REVIEW ARTICLE

Impact of Platelet-rich Plasma and Platelet-rich Fibrin in Mandibular Third Molar Extraction: A Systematic Review

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Abstract

Aim: This study aims to evaluate the impact of platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) on pain, swelling, trismus, soft tissue healing and bone regeneration following mandibular third molar extraction.

Material and methods: A systematic review was conducted from a period of January 2014 to June 2024 using PRISMA guidelines. The search strategy included databases such as Scopus, PubMed, Google Scholar, and Cochrane Central Register of Controlled Trials, using key terms related to "PRF", "PRP", oral surgery, and third molars. PICO criteria followed were - Patient and population (P): Patient with mandibular third molar impacted tooth. Intervention (I): PRF; Comparator or control group (C): PRP; Outcomes (O): Impact on pain, swelling, trismus, soft tissue healing and bone regeneration following mandibular third molar extraction. National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool was also employed. Data was extracted and analyzed.

Results: Six articles met the inclusion criteria. Both materials showed potential in promoting bone and soft tissue regeneration. Out of which 1 was a split-mouth prospective clinical study, 3 were split-mouth comparative study, 2 were unilateral randomized comparative prospective study. While four studies showed a significant improvement in the soft tissue wound healing and increase in bone density in PRF site comparatively, two studies showed no significant difference between PRF and PRP with regard to pain, trismus, swelling and bone formation in the third molar extraction socket region after the placement. Based on NHLBI quality assessment tool, all the studies scored predominantly one, and hence were found good.

Conclusion: Both "PRF" and "PRP" positively influence healing after mandibular third molar extraction. Platelet-rich fibrin offers an advantage due to its ease of preparation and complete autologous nature.

Clinical significance: The impacted third molars created a variety of problems and required their extraction. Because mandibular third molars have denser cortical bone, they are more likely to experience postoperative complications. Successful surgical extraction typically occurs between ages 24 and 30, but outcomes vary based on several factors, including operator experience and patient characteristics. Recent advancements emphasize the role of oxygen and growth factors in wound healing, particularly "PRP" and "PRF".

Keywords: Bone regeneration, Extraction, Mandibular third molar, Platelet-rich fibrin, Platelet-rich plasma, Tissue healing.

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Introduction

Impaction is a pathological condition, that occurs when a tooth fails to erupt in its natural position in the oral cavity. Impacted third molars are common during standard dental operations. Wisdom teeth, or third molars, are present in approximately 90% of people, with about one-third experiencing at least one impacted molar. These impacted teeth can lead to problems such as cysts, decay on nearby teeth, and frequent pericoronitis. Third molar extractions offer a unique opportunity to study bone healing, with insights that can be applied to other parts of the jaw in clinical practice. This makes the procedure an excellent opportunity for researchers to examine various aspects like pain management, flap techniques, and the wound healing process.[1]

In efforts to enhance healing, reconstructive and regenerative surgeons have focused on bone regeneration. Effective bone regeneration is crucial for dental implants, maxillofacial reconstruction, and other oral and maxillofacial surgeries. Various bone-regenerating techniques use graft materials and barrier membranes. Additionally, several pharmacological and non-pharmacological methods are employed to reduce healing time after lower wisdom tooth extraction.[2]

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Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have gained popularity for their potential to accelerate healing. Platelets are not just involved in hemostasis; they also secrete key growth factors that promote cell division, collagen production, cellular recruitment, vascular growth, and differentiation, all of which are crucial for wound healing. Platelet-rich plasma, which has a high concentration of platelets, is used to enhance natural healing and improve tissue regeneration in periodontics, dental implantology, and orthopedic surgery. Platelet-rich plasma, when combined with autogenous bone, has shown to significantly improve bone healing and density.[3]

Platelet-rich fibrin, a second-generation platelet concentrate, differs from "PRP" in that it requires simpler preparation without biochemical processing, making it fully autologous. Platelet-rich fibrin is composed of leukocytes, cytokines, structural glycoproteins, and growth factors in a dense fibrin network, which is crucial for wound healing. It is widely used in dental and maxillofacial surgeries for bone defect restoration, post-extraction socket filling, and other regenerative procedures.[4]

Both "PRP" and "PRF" are biocompatible and biodegradable, reducing the risk of allergic reactions. Very limited data is available on the comparison between these two in the regeneration of bones. Hence, the present systematic review was carried out to assess the impact of "PRF" and "PRP" on the regeneration of bone, soft tissue healing, trismus and the reduction of pain and swelling ensuing mandibular third molar extraction.

