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*Original Research Article.*

# Comparative Effectiveness of Platelet Rich Fibrin on Hard and Soft Tissue Healing After Third Molar Extraction: A Clinico-Radiographic Study

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## ABSTRACT

**Objective:** To determine the effects of a local application of platelet rich fibrin (PRF) on socket and soft-tissue healing after third molar extraction.

**Methods:** Twenty adult patients aged 18-30 years (15 female, 5 male) were included in a randomized, split-mouth design. PRF was inserted into the freshly prepared extraction socket of the third molar in one random side of the maxilla and mandible and the other side served as the control and received normal conservative treatment. The amount of hard tissue healing was assessed using radiographic bone density on weekly interval, at 0th day (T0), 1 week (T1), two weeks (T2), three weeks (T3) and four weeks (T4). Soft tissue healing was assessed at 3rd, 7th and 15th day of treatment using healing index.

**Results:** The PRF group showed significantly greater bone density in both maxilla and mandible as compared to control side. The bone density was higher in the mandibular arch as compared to maxillary arch. Soft tissue healing was also found to significantly higher in the PRF side as compared to control side.

**Conclusions:** Local application of PRF resulted in a increase in the bone density and improvement in soft tissue healing.

**Key words:** Platelet Rich Plasma, Platelet Rich Fibrin, Mandible, Maxilla, Wound Healing.

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## INTRODUCTION

Dental extraction is one of the most commonly employed routine procedure in the management of tooth decay, periodontal disease, severe fractures, infections, and the provision of orthodontic space, procedure.[1,2] One of the common sequelae of dental extraction is development of wound due to loss of tissue integrity. To restore tissue integrity after an injury, numerous cellular and extracellular pathways are activated in a carefully controlled and coordinated manner.[3]

Wound healing post dental extraction is a delicate and complex process that is prone to interruption or failure, resulting in delayed or non-healing wounds.[4] In the absence of controlled healing, alveolar ridge height and width may be greatly reduced due to lack of enough stimulation for the surrounding ligament. In order to consistently restore function and aesthetics, post-extraction bone loss requires bone-grafting treatments.[5]

After extraction, a variety of techniques are used to avoid post-extraction bone loss and provide predictable implant placements, such as socket preservation with grafts (biomaterials) and early or immediate implant insertion. Although there are many graft materials available to the clinician, some bone graft materials require more healing time before even a tiny quantity of new bone may be incorporated into the graft site.[6]

Numerous allografts, alloplastic graft materials or xenografts, such as demineralised freeze-dried one grafts, hydroxyapatite, freeze-dried bone grafts, bioactive glass, etc., are frequently used for bone regeneration procedures and have been shown to have good osteo-conductive and osteo-inductive properties.[7] Yet, the risk of disease transmission and frequently unpredictable results prompted researchers to look for substances that may either independently cause predictable regeneration or enhance the capabilities of these graft materials.

Platelets are among the first cells to respond at a wound site during wound healing, and they are critical to the initiation of this process. Therefore, lately researchers become quite interested in

platelet-rich derivatives due to their potential in tissue regeneration. Pure platelet-rich plasma (P-PRP), leukocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), and leukocyte- and platelet-rich fibrin (L-PRF) are the four subtypes of platelet-rich derivatives.[8] Among them while PRP represents the first generation, PRFs are the second generation with additional advantage of easier formulation and longer eggects.[9,10]

Platelet rich plasma (PRP) is one among novel strategy for tissue regeneration which is frequently employed in a variety of medical or dental surgical specialties. Platelet Rich Fibrin is a fibrin framework that traps and gradually releases platelet cytokines, growth factors, and cells over time. PRF can be used to improve bone healing by acting as a resorbable membrane.[11] It is made up of a fibrin matrix polymerized in a tetra molecular structure, with platelets, leucocytes, cytokines, and circulating stem cells incorporated into the matrix. Autologous Platelet Rich Fibrin is regarded as a healing biomaterial capable of accelerating physiologic wound healing and the formation of new bone.[12]

Although studies have shown the effect of PRF on extraction socket healing but the results have shown contrasting results. Moreover, to the best of our knowledge, practically none have assessed any potential role of post extraction soft tissue healing around the socket. Therefore, to bridge this gap, this clinical study was done to assess the effect of PRF in hard and soft tissue healing of the post-extraction socket.

