelet rich fibrin (PRF) and gelatin sponge are compared for their properties in terms of handling, pain control and assisting in the recipient site healing. **Materials and Method:** In the present randomized clinical trial, 14 patients were taken and donor area was randomly assigned into test and control sites after harvesting of FGG. Dimensions of the graft was similar and obtained from same site with 4mm spacing in test and control sites that was used to rise the attached gingiva width with or without recession. The test sites are dressed with Platelet Rich Fibrin (PRF) dressings and the control site with the gelatin sponge (GS). Complete wound epithelialization (CWE), Pain

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measurements using visual analogue scale (VAS), Healing index (Laundry et al.) were evaluated one, two, three and four weeks postoperatively. Independent t test, ANOVA and pearson's correlation coefficient were used for statistical analysis. **Results:** The results showed faster epithelialization, lesser discomfort during the healing for the test group. The negative correlation for the pain and remaining tissue is observed. **Conclusion:** PRF membrane as a palatal dressing helps in reducing pain and post-operative complications associated with donor sites, thereby accelerating the healing of donor tissue. On the other hand, the handling properties and immediate haemostatic properties are better for gelatin sponge and it can be comfortably used in places such as high palatal vault areas where the retaining of PRF becomes difficult.

Key words: Gingival Recession, Gelatin Sponge, Platelet Rich Fibrin, Wound Healing

Introduction:

Hard palate area is one of the most common site for harvesting the epithelialized free gingival graft (EFGG). This provides a steady and thicker tissue apt for use in successful root coverage and in increasing the width of attached gingiva.[1] The success of these recession treatments and harvesting the grafts mainly depends on the case selection and patient compliance.[2] After all hiccups of convincing the patient for graft procurement from the palate, complications such as postoperative bone exposure, paraesthesia, excessive haemorrhage, arteriovenous shunt, excessive post-operative pain, recurrent herpetic lesions during healing of the wound infections and delayed epithelialization were encountered at times.[3] These plastic procedures are always technique sensitive and each case is a new one because of varied anatomies of palate in individual patients.[4] The palatal donor site is ideal to evaluate haemostatic agents since it is a superficial wound and we can measure various parameters related to wound healing externally. The palatal donor site after harvesting is accessible for observation of haemostasis and healing.[5]

Materials like stents made of acrylics, propylene mesh, cyanoacrylates and haemostatic agents were tried for controlling the post-operative bleeding and aid in acceleration of healing. Usage of collagen sponge (CS) is much noted because of its bio and haemocompatibility, cheaper price and non-toxic.[6] Study done by Rossman and Rees[7] suggested the use of haemostatic dressings, where donor sites were covered with haemostatic dressings which had assisted healing. A recent study done by Mauricio J M et al.,[8] 2023 utilized collagen sponge and flowable resin composite on palatal wound after graft harvest for assessing the post-operative management of pain perception and concluded that addition of resin composite as a covering for collagen sponge helped in reducing the pain and hence it can be incorporated. Though the benefits of collagen sponge is known, but autogenous

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products usage in dentistry is predominated gradually. This lead to the usage of platelet concentrates (PC) for palatal wound healing.

As it is established that Platelet Rich Fibrin (PRF) is enriched with various growth factors (GF), it will help in healing of soft and hard tissues. Study done by Kulkani MR et al.,[9] 2014 and Sharma V et al.,[10] 2019 in their studies concluded that PRF and Colla cote help in wound healing and effective in reducing the post-operative morbidity. Though some literature is available regarding these materials, but present study was aimed to revisit the area and link the role of PRF and gelatin sponge (GS) in the healing of the palatal donor sites and in reducing patient's morbidity.

