ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

A Comparative Analysis of Platelet-Rich Fibrin and Platelet-Rich Fibrin Combined with Hydroxyapatite to Enhance Healing of Impacted Mandibular Third Molar Sockets

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Abstract

Aim: This study aimed to compare the effectiveness of platelet-rich fibrin (PRF) alone versus platelet-rich fibrin (PRF) combined with hydroxyapatite (HA) in reducing postoperative pain, swelling, improving soft tissue healing, and promoting osseous regeneration in the extraction sockets of impacted mandibular third molars in human patients.

Materials and Methods: This prospective study included 40 patients from the Department of Oral and Maxillofacial Surgery (OMFS) at Rama Dental College hospital and Research Centre Kanpur (U.P.). The participants were divided into two groups: one group received PRF treatment, while the other received PRF combined with HA for the management of impacted mandibular third molar extraction sockets. The patients were evaluated based on the following parameters: pain and swelling at 1st, 3rd, and 7th days; soft tissue healing at 3rd, 7th, and 14th days; and osseous regeneration at 1st, 3rd, and 6th months postoperatively.

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Results: The PRF with HA group exhibited lower levels of pain and swelling compared to the PRF-only group. Soft tissue healing was also more favorable in the PRF with HA group. Furthermore, the study demonstrated faster bone regeneration in the extraction socket treated with PRF and HA, as opposed to the PRF group. Additionally, patients in the PRF with HA group experienced less postoperative discomfort.

Conclusion: PRF, as a mitogenic agent, combined with a bone graft, creates a supportive scaffold that enhances early healing, proving to be both beneficial for the patient and cost-effective.

Introduction

The trans-alveolar extraction of impacted mandibular third molars is one of the most frequently performed minor surgical procedures in the OMFS department [1]. Traditional removal of mandibular third molars often results in tissue trauma, which triggers an inflammatory response and leads to common postoperative issues such as pain, swelling, and trismus, all of which can affect the patient's recovery process [2]. In addition to these complications, wound healing is another important concern following the procedure.

Autologous and homologous fibrin adhesives, derived from plasma, represent the final stage of the coagulation process and have been used in various departments, including Orthopaedics, Periodontics, and OMFS, to promote soft tissue healing. Autologous fibrin adhesives offer additional advantages, particularly by reducing the risk of viral disease transmission (e.g., HIV, hepatitis B). Furthermore, the presence of fibrinogen in autologous products helps them withstand mechanical stresses such as pressure and tearing [3].

There are five main types of platelet concentrates, classified based on their leukocyte and fibrin content: P-PRP, L-PRP, P-PRF, L-PRF, and I-PRF. Each type varies in its biological composition and intended use [4, 5].

PRF is preferred over other platelet concentrates because it releases growth factors at a sustained rate over an extended period, thereby promoting optimal wound healing [6]. Acting as a resorbable membrane, PRF consists of a fibrin matrix that contains cytokines and various cells [7]. In vitro studies have shown that PRF facilitates the growth of human periosteal cells and supports bone tissue engineering applications [8, 9], contributing to wound healing through the release of growth factors and other proteins.

To enhance bone healing, the addition of HA to PRF is beneficial, as HA offers excellent biocompatibility and osteoconductive properties [10]. However, there are some limitations to using PRF, such as its lack of osseous regeneration in extraction sockets after 4 weeks following impacted lower third molar surgery. Further research is needed to compare the effectiveness of PRF alone versus PRF combined with bone grafts for osseous regeneration, as well as to identify the most suitable graft material for bone regeneration.

Patients and Methods

Patients were selected from the OPD of the OMFS Department at Rama dental college Hospital and research centre Kanpur (U.P.) for the surgical removal of mesioangular, horizontally, or distoangular impacted mandibular third molars between December 2023 and

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January 2025. Ethical approval for the study was obtained from the Ethical Committee of RDC, Kanpur. Informed consent was obtained from all study participants in both Hindi and English, and a total of 40 patients were included, with ages ranging from 17 to 35 years, all meeting the criteria for the study.

Inclusion criteria were: patients aged 17–35 years, free from systemic diseases, with mesioangular, horizontal, or distoangular lower third molar impaction as defined by Quek et al. [11], and a Pederson difficulty index score ranging from 3 to 7.

