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Original Research

Evaluation of platelet rich fibrin and connective tissue graft in coverage of immediate Dental implants: A comparative study

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ABSTRACT:
Background: The use of Platelet rich fibrin along with connective tissue graft had been shown to have bone augmentation effects. **Aim**: The aim of this study was to compare the effectiveness of platelet rich fibrin and connective tissue graft in coverage of immediate dental implants. **Materials and methods**: This prospective randomized controlled two-armed parallel group double-blinded clinical study trial was conducted on 100 patients selected for immediate dental implants. Informed signed consent was obtained from patients before study. Ethical approval was obtained from Institutional Ethical committee. Inclusion criteria were a) Patients aged between 20-40 years; b) Patients with non-restorable single-rooted teeth; c) Intact Labial or buccal plate; d) Recipient implant site must be free of infectious/inflammatory disease or e) Must not have periodontal disease. Exclusion criteria were a) Smokers b) Pathologies at implant site c) Psychological diagnosis d) Systemic disorders e) Pregnancy and/or hormonal imbalances. **Statistical analysis**: Student's t test, One-way ANOVA and Mann-Whitney U tests were employed for statistical assessment. **Results**: Statistically significant differences in width of keratinized tissue, bio-type of tissue, gain in alveolar bone height, pink esthetic score and patient satisfaction score were obtained in the study group which received augmentation with PRF along with connective tissue graft. **Conclusion**: The use of PRF and connective tissue graft can sufficiently augment immediate implant sites when compared with no augmentation.
Keywords: PRF, connective tissue graft, immediate, implants, osseointegration

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INTRODUCTION

Platelets play a central role in the healing of wounds via formation of a clot from accumulated blood which then releases variety of growth factors that help in initiating and supporting healing of wound. [1] Platelet rich fibrin or PRF is 2nd generation derivative of platelets following the introduction of platelet-rich plasma or PRP. Platelet rich fibrin is prepared in single step and has no requirement of additives. [2] PRF has a fibrinous matrix that is rich in platelets, leukocytic components as well as growth factors. [3] Platelet fibrin plexus is an excellent medium for proliferation as well as migration of cells which a is requisite for regeneration of tissues. When fibrin is combined with autogenous bony graft, an increase in formation of bone is observed that acts as scaffold for filling up of osseous defects. [3] Fibrin acts as a supportive matrix as it contains bone morphogenic protein. Platelet Rich Fibrin acts as a natural and optimal adjuvant for clotting of blood for promoting guided tissue regenerative process. [4] The primary difference between Platelet rich fibrin and PRP system is the natural process that involves no use of anti-coagulants during harvesting of blood or use of bovine derived thrombin along with calcium chloride for activating platelets as well as polymerization of fibrin. PRF is enriched in growth derived factors like platelet derived growth factor or PDGF; transformation growth factors (TGFs) alpha and beta. [5] The enriched growth factors are then released in a sustained manner for a minimum of one week which may extend till 28 days. [6] This allows the Platelet Rich Fibrin to simulate an optimal environment for

significant period of time during the period of wound healing.

Platelet Rich Fibrin can be utilized in conditions such as filling up of periodontal bony defects by use of probes for measurement of pocket depth, gain in clinical periodontal attachment and radiographic evaluation for a period of six months. [7,8] The connective tissue derived grafts were first introduced by Edel in the field of Periodontology as an instrumental tool for increasing overall width of keratinized mucosal tissue and as modality for treatment in recession of tooth root.[9] Additionally, soft tissue thickening using connective tissue grafting might result in maintaining volume or level of bone labially. [10] Investigators have demonstrated that using connective tissue graft causes improvement in local metabolism related environment in superficially localized soft tissues which helps n preservation of keratinized mucosal tissue, thereby creating an adequate peri-implant marginal tissue seal. [11] Thus, based upon scientific literature available, the aim of present study was determined as to comparatively evaluate platelet rich fibrin and connective tissue graft in coverage of immediate dental implants.