## AIM OF THE STUDY

To determine whether autologous platelet rich fibrin has the potential to enhance alveolar bone and soft tissue healing after placement of PRF in one of the sockets following bilateral surgical removal of an impacted third molar, and to compare these results with alveolar bone healing and bone regeneration in the opposite side socket closed primarily without PRF.

## MATERIALS AND METHODS

### Patient selection

The present study was undertaken at the outpatient department of Oral and Maxillofacial Surgery, Awadh Dental College and Hospital, Jamshedpur, India between a period of six months from June 2022 to December 2022. Prior to commencement of the study, ethical approval was taken from the Institutional ethical committee. This study included both male and female patients who were referred to the Oral and Maxillofacial Surgery department for tooth extraction. A thorough clinical examination and investigation were performed on all patients to rule out any systemic problems.

The sample size was calculated using the formula $n= f(\alpha,\beta) \times \sigma^2 / (\mu_1 - \mu_2)^2$ presented by Pandis N et al[13] which has been used by previous studies as a standard for spilt mouth design. Where, σ is the standard deviation of the within-person differences (μ1 - μ2), and $f(\alpha,\beta)$ is a function of power and significance level. Therefore with 90% power and 95%confidence interval and based on the within person differences of earlier studies published in literature the sample was calculated to be 20.

**Inclusion criteria:** All patients between the ages of 18 and 30 who were undergoing exodontia procedures under ASA 1 and 2 and who agreed to participate in the study protocol.

**Exclusion criteria:** Patients with contraindications to local anaesthesia or surgery, uncontrolled medical conditions, periodontally weakened and compromised patients, those with platelet disorders or patients with a history of platelet disorders, and those with harmful smoking and other deleterious habits.

The patients were randomly distributed into 2 groups, Group I (test group-n =20): Extraction sockets which received platelet rich fibrin and Group II (control group-n =20): Extraction sockets left for normal healing (blood clot). By using the Microsoft Excel (Microsoft Office 2022, Microsoft, Random, Wash) computer-generated random number generating tool, the right or left side of the patients was randomly chosen as the experimental side, and the side opposite the experimental side was chosen as the control side.

### Patient preparation

A thorough history of the patients was meticulously recorded before recruiting, and eligibility was determined. The patients were informed of the benefits and dangers, and a written consent was acquired using the recommended format. Following this, bilateral third molar extraction was performed by single surgeon using necessary intraoral nerve blocks with 2% solution of lignocaine hydrochloride and a 1:2, 00,000 adrenaline solution. Post extraction instructions were given and paracetamol 1000gm was prescribed every 6 h in case of pain for 3 days. Debridement was completed thoroughly, and the socket was prepared for PRF gel (group 1).

**Preparation of PRF:** Choukroun et al.[14] protocol was used for PRF preparation where the blood samples are collected in a pree-sanitized rube, without anticoagulant or gel separator, and are immediately centrifuged according to the following program: 30 s acceleration, 2 min at 2,700 rpm, 4 min at 2,400 rpm, 3 min at 3,000 rpm, and 36 s deceleration and stopping.

The PRF clot that had formed in this manner was taken out of the test tube and immediately placed in an open extraction socket. A 3-0 mersilk suture was used for the initial closure. The patients in group II, the control group had their extraction socket painstakingly cleaned before getting a 3-0 mersilk suture/pack for primary closure. The patients were informed regarding the routine post operative care followed by suture removal on the seventh post operative day.

Bone density was measured and compared (using DIGORA® Optime Digital software 2.5 version) at the following intervals: on the day of extraction (T0), 4 weeks after extraction (T1), 8weeks after extraction (T2), 12 weeks after extraction (T3), and 16 weeks after extraction (T4) in order to evaluate the post-extraction hard and soft tissue healing of PRF gel as compared to the control group on RVG.