Exclusion criteria included: patients with habits such as smoking or alcohol consumption, those with systemic diseases, patients presenting with abscesses or any pathology related to the impacted third molars, and those outside the age range of 17 to 35 years.

The patients were selected based on the criteria established for the study and were divided into two groups. In the PRF group (20 patients), following the surgical removal of the impacted mandibular third molar, 5–10 ml of venous blood was drawn and centrifuged at 3000 rpm for 10 minutes to prepare the platelet-rich fibrin [12]. The extraction socket was then filled with PRF, and the flap was approximated. In the PRF with HA group (20 patients), after the surgical removal of the impacted mandibular third molar, the extraction socket was filled with a mixture of PRF and HA, followed by flap approximation.

Patients did not receive any preoperative antimicrobials or other medications that could affect healing, and a standardized protocol was followed for all participants. A brief case history, including a medical history, general examination, and local extraoral and intraoral examination, was conducted for each patient. Preoperative investigations included a panoramic radiograph (OPG) to assess the difficulty level, determine the Pederson difficulty index, and evaluate Winter's line. Additionally, baseline laboratory tests, including a complete blood count, were performed 24–48 hours prior to the surgical procedure.

Operative Procedure

A standardized surgical technique was followed for all groups, performed by the same experienced oral and maxillofacial surgeon. The disimpaction of the mandibular third molar was carried out under local anesthesia using the standard approach. A triangular flap was raised using either a Ward-I or Ward-II incision, or an envelope flap. Buccal guttering and ditching were performed with a tungsten carbide bur and micromotor handpiece. After the tooth extraction and achieving hemostasis, the socket was thoroughly irrigated with 40 ml of normal saline. The patients were then randomly assigned to one of two groups, each consisting of 20 patients (sample size = 20/group).

- The PRF-treated group consisted of patients whose extraction socket was filled with PRF before the socket was closed (Figs. 1, 2).
- The PRF with HA-treated group included patients whose extraction socket was filled with a combination of PRF and HA before the socket was closed (Figs. 3, 4).

Postoperative Monitoring and Variables:

Patients in all groups were evaluated on the 1st, 3rd, and 7th days post-surgery to assess pain and swelling, and on the 3rd, 7th, and 14th days for the evaluation of soft tissue healing (Figs. 1, 3). Osseous regeneration was assessed using radiographs

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(OPG) on the 1st, 3rd, and 6th months after surgery for both the PRF and PRF with HA groups (Figs. 2, 4). Data were collected for statistical analysis.

Data were collected for statistical analysis as follows:

- Pain assessment was performed using the method described by Heller et al. [13], based on the Visual Analog Scale (VAS) score [13].
- Swelling estimation was carried out using the technique outlined by Dutta et al. [14].

Facial swelling was assessed by modifying the three-line measurement method (in cm), utilizing five fixed points on the surgical side of the face. Measurements were taken before surgery and again on the 1st, 3rd, and 7th days post-surgery (Fig. 5).

- Evaluation of soft tissue healing was also based on the standard described by Landry et al. [15].
- The mean radiographic score (using OPG) was used to assess bony healing at different time points across groups. The criteria for evaluating bone healing, which included lamina dura, overall density, and trabecular pattern, as well as the scoring system, were based on the method outlined by Ogundipe et al. [16].