Materials and methods:

Present study was a prospective randomized clinical trial. A total of 25 patients were initially screened for the study but after establishing the proper criteria 14 (12 males and 2 females with mean age of 35±8 years) patients having millers class I or II recession defects were included. Study was performed on the out patients from Department of Periodontics, GITAM Dental College and Hospital, Visakhapatnam during January 2018 to January 2019. Five people didn't meet the inclusion criteria and 6 people declined to participate in the study. Present study was performed according to CONSORT guidelines to as much extent as possibl (Figure 1)e with a proper Helsinki Declaration of 1975 modified in 2008. Pros and cons of the study was explained to the patient and if they are willing then only they were included. Patients know about the undergoing of surgery and protocol but don't know which surgical area what material that was placed. EFGG harvesting site was divided in to two parts with 4mm space of epithelium tissue in between and those areas were randomly divided into test and control sites where PRF was placed in test area and GS (Axiostat[TM] Axio Biosolutions, Ahmedabad, Gujarat, India) was placed in control site (Figure 2 and 3).

Inclusion and Exclusion criteria

Patients who are systemically healthy with full mouth plaque and bleeding index scores less than 20% at the time of surgery. Patients with Miller's class I and class II defects with lack of attached gingiva. Those who want the treatment for recession and willing to participate in the study were included. While patients who are smoking or using other forms of tobacco, with poor oral hygiene or patients taking medications effecting the periodontal status were excluded. Apart from this patients with mobile teeth at the site of surgery and non-compliant were also excluded.

Clinical Parameters

Clinical Parameters like Plaque index (PI)[11], Gingival index (GI)[11],Thickness of the palatal gingiva[12], complete wound epithelialisation (CWE) by 3% H_2O_2 using wound evaluation scale of Quinn et al.,[13] 1995, Healing Index by Laundry et al.,[14] and Verbal rating scale (VRS) to rate the intensity of pain. These PI and GI were assessed only to identify whether patients periodontal status was sufficient to perform the therapy.

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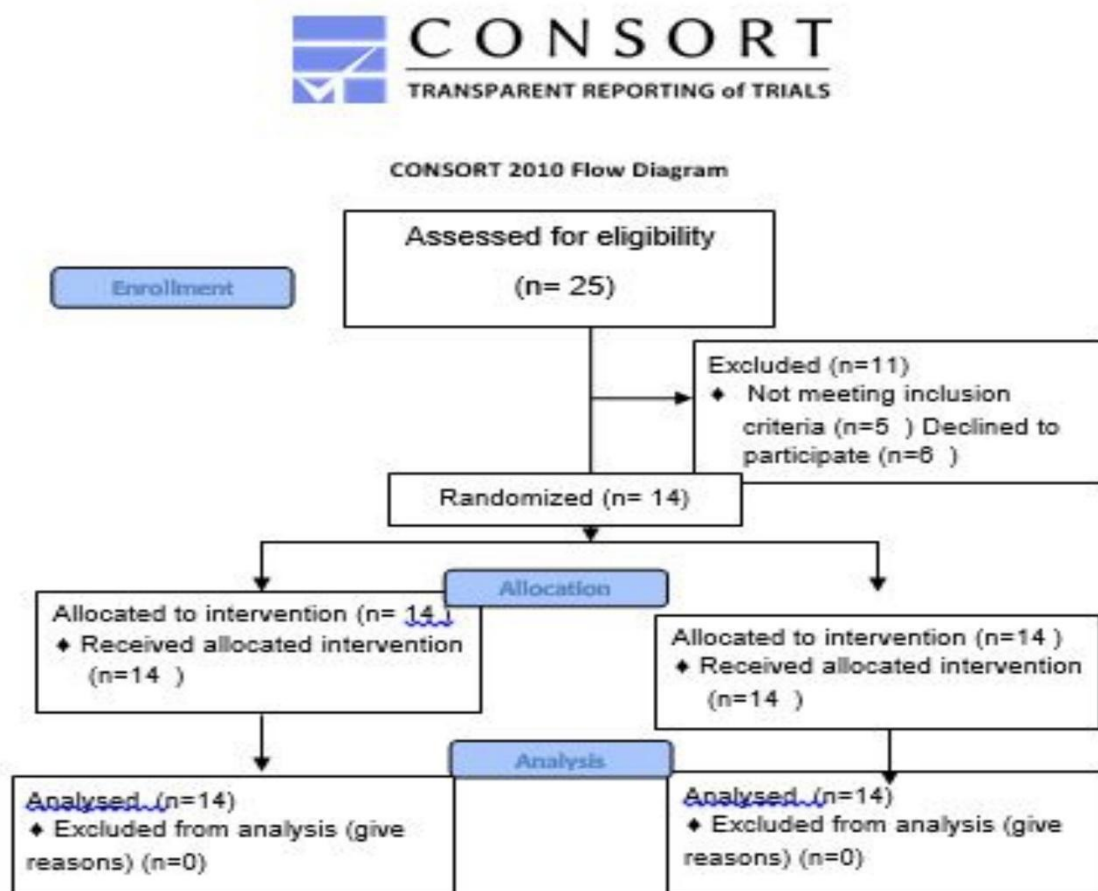
Figure 1 depicts the flow diagram of patient recruitment and allocation in the study and their follow up