MATERIALS AND METHODS

Study design: This was a prospective, randomized controlled two-armed parallel-group double-blinded clinical study trial that was conducted on 100 patients who were scheduled to receive immediate dental implants. All selected patients were explained about the study objective before initiating the study and informed signed consent was obtained from them before beginning the procedure and study. Ethical approval was obtained from Institutional Ethical committee before hand. Total study duration was six months starting from February 2023 to July 2023. Inclusion criteria determined for studied patients were as follows a) Patients must age between 20 to 40 years b) Patients must have a non-restorable single-rooted tooth preferably in the incisor and canine area c) Labial or buccal plate must be intact d) the recipient site for the implant should be free from any infectious or inflammatory disease and e) The site of implant placement must not be periodontally involved. Exclusion criteria selected were as follows a) Patients with smoking habit b) Any pathology such as radicular cyst at site of implant insertion as it might impact the process of osseointegration c) Any psychological issues d) Any systemic diseases e) Pregnancy or hormonal disturbances which can cause peri-implantitis.

Clinical assessment of selected patients: Clinical studied parameters were evaluated at baseline (time of implant placement) and after six months following placement of implants. Width of keratinized tissue was assessed by measurement of distance between muco-gingival junction and free marginal gingiva by using a caliberated UNC periodontal tissue probe. Roll technique was used for identifying mucogingival junction by fabricating customized acrylic material stent. Tissue biotype was then measured following administration of anesthesia following piercing of keratinized gingiva in a perpendicular direction to tooth against underlying alveolar bone by inserting a 'UNC' graduated periodontal probe 2 millimeters apically to gingival soft tissue margin.

Pink esthetic score measurement: Pink Esthetic scores were measured at 6 month interval following prosthetic placement wherein 2 clinical photographs facially and occlusally were taken. Seven different variables were then evaluated a) Mesial as well as distal interdental papillae, b) Level of soft tissue, c) Contour of gingival soft tissue, e) Defects in alveolar bone, f) Color of gingival soft tissue and g) Gingival texture. Scoring index used was 0 being the lowest while 2 being the highest score value and maximum index score equivalent to 14.[12] Observation of these clinical photographs was done by two independent blinded observers on a computer monitor screen for evaluation of esthetics. The treatment satisfaction by patients was evaluated by asking the patients to fill up a questionnaire six months following placing final prosthetic restoration. The questionnaire comprised of points related to final prosthesis as well as peri-implant mucosal health and esthetics.

Power of the study and Calculation of sample size: This was calculated by using the Power and Sample size software (Version 3.1.2, Vanderbilt University, Nashville, Tennessee, US). The operative person who had to perform the surgeries could not be blinded. However, the individual who was responsible for assessment of outcome and analysis of collected data were blinded from the allocation. Moreover, the study investigator responsible for outcome assessor was blinded to the group allocation during the follow-up along with statistical data analyst who was completely unaware of hypothesis of the study. The selected patients were then randomized into two groups as follows a) Group I was control study group that had only placement of immediate dental implants and b) Group II was test study group that had placement of immediate dental implants along with connective tissue graft and platelet rich fibrin.

Radiographic evaluation: Radiographic measurement of changes in crestal bone level was conducted at baseline i.e., prior to performing tooth extraction and immediately following placement of an implant by means of an intraoral periapical radiograph for evaluation of mesio-distal dimensions. Cone-beam computed tomography or CBCT was employed at baseline observation i.e., before performing extraction and following six months for recording height of bone at pre-operative observation. Bucco-lingual bone width and highest coronal point

of platform of implant were utilized as 'static' references for measurements. Super-imposition technique for measurement of level of bone was then recorded over facial aspects of placed dental implant at baseline and at sixth month follow-up. For standardizing measurements, incisal surfaces along with cuspal tips of adjacent teeth were used.