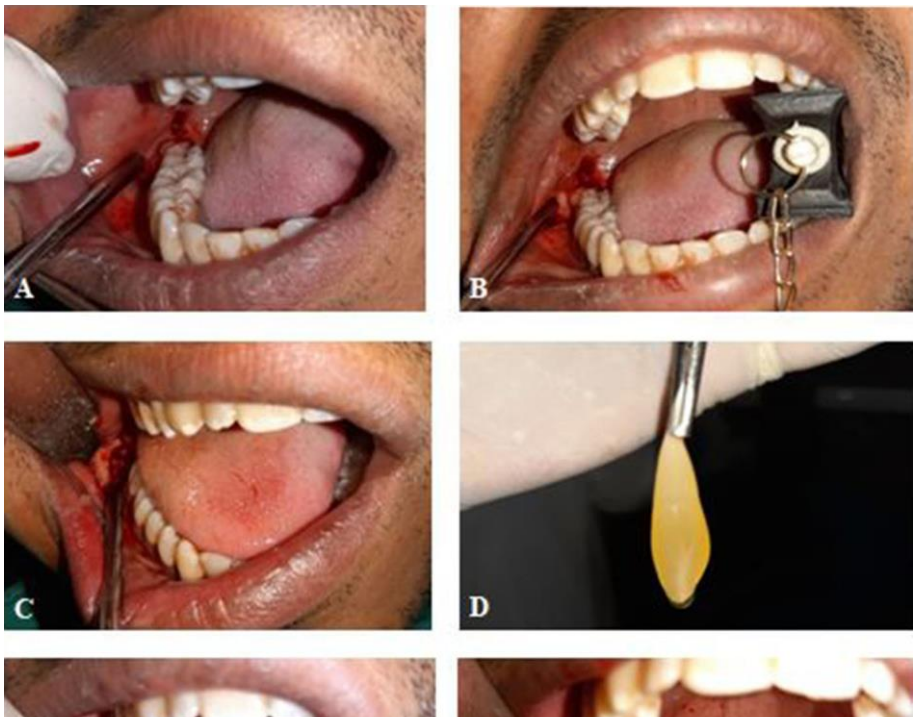

Fig. 1 Representative pictures showing PRF placement in mandibular third molar extraction socket. a Incision,

b surgical site exposure,

c empty extraction socket,

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d PRF separated from RBCs,

e PRF placement and f closure

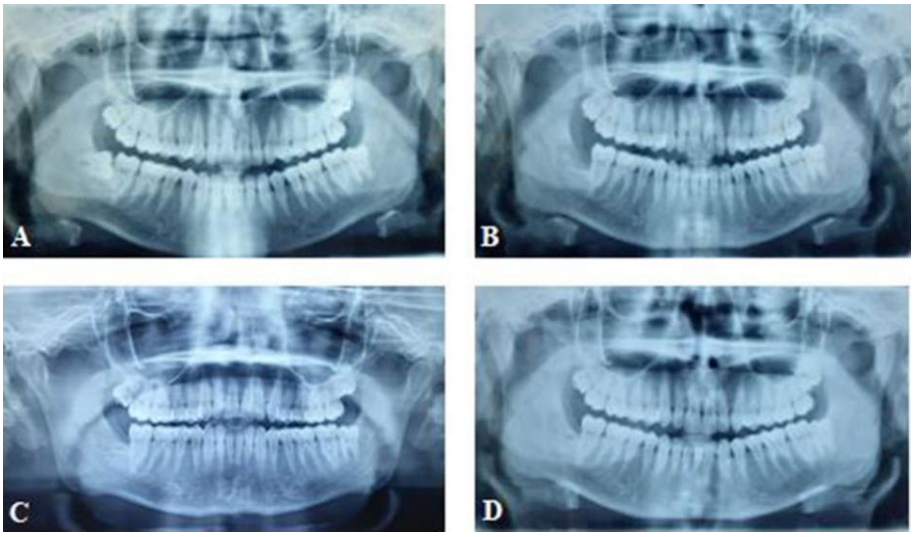

Fig. 2
Representative radiographs (OPG) showing bone healing in PRF-treated patients. a OPG preoperative,

b OPG 1st month after surgery,

c OPG 3rd month after surgery and d OPG 6th month after surgery

(Line 1): A horizontal line drawn between two key anatomical points: the outer corner of the mouth and the midpoint of the ear's tragus.

(Line 2): A horizontal line connecting two important anatomical points: the pogonion and the midpoint of the ear's tragus.

(Line 3): A vertical line linking two significant anatomical points: the outer canthus of the eye and the mandibular angle. The average data were determined by calculating the difference between the postoperative and preoperative measurements [14].

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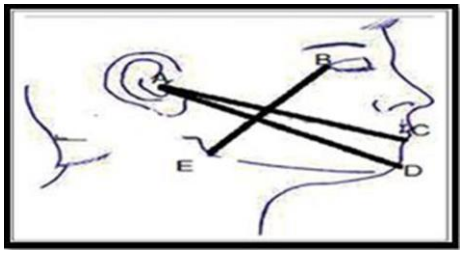

Fig. 5 Representative picture showing facial swelling measurement by joining the three lines AC, AD, and BE

- Evaluation of soft tissue healing was also based on the standard described by Landry et al. [15].
- The mean radiographic score (using OPG) was used to assess bony healing at different time points across groups. The criteria for evaluating bone healing, which included lamina dura, overall density, and trabecular pattern, as well as the scoring system, were based on the method outlined by Ogundipe et al. [16].

