Effect of Autologous Platelet Rich Fibrin (PRF) on Post-operative Complications and Healing Following the Extractions of Impacted Mandibular Wisdoms: An Open Label Randomized Controlled Trial

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ABSTRACT

Background: The extraction of impacted mandibular third molars is a commonly performed oral surgical procedure associated with various post-operative complications, including pain, swelling, and delayed soft tissue healing.

Objective: This study aimed to evaluate the effect of PRF on post-operative complications and healing following the extraction of impacted mandibular third molars.

Methods: A total of 134 participants with impacted mandibular third molars were randomly allocated into two groups: Group A (PRF treatment) and Group B (control, natural clot formation). Post-operative pain, swelling, and soft tissue healing were assessed on the 3rd and 7th post-operative days. Swelling was measured at two sites, and soft tissue healing was evaluated using Landry and Turnbull criteria.

Results: The mean age of participants was 27 years in Group A and 26.2 years in Group B. Pain incidence was lower in Group A (10.4%) compared to Group B (20.8%), although the difference was not statistically significant (p > 0.05). Group A showed a significantly lower rate of swelling (68.5%) compared to Group B (100%) (p = 0.000). Soft tissue healing was significantly better in Group A, with 100% of patients exhibiting excellent healing compared to 80.5% in Group B (p = 0.0001).

Conclusions: The application of PRF following impacted mandibular third molar extraction significantly reduces post-operative swelling and enhances soft tissue healing. While pain reduction was not statistically significant, the overall improvement in post-operative recovery suggests that PRF may be a beneficial adjunct in oral surgery to promote faster healing and reduce complications.

Keywords: *Platelet Rich Fibrin, Third molar, Extraction Site, wound healing, surgical recovery, tissue regeneration.*

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1. INTRODUCTION

The extraction of impacted mandibular third molars, commonly known as wisdom teeth, is a frequently performed oral surgical procedure. These extractions are often associated with a range of post-operative complications, such as pain, swelling, infection, dry socket, and delayed wound healing [1]. These complications can not only affect patient comfort but may also lead to extended recovery periods and increased healthcare costs. Managing these complications is a critical aspect of ensuring a smooth recovery and optimal surgical outcomes [2]. A significant portion of the population undergoes wisdom tooth extraction annually due to a multitude of causes ranging from caries to impaction of teeth within the jaws [3]. Most commonly, a surgical extraction is deemed necessary for the removal of such teeth, and so, the risk of complications in this site is high. Common complications associated with extractions include pain, bleeding, trismus, swelling, post-operative infections, damage to adjacent structures, including nerve injury, and delayed wound healing. Considering the surgical morbidity of local structures such as bone, nerve, and proximity of sinus is necessary, as well as factors that impact wound healing, both locally and systemically, must be considered [4]. Many adjunctive measures have been implemented for the control of complications to maintain a comfortable post-operative period including but not limited to, the use of antibiotics, analgesics, intravenous and local injection of corticosteroids. The application of second-generation platelet concentrate, Platelet-rich fibrin (PRF) socket therapy has gained mainstream attention more recently [5,6]. PRF is a blood product, obtained from uncoagulated blood after subjecting to centrifugation. Similar to the fibrin complex, PRF provides a network constituting concentrated platelets, growth factors and cytokines, that is known to promote and accelerate wound healing [7]. PRF has proven to be versatile in terms of being an autologous product, relatively easy handling with many advantages for the healing socket such as regenerative bone potential and decreased post- operative pain [8]. Various studies have reported an improvement in post-operative complications with the use of PRF which formed the basis of our study where PRF therapy was useful for reducing certain complications in extraction sites associated with mandibular molars [9]. Another significant benefit of PRF is its ability to reduce the need for additional pharmacological interventions. Traditional pain management following wisdom tooth extraction often involves the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, both of which can have side effects, including gastrointestinal discomfort and dependency [10]. By promoting natural healing and reducing inflammation, PRF may help minimize the reliance on these medications, leading to a more comfortable and safer recovery process for the patient [11]. Moreover, the use of PRF may shorten the recovery time, allowing patients to return to their normal activities sooner and with fewer complications. While the initial results of PRF in oral surgery are promising, the body of research remains limited, and additional clinical trials are necessary to fully establish its benefits and optimal application techniques [12]. Some studies have reported mixed results, with varying levels of success depending on the type of procedure, the patient's overall health, and the specific PRF preparation method used. It is important to consider these variables when evaluating the effectiveness of PRF in wisdom tooth extractions [13].