Surgical placement of implant systems: Group I or Control Group: Single operator was responsible for performing entire surgical procedural steps under localized anesthesia (2% lignocaine in 1/200 000 adrenaline). Atraumatic non-surgical extractions were performed by using a periotome so as to preserve the intactness of walls of socket. Tapered self-drilling and self-tapping dental implants (JD Evolution® S, two-piece implants) were then placed till the platform of the implant was placed 2 millimeters apical to alveolar crestal bone height. Jumping gap measurement was performed following placement of the implant. Group II or test group: After placement of an implant, connective tissue graft was subsequently harvested from palatal mucosa by single incision. Platelet Rich Fibrin (PRF) preparation was done with 10 ml venous blood which was collected from ante-cubeital vein. The collected blood sample was then transferred to a anti-coagulant free test-tube and was immediately subjected to centrifuge at 3000 rpm for 10 to 12 min. The obtained fibrin clot was then compressed in a PRF box for obtaining uniformly thick Platelet rich fibrin membrane. This PRF membrane was adapted and placed over connective tissue graft over the implant. Following this, stabilization of connective tissue graft was done by horizontal mattress technique of suturing, following creation of buccal as well as lingual pouches using an absorbable type of surgical suture (Vicryl, 6-0). Surgical flaps were then approximated using a non-absorbable poly-amide suture material.

Pre-operative and post-operative medications: All the patients were prescribed Amoxycillin pre-operatively in dosage of 1 grams per hour prophylactically and after treatment every 12 hours for five days. Ibuprofen was prescribed twice daily for five days to reduce pain and swelling. Chlorhexidine mouthwash in a concentration of 0.12% was prescribed twice daily in diluted form for maintaining a microbial free oral environment.

2nd stage of implant surgery: At sixth month follow-up, CBCT radiographic scan was performed and by means of super-imposition software program, manual method of image registration was selected. For accurately evaluating the parameters, two points (T1 at base-line prior to extraction and T2 following six months after placement of implants) were utilized. Using the superimposition technique, the 'T2' image was kept as much close T1 image in terms of axial, sagittal and coronal slices. After this, auto-registration mode was activated wherein superimposition of 'T2' image was done over T1 image using automated program using common axial coordinates. Both the superimposed images were then visualized by use of fusion mode of software. Procedure for exposing the implant was done under local anesthetic. Healing implant collars were then inserted for a period of one week following which they were replaced with permanent abutments. Impressions were made and then, fixed prosthetic fabrication was done. Pink esthetic score was measured clinically six months following prosthetic phase wherein 2 clinical images facial as well as occlusal were taken. Seven clinical parameters were evaluated- mesial/distal papillae, level of gingival soft tissue, contour of soft tissue, defect in alveolar bone, coloration of gingival tissue along with soft tissue texture. Score system used was 0 being lowest score and 2 was the highest score with maximal score =14.

STATISTICAL ANALYSIS

Collected data was analyzed by SPSS advanced statistics (Statistical Package for Social Sciences), version 21.0 (SPSS Inc., IBM, Chicago, IL). Numerical data was described in form of mean ± standard deviation (S.D.) or median and range while categorical type of data was described in form of numbers and their percentages. Normality of data was analyzed by using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Inter-group comparisons were performed by Student's t-test whereas non-normal numerical variables were analyzed with Mann-Whitney U test. Comparison between categorical variables was conducted using Chi-square test. P-values which were lesser than or equivalent to 0.05 was considered as with statistical significance.

RESULT AND OBSERVATIONS

(I) Width of keratinized mucosal tissue: Inter-group comparison demonstrated higher mean ± S.D. values in test group when compared with control group, although no statistical significance was obtained between both the groups. On the other hand, intra-group comparison demonstrated highest mean ± S.D. score of control subjects at baseline while lowest mean ± S.D. value was obtained at 6th month follow-up. However, there was no statistically significant difference between these follow-ups (table 1 and Graph 1).