Preparation of Protein-Rich Fibrin

Protein-Rich Fibrin (PRF) was prepared according to the protocol established by Choukroun et al. [17]. A 5–10 ml sample of venous blood was drawn from the patient into a test tube without the use of any anticoagulant. The blood was then centrifuged promptly at 3000 rpm for 10 minutes. The centrifuged blood separated into three layers: the top layer consisted of acellular platelet-poor plasma (PPP), the middle layer contained the PRF clot, and the bottom layer held red blood cells (RBCs). The PPP layer was removed, and the PRF clot was extracted from the middle layer [12].

Graft Material

The graft material used was G–Bone (SHAG–31 G.Surgiwear Limited), a synthetic hydroxyapatite granule composed of HA, tricalcium phosphate (TCP), calcium carbonate, and bicalcium phosphate. The grafts, which were sponge-like in texture, measured between 0.8 and 1.8 mm in size after being wetted. The material was provided in sterile, disposable 1 cc blister packs [18] (Fig. 6).

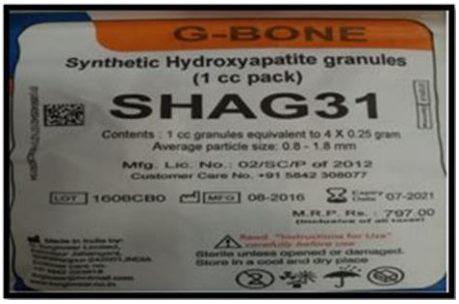

Fig. 6 Representative picture showing material used in extracted socket as Graft material

Statistical Analysis

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

Statistical analysis was performed using the t-test, Fisher's exact test, and Chi-square test with the assistance of SPSS software version 21. The t-test was used to assess whether there were significant differences between groups in the measured parameters. When necessary, proportions were compared using the Chi-square test.

Results

A total of 40 patients were randomly selected for the study and divided into two groups: the PRF group and the PRF with HA group, with each group consisting of at least 20 patients. Among the 40 participants, 19 were male and 21 were female. The age range of the patients was between 17 and 35 years.

Pain and swelling intensity were assessed on the 1st, 3rd, and 7th days. The results, shown in Table 1, indicate a reduction in both pain and swelling across all groups starting from day 1. The most significant reduction in pain and swelling was observed in the PRF with HA group ($p < 0.05$).

Soft tissue healing was evaluated on the 3rd, 7th, and 14th days. As seen in Table 2, a decrease in the healing index was noted across all groups from day 3, with the greatest reduction in the healing index observed in the PRF with HA group ($p < 0.05$).

Radiographic Assessment

Radiographic evaluation of osseous regeneration was performed using orthopantomogram (OPG) images, assessing lamina dura, overall density, and trabecular pattern scores [16] at the 1st, 3rd, and 6th months postoperatively. The lamina dura score showed a significant increase in the PRF with HA group at both the 3rd and 6th months post-surgery, with a notably higher score ($p < 0.05$) in this group. Table 3 presents the mean bone healing scores for overall density and trabecular pattern at the 1st, 3rd, and 6th months postoperatively for both the PRF and PRF with HA groups. Both overall density and trabecular pattern demonstrated significantly higher scores ($p < 0.05$) in the PRF with HA group.

Discussion

Several studies indicate that biological mediators, such as growth factors, can help accelerate the healing of both soft tissue and bone. Our study showed that the combination of PRF with HA in the extraction socket was more effective in reducing pain and swelling, as well as promoting faster soft tissue healing compared to PRF alone. PDGF and epidermal growth factor play key roles in fibroblast migration, proliferation, and collagen synthesis, thereby facilitating soft tissue wound healing [19]. Additionally, the use of HA mixed with PRF in the extraction socket supported earlier bone formation. Other studies have also demonstrated that surgical sites treated with PRF heal 2–3 times faster than those treated by conventional methods [20].