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Figure 2 shows the pre-operative donor site of palate 1(a), 1(b) the tin foil placement, 1(c) incisions on palate, 1(d) donor site after graft harvested, 1(e) harvested free gingival grafts, 1(f&g) free gingival grafts sutured at recipient site
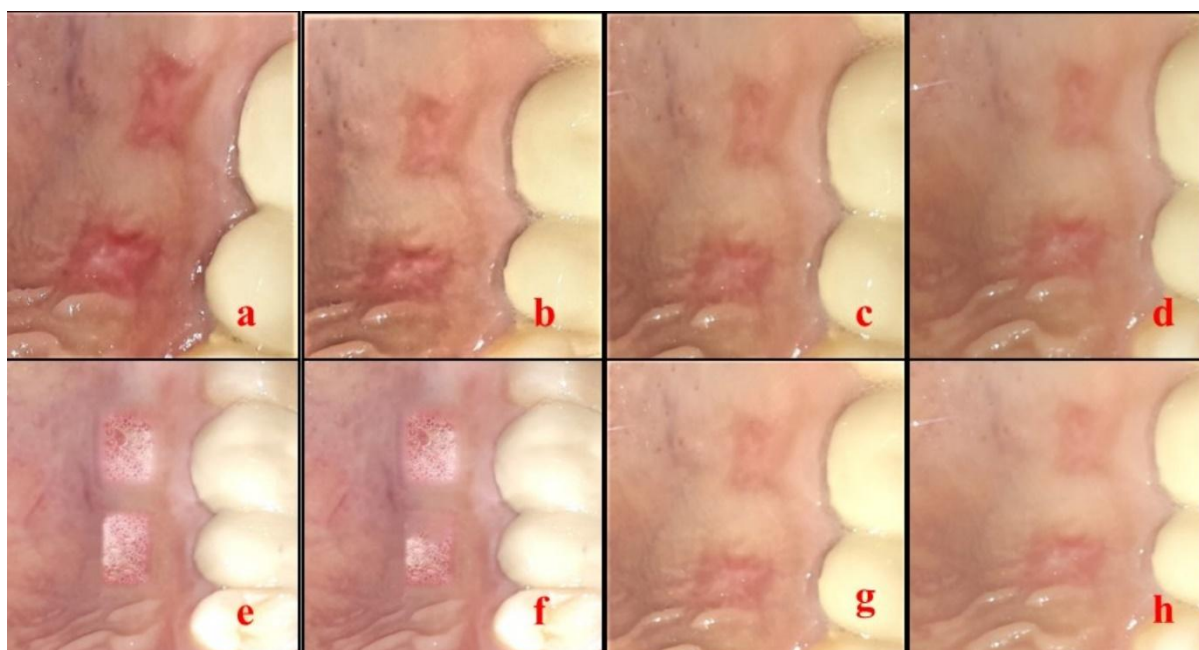

Figure 3 shows the post-operative healing of palatal site using Laundry Healing Index at 1,2,3 and 4 weeks respectively(2a-2d). While 2e-2h show the complete wound epithelization using hydrogen peroxide test

Procedure

For included patients, initial scaling and root planing was performed. Modified stillman's brushing technique was advocated for progressive gingival recession, oral hygiene instructions were explained and recalled after 6 weeks for review. On re-evaluation when good oral hygiene was maintained by patient EFGG were harvested from the palate with 4mm space in between them so that PRF and GS can be placed and sutured.