(II) Tissue bio-type: After baseline observation, inter-group comparison observed no statistical significance between both the groups. However, follow-up observation at 6th month showed statistical significance between both the groups wherein group reported greater mean ± S.D. values when compared with control subjects with independent t-test. 'One-way' ANOVA reported no statistically significant difference between the follow-up intervals. (table 2 and Graph 2)

(III) Level of buccal crestal bone: Group I (test group) had higher mean ± S.D. score than Group II (control) using independent 't'-test statistical result showed no statistical significance (table 3 and Graph 3).

(IV) Pink esthetic score: Pink Esthetic Score in group I had high score than group II. Mann-Whitney statistical test had shown nil significance between both the studied groups. Group II (Control) had greater score of patient satisfaction score when compared to group I showed statistically significance between both the study groups using Mann-Whitney statistical test (table 4 and Graph 4).

(V) Satisfaction of patients: Patients' satisfaction score was found to be higher in control group (Group II) than group I and was found to be statistically significant (table 5).

Table 1: Table showing mean ± S.D. scores and P values for change in width of keratinized mucosal tissue

Follow-up intervals	Mean ± S.D.		Mean differences	Confidence interval (95%)	P value
	Test	Control			
At base-line	13.12±8.20	6.13±09.21	-18.42	-43.30 -2.40	0.02
On 6 month follow-up	-2.07±09.1	0.00±0.00	-3.82	13.45 5.12	0.43

Graph 1: Graph showing P values of changes in width of keratinized mucosal tissue

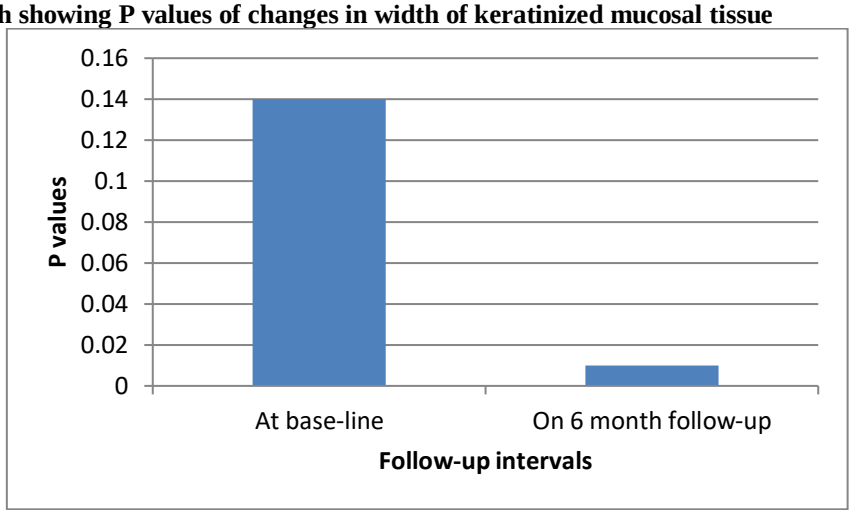

Table 2: Table demonstrating mean ± standard deviation (S.D.) scores and P values of tissue bio-type

Follow-up intervals	Mean ± S.D.		Mean differences	Confidence interval (95%)	P values
	Control	Test			
At base-line	0.43±0.06	1.12±0.01	-0.28	-0.28-0.09	0.15
On 6 month follow-up	0.37±0.02	2.95±0.71	-0.89	1.97-0.12	0.01