PRF with HA is often preferred over other concentrates because PRF releases growth factors at a sustained rate over a longer period, thereby optimizing wound healing [5], while HA further promotes bone healing. Radiographic results showed better bone healing at the PRF with HA site compared to the PRF-only site, indicating that HA has superior osteoconductive properties. The porous structure of HA allows osteogenic cells to grow from existing bone surfaces into the adjacent bone graft material [21].

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The two groups were compared based on four parameters: pain, swelling, soft tissue healing, and osseous regeneration. In our study, pain was measured using the VAS scale [13]. When comparing the PRF group with the PRF with HA group, pain levels were found to be lower in the PRF with HA group, with a p-value < 0.05, which was statistically significant for the PRF with HA group.

The results of our PRF with HA group compared to the PRF group align with the findings of the study by Dutta et al. [14].

Swelling was recorded using the method described by Dutta et al. [14]. Our measurements showed that swelling was significantly reduced in the PRF with HA group compared to the PRF group, with a p-value < 0.05, indicating a remarkable decrease in swelling for the PRF with HA group. These findings are consistent with the study by Asutay F et al. [22].

For soft tissue healing, we followed the criteria established by Landry, Turnbull, and Howley [15]. The results showed a reduction in the healing index for the PRF with HA group compared to the PRF group, with a p-value < 0.05, suggesting a significant improvement in soft tissue healing for the PRF with HA group. This outcome aligns with the study by Al-Hamed et al. [23].

In our study, osseous regeneration was evaluated using radiographs (OPG), following the criteria outlined by Ogundipe et al. [16]. The radiographic results showed that osseous regeneration was significantly better in the PRF with HA group, particularly after the sixth month post-surgery. Early bone formation was observed in the PRF with HA group, with a p-value < 0.05, indicating high significance.

In the study by Singh et al. [24], grayscale values on IOPA radiographs were used to assess mean bone density in the PRF and control groups, showing values of 18, 20 for the PRF group and 10, 20 for the control group at the 2nd and 3rd months postoperatively, which were not statistically significant. Based on our findings, it can be concluded that adding HA to PRF enhances osseous regeneration at the 1st, 3rd, and 6th postoperative months, making this combination beneficial for improving post-surgical bone regeneration.

The findings of this study, along with previous literature, indicate that the combination of PRF and hydroxyapatite is both economically feasible and an effective approach for reconstructing bony defects and promoting better healing.

In summary, our study assessed the effectiveness of PRF and PRF with HA in third molar extraction sockets, focusing on postoperative pain, swelling, soft tissue healing, and osseous regeneration, both clinically and radiographically. The results revealed that PRF with HA significantly reduced pain on the 3rd and 7th postoperative days, decreased swelling on the 7th postoperative day, enhanced soft tissue healing by the 14th postoperative day, and improved bone healing by the 6th postoperative month. These findings suggest that PRF with HA is superior to PRF alone in promoting both soft and hard tissue healing. However, further studies with larger sample sizes and extended follow-up are needed to make more definitive conclusions on this topic.

Conclusion

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This study evaluated pain, swelling, soft tissue healing, and osseous regeneration. The results indicated that the PRF with HA group experienced a greater reduction in pain and swelling. Additionally, this group demonstrated more significant improvements in soft tissue healing and osseous regeneration compared to the PRF group.

The present study, despite its limitations, demonstrated the following findings:

1. A clinically significant reduction in postoperative pain was observed in the PRF with HA group compared to the PRF group on the 1st, 3rd, and 7th days.
2. Postoperative swelling showed satisfactory improvement in 19 patients and unsatisfactory results in 1 patient within the PRF with HA group, with clinically significant differences compared to the PRF group on the 1st, 3rd, and 7th days.
3. Postoperative soft tissue healing was significantly enhanced in the PRF with HA group compared to the PRF group on the 3rd, 7th, and 14th days.
4. Postoperative osseous regeneration showed significant improvement in the PRF with HA group compared to the PRF group on the 1st, 3rd, and 6th months.

PRF with HA proves to be an effective and straightforward method for reducing postoperative complications across all evaluated parameters. However, further studies with larger sample sizes are necessary to validate these findings.

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