Materials and Methods

The Original research was conducted using PRISMA guidelines from a period of January 2014 to June 2024 with Prospero registration number CRD42024580199 (Flowchart 1). The focused research question of the present study was, is the efficacy of "PRF" better than that of "PRP" when used in post extraction sockets of Mandibular 3rd Molars? The databases Scopus, PubMed, Google Scholar, Cochrane Central Register of Controlled Trials, and other relevant journals were searched electronically using the key terms-platelet-rich fibrin, PRP, oral surgery, and third molar. PICO criteria followed were- Patient and population (P): Patient with mandibular third molar impacted tooth. Intervention (I): PRF; Comparator or control group (C): PRP; Outcomes (O): Impact on pain, swelling, trismus, soft tissue healing and bone regeneration (Table 1).

Eligibility Criteria

All randomized clinical trials (RCTs) and controlled clinical trials (CCTs) conducted in the English language that compared the effectiveness of "PRF" injection against "PRP" in recently removed mandibular third molar sockets fulfilled the inclusion criteria.

Animal studies, case reports, case series, and non-English case studies were not taken into consideration. Studies employing "PRF" or "PRP" alone as a socket filler and those evaluating the use of "PRF" in extraction sockets for teeth other than mandibular third molars were excluded.

The present review used the inclusion criteria after conducting an impartial examination of the complete articles. The manual search for pertinent articles that may have been missed in the electronic database was conducted using the references of the included articles.

Using an Excel spreadsheet, the two reviewers separately extracted the data. Discussion was used to settle any disputes. Each of the chosen studies' data was collected and entered the spreadsheet: the data that were retrieved from the selected articles were study design, total sample size, test and control group, mean age and gender, impact on pain, swelling, trismus, soft tissue healing and bone regeneration after the extraction and placement of the factors, results and observations.

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Conflict of interest: None

Quality Assessment of the Selected Articles

National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool was employed for quality assessment of the selected articles (Table 2). Scores of 1 (Yes), 2 (No), or 3 (NA) were assigned based on responses to questions such as the clarity of the research question, sample size rationale, appropriateness of controls, consistency of definitions and criteria, random selection of participants, and the presence of potential confounding factors. Each article was ultimately classified as having good, fair, or poor quality based on the results of this assessment.

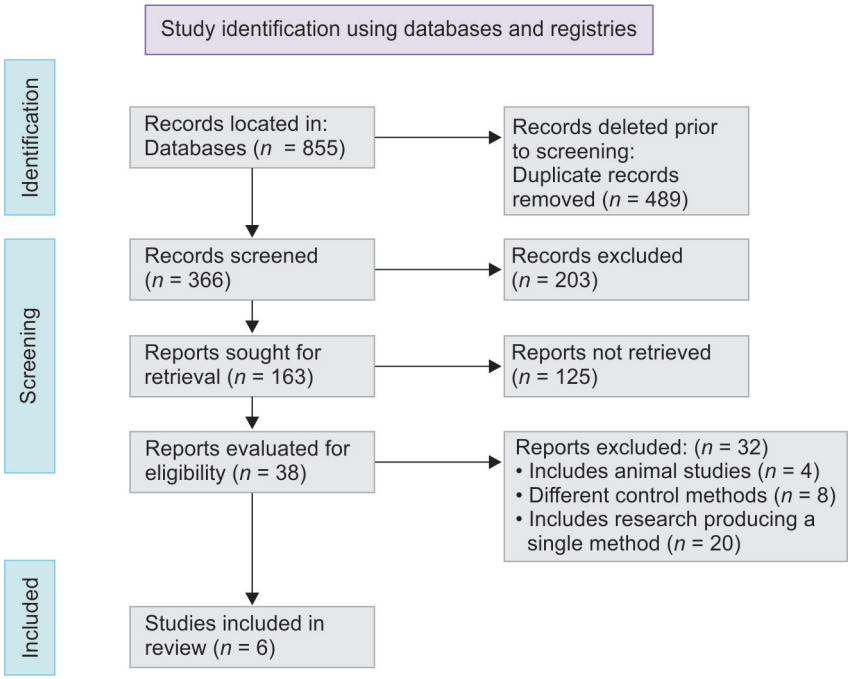
Results

Total of 855 articles were identified from the databases. Only 366 articles were screened after 489 duplicate articles were excluded after titles and abstracts were examined. Due to lack of relevance, 203 articles were removed. Out of 163 articles, 125 articles could not be retrieved. The remaining 38 publications were reviewed for eligibility, of 32 articles were excluded as 4 were animal studies, 8 included different control methods and 20 considered a single approach alone. Finally, six articles were selected for the present systematic review.[3–9]