Objective

This study aimed to compare the difference in post-operative complications in patients who underwent third molar extractions and were given conventional post-operative care versus those treated with PRF post-extraction.

2. METHODOLOGY

The study was conducted with patients who were recommended for the extraction of impacted mandibular third molars at the Department of Oral and Maxillofacial Surgery, Dr. Ishrat ul Ebad Khan Institute of Oral Health and Sciences, DUHS, Pakistan, from September 06, 2022, to March 6, 2023. The study protocol was reviewed and approved by the Institutional Review Board (IRB), and written informed consent was obtained from all participants before enrollment. All patients were provided detailed information about the study, including its objectives, procedures, and potential risks. The sample size was calculated using the OpenEpi sample size calculator, with a 95% confidence level and 80% statistical power. Based on these parameters, a total of 134 participants (n=134) were estimated as the required sample size for sufficient statistical power to detect meaningful differences between the two study groups.

Inclusion Criteria

- Age between 18 and 30 years,
- Both male and female participants,
- Diagnosis of unilateral or bilateral impacted mandibular third molars that were indicated for extraction,
- American Society of Anesthesiologists' (ASA) grade I (healthy individuals).

Exclusion criteria

- Presence of systemic illnesses that could delay healing, such as diabetes, hypertension, bleeding disorders, immunodeficiencies, mental retardation, and physical disabilities; pregnancy; lactation,
- Fully erupted molars,

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- Active dental infections or periapical pathologies,

- Ankylosed teeth,

- Inadequate oral hygiene,

- Bony diseases or bisphosphonate use,

- Smoking.

Data Collection

Post extraction, each patient's extraction site was randomly allocated to one of two groups:

- **Group A (PRF Group):** Patients who received autologous platelet-rich fibrin (PRF) following the extraction,

- **Group B (Control Group):** Patients who healed naturally with clot formation.

A total of 67 participants were allocated to each group. Randomization was achieved through a computer-generated randomization list to ensure unbiased distribution between the two groups. At the initial visit, participants underwent a screening process to ensure they met the inclusion and exclusion criteria. Those who were deemed suitable for inclusion in the study were provided with detailed information about the extraction procedure, its potential risks, and the treatment protocol. Informed consent was obtained, and all patient inquiries were addressed by a trained professional. Clinical assessments included general health evaluation, oral health status, and periodontal health. Oral hygiene was assessed and categorized as either poor or adequate. Impaction classification was performed using the Pell and Gregory classification system (Classes A, B, C for horizontal, vertical, and mesioangular impactions; and Classes I, II, III for depth of impaction). Patients were then randomly allocated to either Group A or Group B.

Preparation Protocol for PRF

PRF was prepared following the protocol devised by Dr. Joseph Choukroun and his colleagues in 2001. Autologous venous blood was collected from each patient into a 10ml red-cap glass-coated plastic vial, free from anticoagulants, and immediately subjected to centrifugation at 2700-3000 rpm (400g) for 12 minutes. Post-centrifugation, three distinct layers were formed: platelet-poor plasma (PPP) as the top layer, platelet-rich fibrin (PRF) as the middle layer, and erythrocytes at the bottom. The PRF clot was carefully retrieved using sterile tweezers after removing the PPP and erythrocytic layers.

Surgical Technique and Placement of PRF Clot in Extraction Socket

All extractions were performed under strict aseptic conditions. Before the procedure, patients were instructed to rinse with chlorhexidine mouthwash. Local anesthesia was administered using 2% lidocaine with 1:100,000 epinephrine, including an inferior alveolar nerve block and long buccal nerve block for mandibular third molar extractions. A sulcular incision was made with a No. 15 blade, followed by flap reflection, and the tooth was extracted with minimal trauma. After the extraction, the socket was thoroughly debrided and irrigated with saline to remove any loose tissue or debris. In Group A, the PRF clot was placed into the socket, and the flap was sutured with 3-0 silk sutures. In Group B, the socket was left empty, and the flap was sutured without additional material. All surgeries were performed by the same surgeon to maintain consistency. Patients were provided with standardized post-operative instructions. They were advised to rinse with saline starting 24 hours after surgery. For pain management, Naproxen Sodium 550mg (as needed) and Amoxicillin 500mg three times daily for 7 days were prescribed. Patients were scheduled for follow-up visits on the 3rd and 7th post-operative days to monitor recovery and complications. Follow-up visits were scheduled for the 3rd and 7th post-operative days. Trismus was assessed by measuring the distance between the maxillary and mandibular central incisors. Pain levels were assessed on the 7th post-operative day using a Visual Analog Scale (VAS), where scores ranged from 1 (worst pain) to 10 (no pain). Soft tissue healing was evaluated using the Landry and Turnbull criteria, which classified healing as very poor, poor, good, very good, or excellent based on factors such as tissue color, bleeding on palpation, granulation tissue formation, incision margins, and the presence of any pus or discharge.