The Healing index (HI) by Landry et al[15] (1988) was used to evaluate the soft tissue response in the extraction sockets of experimental and control sites. The scoring was done on 3rd, 7th, and 15th day after PRF placement.

**Statistical analysis:** The statistical package SPSS (Statistical Package for Social Science, Version 21) software was used to examine the data. For continuous data, descriptive statistics with Mean and Standard Deviation (SD) were calculated. Calculations were made for frequency and percentages for categorical variables. Normality of data was checked using Shapiro-Wilk test. Paired and unpaired t test and repeated measures ANOVA was carried out for inter and intra-group comparison across different study visits. All statistical inferences were deemed significant at a p-value of <0.05.

**RESULTS**

The study consisted of 20 participants. Age was categorized into two subgroups: ≤20 years and >20 years. Majority of the study participants (N=14, 70%) belonged to age group of >20 years. The mean age of the study participants was 24.56±2.12 years**.** Majority (75%) of the study participants were females.

Table 1 and 2 shows difference in mean measurement of bone density of experimental and control side from T0 to T5 in maxilla and mandible respectively. In maxilla, statistically significant difference was found in PRF side bone density as compared to control side all time intervals except at T0. Similarly in mandible statistically significant difference was found in PRF side bone density as compared to control side all time intervals including T0. The bone density values were higher in mandible as compared to maxilla which is seen physiologically too. Table 3 and 4 represent the weekly mean difference in bone density in maxilla and mandible respectively. In both maxilla and mandible, there was statistically significant mean weekly difference (T0-T1, T1-T2, T2-T3 and T3-T4) in bone density was observed between experimental and control group with higher difference in mandible as compared to maxilla (Graph 3and 4).

Intra-group comparison (Table 5) of mean change of healing index score for experimental side at 3rd, 7th and 15th day using one way ANOVA test resulted a significant difference for both experimental (4.11±0.51 vs. 4.37±0.44vs 4.79±0.47, p=0.003) and control side (3.54±0.26vs. 3.42±0.60 vs. 4.01±0.25, p=0.034). Inter-group comparison (Table 6) showed a significant difference in mean for both experimental and control side on 3rd (4.11±0.51vs. 3.54±0.26, p=0.028), 7th (4.37±0.44 vs. 3.42±0.60, p<0.001) and 15th day (4.79±0.47 vs. 4.01±0.25, p<0.001) which signifies that soft tissue healing was significantly higher in PRF side as compared to control side.

**Table 1: Comparison of mean measurement in bone density between experimental & control group from T0 to T4 in maxilla**

| Time period | Experimental group | Control group | p value |
|---|---|---|---|
| **T0** | 62.01±0.49mm | 61.76± 0.48mm | p=0.112 (NS) |
| **T1** | 66.92±0.44mm | 64.79±0.44mm | p<0.001(HS) |
| **T2** | 78.13±0.50mm | 69.46±0.43mm | p<0.001(HS) |
| **T3** | 92.30±0.53mm | 81.07±0.44mm | p<0.001(HS) |
| **T4** | 106.12±0.34mm | 92.72±0.19mm | p<0.001(HS) |

**Table 2: Comparison of mean measurement in bone density between experimental & control group from T0 to T4 in mandible**

| Time period | Experimental group | Control group | p value |
|---|---|---|---|
| **T0** | 74.09±0.28mm | 76.28± 0.87mm | p<0.001(HS) |
| **T1** | 83.34±0.28mm | 80.39±0.46mm | p<0.001(HS) |
| **T2** | 97.42±0.65mm | 89.36±0.21mm | p<0.001(HS) |
| **T3** | 109.70±0.51mm | 96.47±0.64mm | p<0.001(HS) |
| **T4** | 127.12±0.74mm | 107.72±0.34mm | p<0.001(HS) |