Initially patients underwent routine blood investigations to rule out systemic health. On the day of muco-gingival surgery intraoral and extra oral antisepsis were performed using Chlorhexidine mouth wash and Povidine Iodine. The recipient site is anesthetized by local infiltration (2% lidocaine with adrenaline 1:80,000) and the nerve impulses of the donor site are blocked by greater palatine nerve block. The recipient site preparation (de-epithelization) done to receive the graft material. Palatal soft tissue thickness (PT) can be clinically determined, at the time of anaesthesia, by penetrating with an endodontic reamer/ needle perpendicular to the palatal bone plate[12] Two epithelial free gingival grafts of equal dimensions will be harvested from the palate with a minimum of 4mm of palatal tissue remaining between the two grafts. Each of the graft materials is sutured to the prepared recipient bed firmly to prevent the mobililty of the grafted tissue using 4-0 silk suture. These graft material is used to cover isolated recession defects or to increase the thickness of attached gingiva. Prior to the surgery 10ml of blood was drawn from antecubital vein and was

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used to prepare PRF clots using Choukroun's protocol[15] 2800rpm for 12 minutes, thus obtained clots were placed in layers (Double PRF layer) which represented the palatal bandage of the test group. Absorbable collagen sponge is used as palatal bandage to cover the experimental site. In both the areas the materials used as palatal bandages are trimmed and sutures were given to prevent bleeding and for retaining the PRF and GS in the place. The sutures will be removed after 7 days. Patients will be recalled every week for 4 weeks for comparison of healing and epithelialisation.

Post-surgical care

Patients were instructed not to brush their teeth in the treated area, but to rinse their mouth with 10ml of 0.2% chlorhexidine di-gluconate (Rexidine[TM]) solution twice daily for 10 minutes. Patients were advised to avoid hard and spicy food for 3 days following surgery. Ibuprofen 400mg, sos was prescribed as an analgesic. The sutures were removed seven days after surgery for both the sites. Patients were monitored at 1, 2, 3 and 4 weeks after surgery for the complete re-epithelialization of the palatal wound (CWE) by spraying 3% H_2O_2 with a syringe. During the initial four weeks, patients will be instructed to brush only the uninvolved teeth. After this period, the patients were instructed in mechanical plaque control of the treated tooth region using a soft bristled tooth brush and a roll technique. Then, the patients were kept on maintenance program.

Statistical Analysis

Entire data was subjected to statistical analysis using statistical package for social sciences (SPSS) version 20. IBM Pvt Ltd, Chicago Illinois, USA. P value <0.05 was considered to be significant. Repeated ANOVA and independent t tests were performed to compare the differences between PRF and CS groups. Pearson's correlation coefficient was also obtained to establish any correlation between VAS and TT among both the groups.

Results

Mean tissue thickness of PRF and GS sites were depicted in Table 1. Regarding pain scores using visual analogue scale PRF site showed a significant (p=0.020*) lower pain scores than GS site during the second week while remaining 1,3 and 4th week values were non-significant (p>0.05) (Table 2). For intra group evaluation of pain scores for PRF sites statistical significance (p=0.00*) was during first and second weeks when they were compared with remaining week combinations where as non-significance (p=0.989) was reported for 3rd and 4th week comparison (Table 3). Further statistical significance was recorded at all the point of times comparisons and follow ups for GS sites during their intra group analysis (Table 4). During inter group comparison regarding Laundry Healing Index values were statistically non-significant at all the time intervals for both the groups (Table 5). While coming to complete wound epithelization inter group comparison of both PRF and GS sites revealed statistical significance during 2nd (p=0.016*) & 3rd weeks (p=0.009*) favouring PRF group and non-significant results were recorded at 4th week (p=0.50#) (Table 6). Further, r values of PRF group were -0.50, 0.115 and -0.28 whereas r values for GS group

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were -0.27, -0.323, -0.564 respectively during 1st 2nd and 3rd weeks of pain scores correlated with tissue thickness (TT) for both groups. Negative correlation was obtained in both groups for pain and TT in both groups for all the three weeks except for test group 2nd week which has a weak positive correlation. A significant positive correlation was obtained when decrease in pain intensity was compared for 1st and 2nd week in both test (0.728) and control (0.811) groups (Table 7 and 8).