Out of the 6 articles, 1 was a split-mouth prospective clinical study, 3 were split-mouth comparative study, 2 were unilateral randomized comparative prospective study.[3–8] Of the six studies, the minimal sample size was 15, while the maximum sample size considered was 60.[3,8] For pain, trismus and swelling, the maximum follow-up period ranged from 7 to 14 days while the bone changes were up to a maximum of 6 months. While only 3 studies evaluated pain and considered the VAS scale, swelling was measured in three studies, trismus in one study alone by vernier caliper, 4 studies evaluated soft tissue swelling.[3,4,6–8] On the contrary, all studies evaluated bone changes. Out of six studies, four studies showed PRF is significantly better at promoting soft tissue healing and also faster bone regeneration after third molar extraction in comparison with PRP.[4–6,8] Two studies showed that in the cases treated with PRP and PRF there was an obvious improvement in the pain, swelling, healing of soft tissue, and bone development.[3,7]

The complete reduction of pain was found in Unakalkar et al.[3] study, in Bhujbal et al.[4] study PRF group showed a complete reduction of pain, but postoperative pain in the Dutta et al.[7] study showed the PRF group was 0.1 ± 0.03 PRP group was 0.3 ± 0.03 at the end of 14 days. Swelling was measured in three studies, The maximum changes in swelling were found in Unakalkar et al.[3] (Baseline: PRF group – 97.27 ± 1.71, PRP group – 97.27 ± 1.87 after 14th day PRF group – 90.07 ± 1.75, PRP group – 90.13 ± 1.72) and Dutta et al.[7] (PRF group – 3.9 ± 0.23, PRP group – 4.2 ± 0.41 after 14th day: PRF group – 0.4 ± 0.16 PRP group – 0.2 ± 0.13) studies. Trismus was evaluated by Unakalkar et al.[3] study using a vernier

Flowchart 1: PRISMA flowchart for the present study



caliper, and changes were found from PRF group – 36.53 ± 1.88, PRP group – 37.2 ± 1.26 to PRF group – 41.53 ± 1.64 PRP group – 41.53 ± 1.64. Out of six studies, four studies (Bhujbal et al.,[4] Amol NV et al.,[5] Yelamali T and Saikrishna,[6] Satish and Baliga)[8] showed PRF is significantly better for faster bone regeneration of bone after third molar extraction, in comparison with PRP.

A total of 12 factors were evaluated in the NHLBI quality assessment tool. Out of 12 factors, 10 factors found a positive response in all the six studies (Unakalkar et al.,[3] Bhujbal et al.,[4] Yelamali and Saikrishna,[6] Doiphode et al.,[10] Dutta et al.,[7] and Satish and Baliga).[8] But two factors found negative response in all the six studies. Hence, all the six articles predominantly fared good.

Discussion

Platelet-rich plasma and platelet-rich fibrin have gained popularity for their potential to accelerate healing. Platelet-rich plasma, a first-generation platelet concentrate, has been utilized to treat a variety of disorders in specialties such as dermatology, orthopedics, and dentistry. Platelet-rich plasma (PRP) includes a high level of growth factors, which have a high development potential and promote faster healing, hence it is becoming popular in regenerative medicine due to the easy availability of growth factors, which simply require extracting blood.[3] Platelet-rich fibrin, a second-generation platelet concentrate, was created to remove anticoagulants to reduce the risk of hypersensitivity reactions and to improve growth factor release. Separating blood layers prior to clotting necessitates a quick and efficient centrifugation operation. The platelet-rich layer forms a fibrin matrix, which binds platelets and leukocytes.[4]

Unakalkar et al.[3] and Bhujbal et al.[4] studies observed no significant difference between "PRP" and "PRF" in managing pain during the first week post-extraction. These findings suggest that both "PRP" and "PRF" can effectively reduce postoperative pain to a similar extent. In contrast, Dutta et al.[7] study found that "PRF" resulted in significantly less postoperative pain compared to "PRP". The difference in outcomes may be due to the prolonged release of growth factors from "PRF", which might provide sustained pain relief. The fibrin matrix in "PRF" also potentially creates a more stable clot, which could further reduce postoperative discomfort. Trybek et al.[9] this study focused solely on "PRF" and demonstrated significantly lower pain scores in the "PRF" group compared to the control group at various time points post-surgery.