Graph 2: Graph showing P values of tissue biotypes

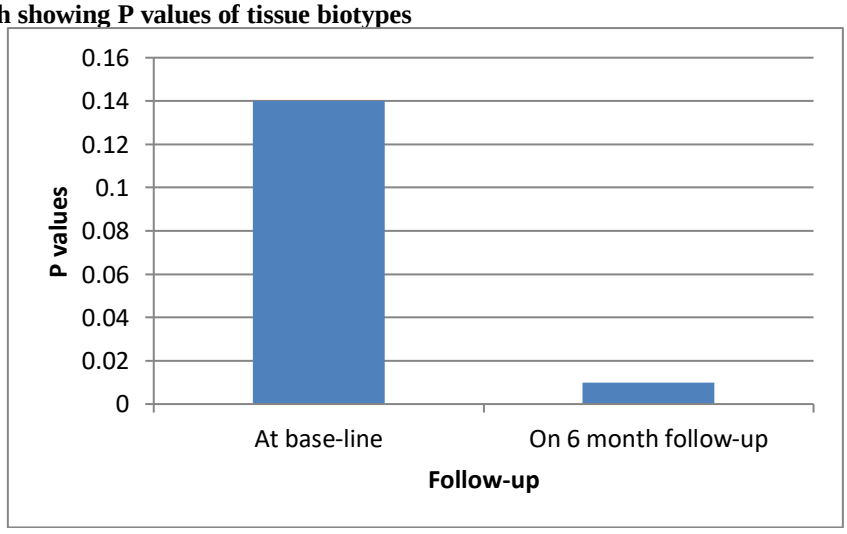

Table 3: Table demonstrating mean ± standard deviation (S.D.) values and P values of buccal crest bone levels

Follow-ups	Mean ± S.D.		Mean differences	Confidence interval (95%)	P values
	Control	Test			
At base-line	0.09 ± 0.12	1.23±0.04	-0.28	-0.28-0.09	0.13
On 6 month follow-up	0.37±0.02	2.34±0.82	-0.89	1.97-0.12	0.02

Graph 3: Graph showing P value scores of crestal bone level

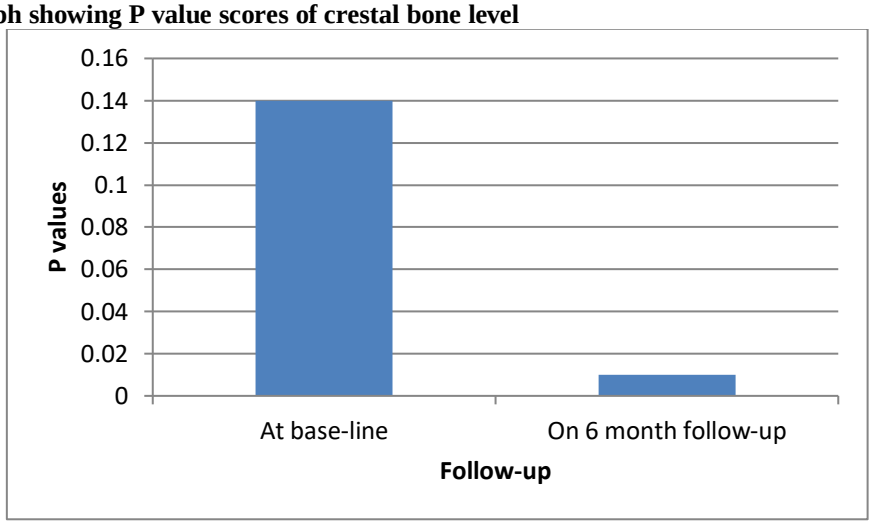

Table 4: Table illustrating mean ± standard deviation (S.D.) values and P values of Pink esthetic score

Follow-ups	Mean ± S.D.		Mean differences	Confidence interval (95%)	P values
	Control	Test			
At base-line	0.34±0.21	1.24±0.02	-0.12	-0.11-0.01	0.14
On 6 month follow-up	0.12±0.02	1.56±0.04	-0.03	1.02-0.09	0.01