Discussion:

Present study, materials used were PRF and GS these are helpful for wound healing and clot stabilization. PRF was an autologous PC and GS was haemostatic agent. PRF has higher GF, cytokines release which would accelerate healing. Present study patients didn't lost the follow up and healing was un-intentional without any abnormalities both at donor and recipient sites. This might be due to improved compliance of patient with doctor and enhanced reinforcement of oral hygiene instructions helped in better outcomes. This is in accordance with a studies done by Yen et al., 2007; Feminella et al.,[16] 2016 and Bahmmam et al.,[17] 2018 where they concluded that PRF helped in rapid healing and rapid regeneration of palatal tissue thickness at 6th and 8th week post-surgery.

Regarding pain scores PRF has significantly lower pain scores when compared to GS during 2nd week and by the end of 3rd week no significance was reported this is in accordance with Bahammam et al.,[17] 2018 and Hassan AA et al.,[18] 2020 where they concluded that patients with PRF as palatal bandage has experienced normalcy for pain almost 3 days after surgery, best results were noted by 7th day and by the end study though PRF had better clinical outcomes both the groups healed properly. This might be due to faster procurement of blood and its centrifugation helped in earlier placement of PRF membrane helped in lesser pain scores.

Current study results were also in accordance with recent study done by Sharma V et al.,[10] and Isler et al.,[19] 2019 where they concluded that though PRF helped in accelerated wound healing and lesser post-operative pain, both PRF and Collacote (collagen membrane) had shown non-significant results regarding pain measures, wound epithelization etc. Shaqir Q J et al.,[20] 2015 reported that patients with PRF palatal dressings showed complete wound closure within 18 days and experienced less postoperative morbidity than a patient whose wounds were not treated with PRF membranes. This reduction in post-operative pain may be due to the presence of various GF which might have stimulated the wound area where progenitor cells will pool up and help in rapid healing and epithelization that might help in lesser pain levels. Current study results also favour the Isler et al.,[19] 2019 study where they concluded that PRF helps in reducing post-operative discomfort for patients who are under-going FGG surgery.

Study done by Alpan and Cin[21] 2020 stated that PRF group has shown significant lower pain scores while at 3rd to 7th post-operative day EHI was low and by the end of 7th to 14th day tissue colour match was first obtained in suture alone group. These results were in accordance with current study where they have reported lower pain scores during intra group

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comparisons while inter group showed significance during 2nd week. While coming to CWE also significance favouring PRF was recorded in 2nd week while end of 4th week both PRF and GS has shown similar results. This favourable response of PRF might be due to stimulation of angiogenesis by the release of cytokines and GF's, it also release the PDGF for a period of 7-28 days which helped in rapid epithelization and healing. Further LHI was non-significant which is in contrast with Alpan and Cin[21] 2020 study where EHI was significant. This variation might be due to presence of platelets in both the materials. PRF inherits the platelets, some living cells, leukocytes and so on, whereas GS when placed absorbs some amount of blood and forms a fibrin stabilized clot. Even this favours the cells to get stimulated at the surgical area which had helped in equal healing in both groups.

Present study results were also in accordance with Ustaouglu G et al.,[22] 2016 where there was a CWE on 14th day, lower pain scores later on after surgery when Titanium- PRF was used as bandage for palatal wound healing. Thus, PRF shown on par results with that of T-RPF

Post-operative lower pain scores was inconsistent and varies in different studies as it is a self-perception of patient himself. Some show favourable results for reduced pain (Bahammam MA et al.,[17] 2018 but some report unfavourable pain reduction (Ustauoglu G et al.,[22] 2016 and Ozgun O et al.,[23] 2015). In the current study VAS pain scores were lowered significantly in PRF group and final follow up showed in-significant for both PRF and GS. This might be due to presence of leukocytes which have anti-nociceptive effects through different chemokines, anti-inflammatory peptides and opioid peptides which have their influence on reducing the pathological pain. Apart from this, both the groups used analgesics for pain control which might have influenced the outcomes.