**Table 3: Comparison of mean difference in bone density between experimental & control group from T0 to T4 in maxilla (Weekly change)**

| Time period | Experimental group | Control group | p value |
|---|---|---|---|
| **T0-T1** | 4.91±0.14 | 3.03±0.14 | p<0.001(HS) |
| **T1-T2** | 11.21±0.15 | 4.67±0.13 | p<0.001(HS) |
| **T2-T3** | 14.17±0.16 | 11.61±0.14 | p<0.001(HS) |
| **T3-T4** | 13.82±0.14 | 11.65±0.10 | p<0.001(HS) |

**Table 4: Comparison of mean difference in bone density between experimental & control group from T0 to T4 in mandible (Weekly change)**

| Time period | Experimental group | Control group | p value |
|---|---|---|---|
| **T0-T1** | 9.25±0.08 | 4.11±0.22 | p<0.001(HS) |
| **T1-T2** | 14.08±0.15 | 8.97±0.11 | p<0.001(HS) |
| **T2-T3** | 12.28±0.18 | 7.11±0.15 | p<0.001(HS) |
| **T3-T4** | 17.40±0.20 | 11.25±0.16 | p<0.001(HS) |

**Table 5: Intra-group mean change in healing index scores between at 3rd, 7th and 15th days**

| Time period | 3rd day | 7th day | 15th day | t value† | p value |
|---|---|---|---|---|---|
| **Experimental group** | 4.11±0.51 | 4.37±0.44 | 4.79±0.47 | 8.35 | 0.003(S) |
| **Control group** | 3.54±0.26 | 3.42±0.60 | 4.01±0.25 | 7.63 | 0.034(S) |
| **One way ANOVA†; Statistically significant (p<0.05)** | | | | | |

**Table 6: Inter-group of mean change in healing index score at 3rd, 7th and 15th days**

| Time period | Experimental group | Control group | t value† | p value |
|---|---|---|---|---|
| **3rd day** | 4.11±0.51 | 3.54±0.26 | 3.09 | 0.028(S) |
| **7th day** | 4.37±0.44 | 3.42±0.60 | 5.00 | <0.001(HS) |
| **15th day** | 4.79±0.47 | 4.01±0.25 | 5.55 | <0.001(HS) |