Graph 4: Graph showing P values of Pink Esthetic score

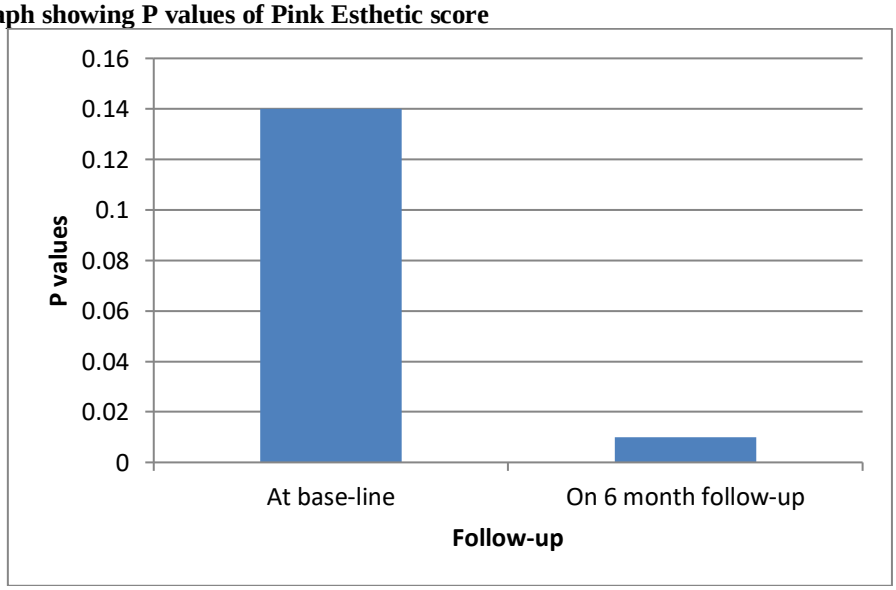

Table 5: Table showing mean ± standard deviation (S.D.) scores and P values of Patient satisfaction scores in both the study groups

Follow-ups	Mean ± S.D.		Mean differences	Confidence interval (95%)	P values
	Control	Test			
On 6 month follow-up	4.32±0.34	2.19±0.03	-0.01	0.45-0.03	0.04

DISCUSSION

The primary reason behind the immediate placement of implants is reduction in the total number of surgical procedures as well as time of treatment as it may decrease the chances of bone resorption. [13] Resorption of alveolar bone might take place between an implant and wall of socket which might result in loss of esthetics especially in anterior region and among patients who have higher smile line. [14] The connective tissue graft causes improvement in facial contouring of alveolar bone and involves less invasive surgical procedure along with reduced period of healing. [15,16] Pink esthetic score assessment was performed by blinded, independent observer for maintaining reliability of the study outcome. In current study, group (I) showed higher Pink esthetic score (1.56±0.04) when compared with control group (0.12±0.02) and was statistically significant (P =0.10). Our findings are supported by Frizzera et al (2019) who have reported higher pink esthetic score in patients of immediate implants along with connective tissue graft.[17] Similarly, Migliorati et al (2015) reported significant PES with use of connective tissue graft. [18] Also, in the present study, width of keratinized tissue showed high score in test study group (13.12±8.20) than control study group (6.13±09.21) and there was statistical significance obtained (P value =0.01). It has been suggested that connective tissue grafts can induce epithelial keratinization.[19] Keratinized mucosa surrounding an implant causes improvement in the outcome related to esthetics, stabilization of soft tissues and preventing accumulation of plaque, recession, and peri-implantitis. [20,21] On analyzing tissue bio-type in present study, group I had statistical significance (P, 0.01) while on studying the buccal crestal bone level after 6 months, the test group had high mean score (2.34±0.82) when compared with controls (2.34±0.82) and was statistically significant (P =0.01). However, our findings are contrasted by Wiesner et al. (2010) who found no significant loss of bone between connective tissue graft group and group which received no augmentation.

CONCLUSION

Hence, it can be concluded that use of connective tissue graft along with PRF in immediate loading implants can substantially improve the treatment outcome. However, limitations of this study was short period of follow up due to which further significance of effectiveness of PRF with connective tissue grafting in immediate implant cases could not be ascertained.

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