Results of present study followed the similar pattern of recent systematic review done by Matheus H R et al.,[24] 2021 and Martins A A et al.,[25] 2022 where they concluded that PRF had an ability to reduce the post-operative pain create a comfortable environment to heal and reduce the pain morbidity. PRF doesn't decrease the cause for delayed bleeding. In the present study, no case of delayed bleeding reported this might be due to placement of materials and approximating the area with sutures to as much extent as possible which might have helped in healing without complications.

Further while making a look into correlation, negative one was obtained between thickness and pain in both the groups for all 3 weeks except for test group during 2nd week which was a weak negative one. This indicates that thinner tissues has more pain reduction. A significant positive correlation was reported in 1st and 2nd weeks in both test and control groups. From this it was inferred that GS showed increased pain intensity. Study done by Bechert K and Abraham S E 2009[26] stated that wound related pain had negative effect on wound healing. This might be an apt explanation of lower pain scores of PRF had influenced for rapid wound healing. Present study results are in harmony with this study done by Burkhardt R et al.,[27] 2015 stated that GT showed a correlation with pain perception with increased palatal mucosal thickness before harvesting and reduced pain levels after graft removal.

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Limitations of the present study might be smaller sample size and shorter follow up period. In addition to this histological sectioning was not performed for both the groups because of ethical reasons. If it was done exact healing and various outcomes would been assessed more accurately.

Conclusion

Though GS had a better handling of adaptation and rapid haemostatic properties than PRF where GS can be easily adapted in high palatal vault patients. But within limitations PRF helped in good healing and reduced patient discomfort, it is easy to make, price friendly and autologous biomaterial. Thus, utility of PRF membrane provides the clinician a great treatment tool to treat recession defects with optimal aesthetic results and it also holds promise as a biomaterial for various other procedures.

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Conflicts of Interest: Nil

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Tables

Table 1depicts the mean tissue thickness among PRF and Gelatine sponge sites

Tissue thickness	Total Subjects	Mean	Standard Deviation
PRF site	14	1.52	0.03
Gelatine sponge site	14	1.47	0.07

Table 2 show the intergroup Comparison of mean pain scores (Visual Analog Scale) between PRF and Gelatine sponge groups for at 1st , 2nd 3rd and 4th weeks

*indicates significance P<0.05, PRF- Platelet Rich Fibrin, GS- Gelatin Sponge

Pain	Group	N	Mean	Standard Deviation	Mean difference	P value
1st week	PRF	14	3.43	1.01	- 0.71	0.136
	GS	14	4.14	1.40		
2nd week	PRF	14	1.21	0.80	- 0.78	0.020*
	GS	14	2.00	0.87		
3rd week	PRF	14	0.14	0.36	- 0.21	0.20
	GS	14	0.36	0.49		

Table 3 show the intragroup comparison of pain scores in PRF group at1^{st} , 2nd 3rd and 4th weeks

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*indicates significance, P<0.05

Table 4 show the intragroup comparison of pain scores in Gelatine Sponge group at different

Time Interval in weeks	Weeks	Mean	Mean difference	Standard Error	P value
1st	1st week	3.429	2.214	0.187	0.000*
	2nd week	1.21			
	3rd week	0.14	3.286	0.286	0.000*
	4th week	0	3.429	0.272	0.000*
2nd	2nd week	1.214			
	3rd week	0.14	1.017	0.195	0.001*
	4th week	0	1.214	0.214	0.000*
3rd week	3rd week	0.14	0.143	0.097	0.989
	4th week	0			

time intervals

*P <0.05 indicates significance

	Weeks	Mean	Mean difference	Standard Error	P value
With 1st week	1st week	4.14	2.143	0.231	0.000*
	2nd week	2.00			
	3rd week	0.357	3.786	0.366	0.000*
	4th week	0	4.143	0.376	0.000*
With 2nd week	2nd week	2.000	1.643	0.225	0.000*
	3rd week	0.357			
	4th week	0	2.000	0.234	0.000*
With 3rd week	3rd week	0.357	0.357	0.133	0.112*
	4th week	0			