Unakalkar et al.[3] and Bhujbal et al.[4] studies found that "PRP" and "PRF" are equally effective in reducing swelling following surgery. The lack of difference might suggest that the initial anti-inflammatory effects provided by both "PRP" and "PRF" are sufficient to control postoperative edema similarly. Dutta et al.[7] reported that "PRF" was more effective than "PRP" in reducing swelling. This could be due to the better clot stabilization and prolonged release of growth factors with "PRF", which may help reduce inflammation over a longer period.

Unakalkar et al.[3] study found no significant difference between "PRP" and "PRF" in terms of trismus. This outcome suggests that the ability of both treatments to reduce muscle spasm or inflammation around the surgical site is similar. Trybek et al.[9] found a noteworthy decrease in trismus in the "PRF" group vs to the control group. Because "PRF" may have anti-inflammatory qualities, this suggests that it might be helpful in lowering trismus after extraction.

Bhujbal et al.,[4] Yelamali and Saikrishna,[6] Doiphode et al.,[10] Dutta et al.,[7] and Satish and Baliga[8] studies consistently found that "PRF" promotes superior soft tissue healing compared to "PRP". The fibrin matrix in "PRF" supports cell migration and proliferation, creating a more conducive environment for tissue regeneration. The sustained release of growth factors like vascular endothelial growth factor (VEGF) from "PRF" also promotes angiogenesis, which is crucial for healing.

Afat et al.[11] study also supports the use of "PRF", highlighting its effectiveness in enhancing soft tissue healing when used alone or in combination with hydroxyapatite (HA). The combination of

Table 1: Characteristics of all included studies in the present study

Author	*Study design*	*Sample size*	*Mean age/age range and gender distribution*	*Test group*	*Control group*	*Follow-up period*	*Outcomes evaluated*					*Result*	*Conclusion*
							Pain VAS scale	*Swelling*	*Trismus Vernier calliper*	*Soft tissue healing*	*Osteo-blastic activity*		
Unakalkar et al.[3]	Split-mouth study	15 patients	18–40 years	PRF group – 15 sites	PRP group – 15 sites	Pain, trismus, swelling – 1st, 3rd, 7th, and 14th postoperative day. Bone healing - 8th and 16th week postoperative day	Baseline: PRF group – 6.33 ± 1.113 PRP group- 5.93 ± 1.280 14th day– PRF group – 0 PRP group – 0	Facial measurement with thread- Baseline: PRF group – 97.27 ± 1.71 PRP group – 97.27 ± 1.87 14th day PRF group – 90.07 ± 1.75 PRP group – 90.13 ± 1.72	Baseline: PRF group – 36.53 ± 1.88 PRP group – 37.2 ±1.26 14th day- PRF group – 41.53 ± 1.64 PRP group – 41.53 ± 1.64	–	IOPA- Baseline: PRF group – 0.933 ± 0.07 PRP group – 1.0 ± 0.103 At 16th week- PRF group – 0.95 ± 0.06 PRP group – 0.960 ± 0.09	No significant difference between both the groups over pain, swelling, trismus, periodontal health, and bone healing in the third molar extraction socket	PRF and PRP were not statistically significant for the outcomes evaluated
Bhujbal et al.[4]	A prospective split-mouth study	20 patients	M: F = 7: 13 Mean age - 22 years	PRF group – 20 sites	PRP group – 20 sites	Pain, trismus, swelling – immediate,1st, 3rd, and 7th postoperative days. Bone density - 3rd and 6th months postoperatively.	Baseline: PRF group – 1.9 ± 0.9 PRP group – 2.3 ± 0.7 After 7th day: PRF group – 0 ± 0 PRP group – 0.1 ± 0.2	Facial measurement Baseline: PRF group – 9.68 ± 0.93 PRP group – 9.68 ± 0.93 7th day: PRF group – 9.68 ± 0.93 PRP group – 9.68 ± 0.93	–	–	OPG- Baseline: PRF group – 135.16 ± 4.1 PRP group – 132.49 ± 4.36 After 6th month: PRF group – 140.57 ± 4.52 PRP group – 135.92 ± 4.34	Soft tissue healing, pain scores, swelling and bone density fared well in in PRF site.	A significant improvement in the soft tissue wound healing and increase in bone density in PRF site.
Amol NV et al.[5]	Nonrandomized clinical trial with split-mouth design	45 patients	Mean age of 36.30 ± 6.44 y (range 28–44 y). M:F = 6: 9	PRF group – 15 sites	PRP group – 15 sites	Osteoblastic activity - 9 months	–	–	–	–	Baseline:PRF group – 50.33 ± 10.25 After 9th month: PRF group – 51.33 ± 9.72	There was no significant difference in radiographic bone levels at 9 months' postsurgery ($p > 0.05$). Clinically the use of PRF in both gel and membrane form were effective.	Use of PRF significantly improved the clinical parameters in terms of probing depth and clinical attachment level