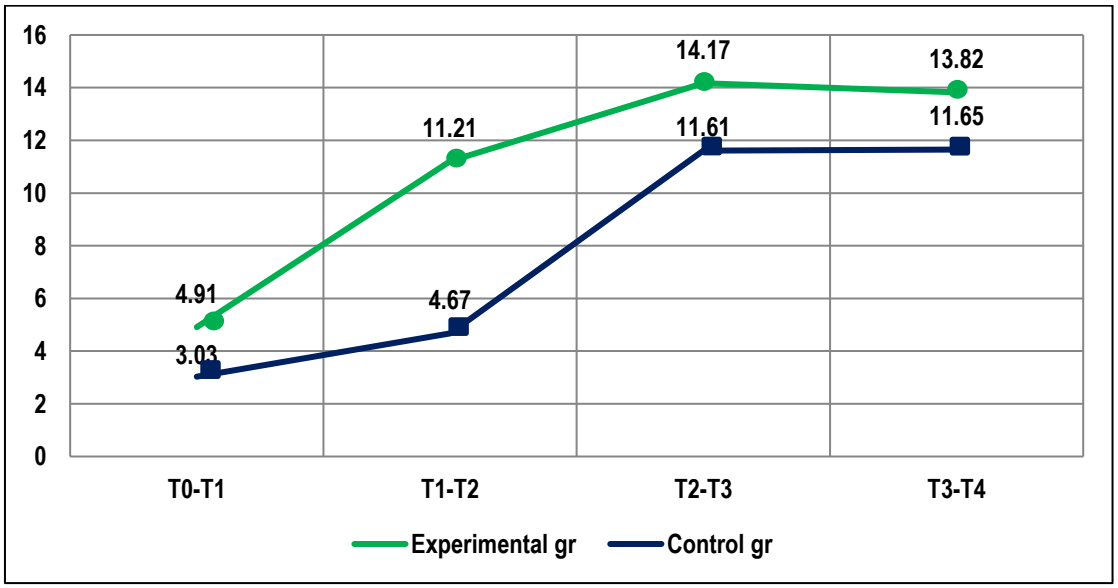


**Figure 1: Mean difference in bone density between experimental & control in maxilla (weekly change)**

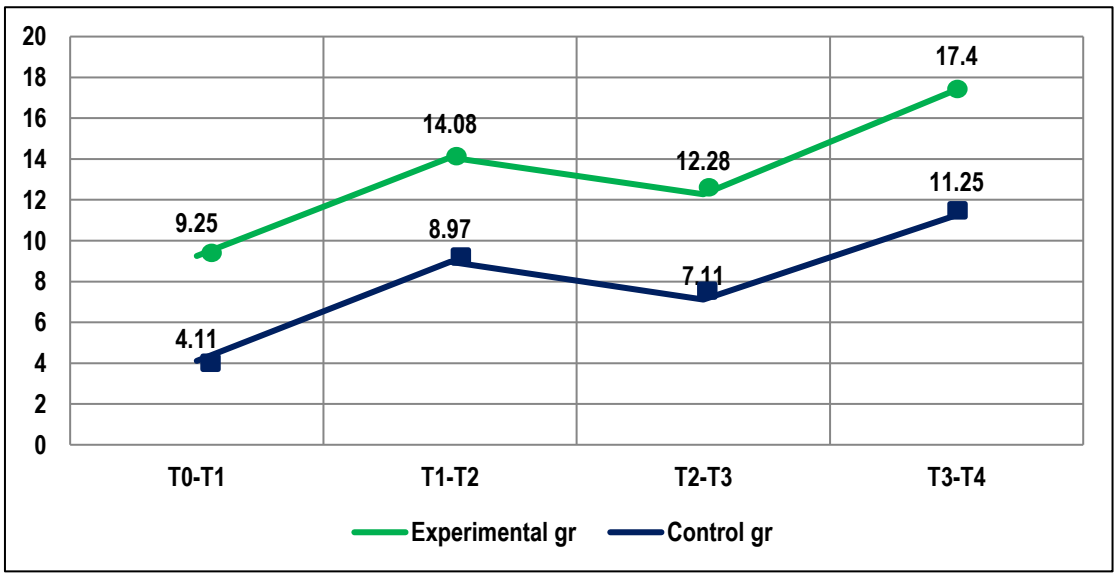


**Figure 2: Mean difference in bone density between experimental & control in mandible (weekly change)**

## DISCUSSION

The study's objective was to assess the clinical and radiographic outcomes of autologous platelet rich fibrin (PRF)-assisted extraction socket in terms of hard and soft tissue healing. The assertion that PRF will hasten the repair of the tooth socket following extraction, as evidenced by greater bone fill and increase in soft tissue healing, was validated. Also, a comparison of the bone density between the experimental and control groups revealed a statistically significant difference between the two groups from tooth extraction, further demonstrating the effect of employing PRF.

It is hypothesised that PRF inclusion boosts cell proliferation effectiveness. Additionally, platelets in the PRF undergo de-granulation, which results in a sustained release of growth factors that affect angiogenesis, epithelialization, stem cell trapping, and immune control. These factors include platelet derived growth factors (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), thrombospondin-1 (TSP-1), and transforming growth factor-beta (TGF-b). This offers crucial components for faster bone repair when PRF is present.[16-19]

Numerous materials have been used in past like xenograft, allograft, or alloplastic graft materials have been employed for bone regeneration treatments. They consist of hydroxyapatite, bioactive glass, demineralized freeze-dried bone grafts, and freeze-dried bone grafts. These biologically active materials are thought to have good bone inductive and conductive properties, but the risk of disease transmission and frequently unpredictable results have prompted researchers to look for materials that can independently produce predictable regeneration or that can enhance the properties of these graft materials.[7]