Statistical Analysis

All statistical analyses were performed using SPSS v.21. The normality of the data was assessed using the Shapiro-Wilk test. For categorical data comparison, Chi-Square or Fisher's Exact test was applied. For quantitative data comparison, the Mann-Whitney U test was used. A p-value of ≤ 0.05 was considered statistically significant for all analyses.

3. RESULTS

In total, 134 participants were engaged with 134 extraction sites, all of which attended follow-ups. The mean age recorded for Group A was 27 years, where 54.3% (n=36) of patients were men, whereas 45.7% (n=31) were women. For Group B, the mean age was determined to be 26.2 years, with 35 men (52%) being men and the remaining 48% (n=32) women. The number of patients in Group A who experienced pain after the extraction was lower, n=7 (10.4%), than that in the control group (Group B), n=14 (20.8%). (p > 0.05). There was a difference noted in swelling between the two groups, Group A

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68.5% (n=46) faring better than Group B 100% (n=67) (p=0.000). Healing of soft tissues was considerably better in the PRF group A, with 100% (n=67) result. (p=0.001).

Table 1. Comparison of Post-Operative Complications and Healing Rate of PRF Treated Socket versus Placebo following the Surgical Removal of Impacted Lower Third Molars.

Outcome Variable	Group A (PRF) Yes (%)	Group A No (%)	Group B Yes (%)	Group B No (%)	P-value
Pain	7 (10.4%)	60 (89.5%)	14 (20.8%)	53 (79%)	0.096
Swelling	46 (68.5%)	21 (31.5%)	67 (100%)	0 (0%)	0.000
Healing of Soft Tissues	67 (100%)	0 (0%)	54 (80.5%)	13 (19.4%)	0.0001

In terms of low pain (VAS 1-3), 17.9% (n=12) of patients in Group A (PRF treatment) experienced low pain compared to 11.9% (n=8) in Group B (control group), with a p-value of 0.452, suggesting no significant difference between the two groups. For moderate pain (VAS 4-6), 37.3% (n=25) of patients in Group A reported moderate pain, while 26.9% (n=18) of patients in Group B reported similar levels of pain, with a p-value of 0.295, indicating no significant difference. Regarding severe pain (VAS 7-10), 44.8% (n=30) of Group A patients experienced severe pain, compared to 61.2% (n=41) in Group B, with a p-value of 0.073.

Table 2. Post-Operative Pain Measurement (VAS) Comparison

| Outcome Variable	Group A (PRF) n (%)	Group B (Control) n (%)	P-value
Pain (VAS 1-10 Scale)			
1-3 (Low Pain)	12 (17.9%)	8 (11.9%)	0.452
4-6 (Moderate Pain)	25 (37.3%)	18 (26.9%)	0.295
7-10 (Severe Pain)	30 (44.8%)	41 (61.2%)	0.073
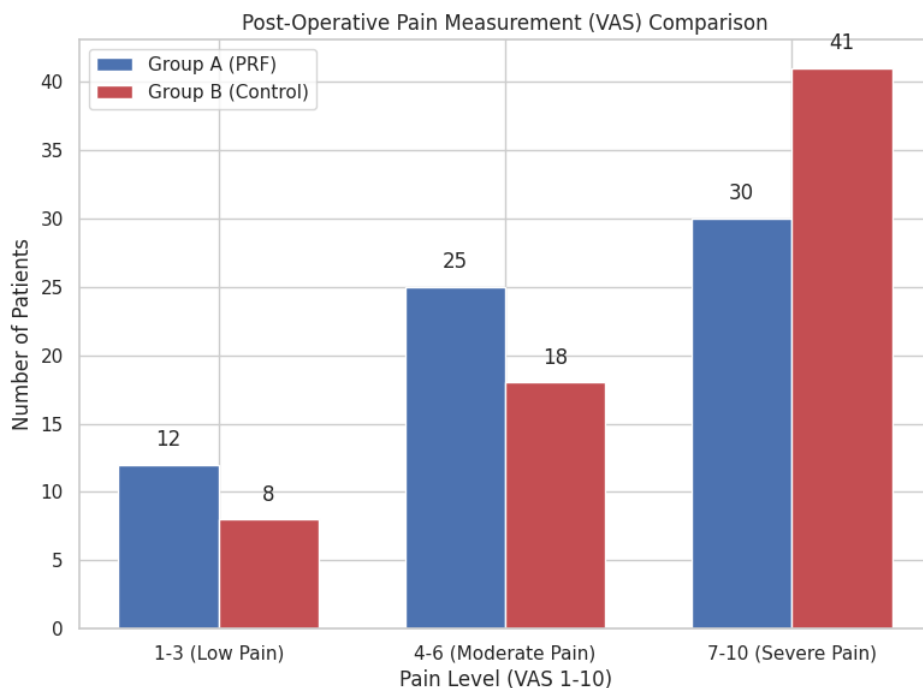
For swelling, the distance measured from the tragus of the ear to the angle of the mouth was significantly lower in Group A (PRF) at 1.5 ± 0.6 cm compared to Group B (control), which had a swelling of 2.0 ± 0.8 cm (p = 0.001). This finding indicates that PRF treatment significantly reduced swelling. Similarly, swelling measured from the lateral canthus of the eye to the