Table 5 show theintergroup comparison of Landry healing Index between PRF and Gelatine Sponge groups at different time intervals

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	Group	Healing Index (N)					P value
		Very poor N(%)	Poor N(%)	Good N(%)	Very good N(%)	Excellent N(%)	
1st week	PRF	1 (7.14%)	13 (92.85%)	0 (0%)	0 (0%)	0 (0%)	0.16#
	GS	4 (28.58%)	10 (71.42%)	0 (0%)	0 (0%)	0 (0%)	
2nd week	PRF	0 (0%)	5 (35.71%)	9 (64.28%)	0 (0%)	0 (0%)	0.65#
	GS	0 (0%)	5 (35.71%)	9 (64.28%)	0 (0%)	0 (0%)	
3rd week	PRF	0 (0%)	0 (0%)	8 (57.14%)	6 (42.85%)	0 (0%)	0.21#
	GS	0 (0%)	0 (0%)	11 (78.57%)	3 (21.42%)	0 (0%)	
4th week	PRF	0 (0%)	0 (0%)	3 (21.42%)	11 (78.57%)	0 (0%)	0.50#
	GS	0 (0%)	0 (0%)	4 (28.58%)	10 (71.42%)	0 (0%)	

*P<0.05 indicates statistical significance, # indicates non-significant, N- score, (%)- Frequency percentages

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Table 6 show theintergroup comparison of Complete Wound Epithelisation (CWE) between PRF and Gelatine Sponge groups at 1st, 2nd 3rd and 4th weeks

	Group	**Complete Wound Epithelisation**		**P value**
		NO (N %)	YES (N%)	
1st week	PRF	14 (100%)	0 (0%)	--
	GS	14 (100%)	0 (0%)	
2nd week	PRF	7 (50%)	7 (50%)	0.016*
	GS	13 (92.85%)	1 (7.14%)	
3rd week	PRF	1 (7.14%)	13 (92.85%)	0.009*
	GS	9 (64.28%)	5 (35.71%)	
4th week	PRF	0 (0%)	14 (100%)	0.500
	GS	1 (7.14%)	13 (92.85%)	

* $p < 0.05$ indicates statistical significance, # indicates non-significant, PRF-Platelet Rich Fibrin, GS-Gelatin Sponge, N- number, (%) –frequency distribution percentages

Table 7: Correlation between tissue thickness and painamong three weeks for PRF (test) group

		TT PRF	1 week pain PRF	2 pain PRF	3 pain PRF
Tissue thicknessPRF group	r	1	-.050	.115	-.208
	p		.866	.695	.475
1 pain PRF	r	- .050	1	.728**	.030
	p	.866		.003	.920
2 pain PRF	r	.115	.728**	1	.415
	p	.695	.003		.140
3 pain PRF	r	-.208	.030	.415	1
	p	.475	.920	.140	

**. Correlation is significant,PRF-Platelet Rich Fibrin, TT-Tissue Thickness

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Table 8: Correlation between tissue thickness and pain among four weeks for gelatin sponge (control) group

		TT GS	1 pain GS	2 pain GS	3 pain GS
Tissue thickness GS group	R	1	-.270	.323	-.564
	P		.351	.260	.036
1 pain GS	R	-.270	1	.811[**]	.251
	P	.351		.000	.386
2 pain GS	R	.323	.811[**]	1	.251
	P	.260	.000		.216
3 pain GS	R	-.564	.251	.353	1
	P value	.036	.386	.216	

**. Correlation is significant,GS-Gelatin Sponge, TT-Tissue Thickness

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