Choukroun et al. from France were the first to describe platelet rich fibrin. Since PRP was the first, it has been referred to as second generation platelet concentrate. During the Second International Conference on Growth Factors in May 2006, Dohan and Diss presented a report on clinical trials contrasting the growth factor composition of PRP and PRF.[14] It has been demonstrated that combining the growth factors can hasten bone repair, promote fibroblast proliferation, and increase tissue vascularity, rate of collagen formation, mitosis of mesenchymal

stem cells and endothelial cells, as well as osteoblasts, playing crucial roles in the rate and extent of bone formation.[20]

In combination with bone grafts, PRF, which comes in the form of a platelet gel, increases wound healing, bone development and maturation, graft stabilisation, wound closure and hemostasis, and enhances the handling characteristics of graft materials. PRF can be utilised as a membrane as well. According to clinical studies, increasing bone density may be possible with a combination of bone transplants and the growth factors found in PRP and PRF.[21]

Similar experiments were conducted to compare a test group where the PRF was inserted in the removed socket with a control group permitted to heal normally in order to assess the effectiveness of PRF in bone healing.[18,22-26] Among these few studies have used the surgically removed third molars in the maxilla and mandible were on both sides.[27-29]

Similar results have been reported by Ruktowski et al. who tracked changes in radiographic density at PRP- treated locations in comparison to ipsilateral not-PRP treated sites using digital radiography and Computer Tomography (CT) scan analysis.[30] Following tooth extraction, the PRP-treated sites showed an early and noticeable increase in radiographic density above baseline measures. he early 2-week post-operative healing period is where PRP is most beneficial; control extraction sites took six weeks to reach comparable bone density, but PRP-treated sites did so in just one week. Similar to the previous study, a more recent study by Celio-Mariano et al. revealed a higher radiographic bone density in the PRP group, demonstrating a significantly better improvement in bone healing in the sockets after extraction of mandibular third molars as compared to the control group.[28]

Arenaz-Bua et al. examined the effectiveness of PRP in stimulating bone repair following extraction of the third molar in a prospective split-mouth trial. At six months, the authors saw no further acceleration of bone development, and they found no statistically significant differences between the groups in terms of discomfort, edema, trismus, or infection.[31] Similarly, applying PRF alone to soft tissue-impacted mandibular third molar extraction sockets did not improve osteoblastic activity in post-surgical weeks 1 and 4 compared to non-PRP-treated sockets in a study by Gurbuzer et al. (2008) (using scintigraphy).[18]

In this study PRF also has shown a statistically significant effect in soft tissue healing in both inter and intra-group comparisons. This is in line with a systematic review where, using PRP/PRF in the alveolar socket following tooth extraction can undoubtedly enhance soft tissue healing.[32] Lundquist was one of the pioneers in studying how PRF affected human dermal fibroblasts.[33] It was discovered that PRF considerably outperformed fibrin sealant in terms of its proliferative effect on cutaneous fibroblasts. Moreover, PRF caused the fast release of collagen I as well as the sustained release and protection of endogenous fibrogenic components from proteolytic deterioration, both of which are crucial for wound healing. Following that, Clipet et al. discovered that PRF increased survival and proliferation of fibroblast and keratinocyte cells.[34] Vahabi et al. in 2015 likewise observed that PRF caused gingival fibroblast proliferation at 24 hours, but they also discovered that at 48 and 72 hours, gingival fibroblast proliferation was considerably higher in the plasma rich in growth factors group.[35] In summation, it can be said that PRF has the ability to stimulate the growth of keratinocytes, gingival fibroblasts, and dermal fibroblasts as well as to take part in their creation of extracellular matrix collagen I ultimately leading to soft and hard tissue healing

## CONCLUSION

According to the study, PRF is a potential biomaterial for the rapid and significant enhancement of bone regeneration following exodontia surgery. Its improvement and increase in bone density emphasise the use of autologous PRF as a legitimate technique for triggering and speeding the regeneration of hard tissues. The PRF membrane benefits from a particularly favourable physiologic architecture to help the healing process thanks to the slow polymerization mode. Further research on the material's anti-inflammatory properties should be conducted, as well as additional clinical trials with longer follow-up periods, a bigger sample size, and accurate bone density measurement devices.

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