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angle of the mandible was also lower in Group A (1.4 ± 0.5 cm) compared to Group B (2.1 ± 0.7 cm), with a p-value of 0.000, further emphasizing the beneficial effect of PRF on reducing post-operative swelling.

Table 3. Swelling and Trismus Comparison

Outcome Variable	Group A (PRF) n (%)	Group B (Control) n (%)	P-value
Swelling (cm)			
From Tragus to Angle of Mouth	1.5 ± 0.6	2.0 ± 0.8	0.001
From Lateral Canthus to Angle of Mandible	1.4 ± 0.5	2.1 ± 0.7	0.000
Trismus (cm)			
Distance Between Central Incisors	3.1 ± 1.2	2.4 ± 1.0	0.045
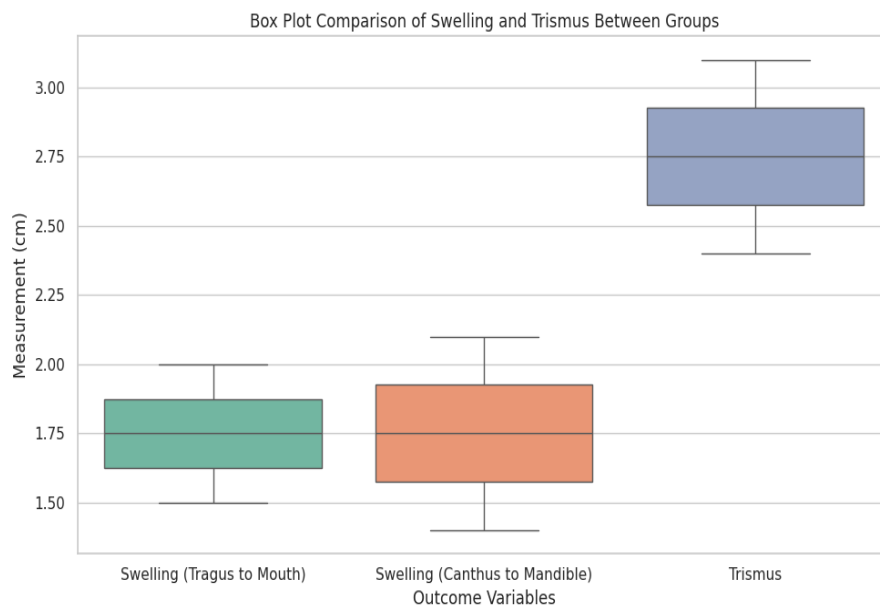
4. DISCUSSION

Surgical removal of mandibular 3rd molars is one of the most common procedures undertaken in the dental office and has a significant impact on quality of life during the post-operative recovery period. Common complications arising after wisdom teeth extraction are pain, swelling, decreased mouth opening, delayed wound healing, infections and damage to adjacent vital structures. Various studies have been conducted to identify methods to reduce postoperative discomfort ranging from administration of antibiotics, analgesics and corticosteroids both locally and systemically. Some newer studies have also supported the use of platelet concentrates to decrease severity of complications, of which, platelet rich fibrin (PRF) therapy has gained momentum for the early rehabilitation of extraction sockets. PRF is classified as a matrix with a low concentration of thrombin that provides an adequate scaffold for the migration of endothelial cells and fibroblasts [14]. It is known to expedite wound healing owing to faster neovascularisation and fibrin remodeling. The mechanisms underlying this action are due to the release of growth factors from PRF, including PDGF, VEGF and TGF-β. Advantages gained by using PRF are due to it being sourced autologously, thereby reducing the risk of foreign body reactions, infections and adverse allergic effects from other synthetic materials and drugs. Successful outcomes have been reported in many studies pertaining to PRF application in various different specialties such as bone grafting procedures, plastic surgery, dermatology and aesthetic medicine, trauma and dentistry [15].

Pain is an unpleasant sensation or discomfort experienced by the patient post-surgically. Many therapeutic agents have been directed towards its management. In our study a VAS was used to ascertain pain experienced. Our study did not report a significant difference in pain perception between the two groups [16]. Contrary to our findings, various animal studies using platelet concentrates have been successful in relieving neuropathic pain via platelet-derived IGF and VEGF owing to axonal regeneration of nerve. Another study reported direct regeneration between the distal and proximal ends of the nerve when PRP was interposed in between giving support to the fact that PRF does aid in the reduction of pain. Thirdly, a more stable

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clot formed after PRF application adequately covers the exposed nerve endings in the socket thereby further decreasing pain. Various studies concluded lesser pain postoperatively in patients with PRF use [17]. Other sequelae to surgical extractions are swelling, trismus and impaired wound healing, caused by local injury and inflammation to surrounding tissues. Surgical techniques such as traumatic extractions, improper technique and aggressive tissue retraction are all implicated in the extent of swelling and delayed wound repair. Swelling attains its maximum impact 3 days postoperatively [18]. Swelling was measured in centimeters from two sites i.e, tragus of ear to corner of mouth in the anteroposterior dimension and lateral canthus of eye to of mouth super inferiorly. In our study, patients receiving PRF fared better in terms of reduction in postoperative swelling as compared to their control counterparts. This is in part due to wound healing mechanisms. The extraction socket healing process consists of three overlapping phases: inflammation, fibroplasia, and tissue maturation. The findings related to soft tissue healing also support the potential benefits of PRF [19]. In Table 1, 100% of patients in Group A exhibited excellent soft tissue healing, compared to 80.5% in Group B, with a statistically significant difference (p = 0.0001). This improvement in soft tissue healing aligns with previous studies that have shown PRF to enhance wound healing by promoting fibroblast proliferation and collagen formation. The formation of a fibrin matrix in the PRF clot provides a scaffold for tissue regeneration and cellular migration, which is essential for optimal wound healing after surgical procedures [20]. The absence of soft tissue healing issues in the PRF group also suggests that PRF may help minimize the risks of complications such as delayed wound healing and infection, which are common concerns after impacted molar extractions. Although pain levels were lower in the PRF group, the difference was not statistically significant. The results showed that 10.4% of patients in Group A reported pain compared to 20.8% in Group B, with a p-value of 0.096. While the trend indicates that PRF may have a potential analgesic effect, it is important to note that pain perception is subjective and multifactorial. Factors such as the surgical technique, the severity of impaction, and individual pain tolerance could have contributed to the observed differences. Moreover, the use of post-operative analgesics, such as Naproxen, could have influenced pain outcomes in both groups. Previous studies have indicated that PRF may not have a direct effect on pain reduction, but its anti-inflammatory properties could contribute to less discomfort during the healing process [21]. The lack of statistical significance in pain levels may also be attributed to the relatively low incidence of severe pain in both groups, making it harder to detect significant differences. While the results of this study are promising, several limitations should be considered. First, the sample size of 134 patients may not be large enough to detect small differences in pain scores between the groups. Further studies with larger sample sizes are needed to confirm the effects of PRF on pain management. Additionally, the study focused on short-term outcomes, with follow-up limited to 7 days post-surgery. Longer follow-up periods would provide more comprehensive data on the long-term healing process, potential complications, and the stability of the observed benefits of PRF. Another limitation is the lack of objective biomarkers for healing and inflammation, such as serum levels of C-reactive protein (CRP) or interleukins, which could provide additional insight into the biological mechanisms behind the observed improvements in healing.

5. CONCLUSION

It is concluded that the use of autologous platelet-rich fibrin (PRF) following the extraction of impacted mandibular third molars significantly improve post-operative outcomes. Specifically, PRF treatment was associated with a marked reduction in post-operative swelling and enhanced soft tissue healing. Although there was no statistically significant difference in post-operative pain levels, the trend towards lower pain in the PRF group suggests that it may have an analgesic effect.

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