(Contd...)

Table 1: *(Contd...)*

Author	*Study design*	*Sample size*	*Mean age/age range and gender distribution*	*Test group*	*Control group*	*Follow-up period*	*Outcomes evaluated*					*Result*	*Conclusion*
							Pain VAS scale	*Swelling*	*Trismus Vernier calliper*	*Soft tissue healing*	*Osteo-blastic activity*		
Yelamali T et al.[6]	Split mouth design	20 patients	Age-group 18–28 years	PRF group – 20 sites	PRP group – 20 sites	Soft tissue healing – day 7 Bone tissue healing – 4 months post operative	–	–	–	Healing index of Landry. PRF group were significantly higher compared to PRP group. The 't' value for 1 week post operative was 4.359	Digital OPG Mean values of bone density for PRF groups were significantly higher as compared to PRP groups. The 't' value for fourth month post-operative is 4.579	The mean values of soft tissue healing and bone density for PRF group were also significantly higher as compared to PRP group	PRF is significantly better in promoting soft tissue healing and also faster regeneration of bone after third molar extraction, in comparison with PRP
Dutta et al.[7]	Randomized, controlled, parallel group study	40 patients	Age-group 17–36 years	PRF group – 20	PRP group – 20	Pain, trismus, swelling – 3rd, 7th, and 14th day. Change in bone density 1, 2, and 6 months	Baseline: PRF group – 2.4 ± 0.75 PRP group – 2.9 ± 0.91 After 14th day: PRF group – 0.1 ± 0.03 PRP group – 0.3 ± 0.03	Baseline: PRF group – 3.9 ± 0.23 PRP group – 4.2 ± 0.41 14th day: PRF group – 0.4 ± 0.16 PRP group – 0.2 ± 0.13	–	Baseline: PRF group – 2.8 ± 0.13 PRP group – 2.6 ± 0.16 After 14th day: PRF group – 4.8 ± 0.13 PRP group – 4.5 ± 0.16	Baseline: PRF group – 0.4 ± 0.16 PRP group – 1.6 ± 0.16 After 6 months: PRF group – 1.2 ± 0.13 PRP group – 0.5 ± 0.16	Pain and swelling were less on PRP and PRF site. PRP and PRF site showed better soft tissue healing. Radiographic assessment showed compara-tively lesser bone density values in PRP, PRF.	Cases treated with PRP and PRF there was obvious improvement in the pain, swelling, and healing of soft tissue.
Satish et al.[8]	Randomized, controlled, trial	60 patients	Age-group above 18 years. M:F – 36: 24	PRF group – 20	PRP group – 20	Soft tissue Swelling – 7th day. Bone changes – 3 months	–	–	–	On the 7th day mean score, PRF – 3.8 PRP – 3.5.	At the end of 3 months, the mean score of group PRF was 1.2 whereas of PRP was 1.1.	PRF showed significantly improved soft tissue healing and a faster bone healing as compared to PRP.	PRF shows better results in terms of soft tissue and bone healing as compared to PRP.

– Indicates data not available

Table 2: Quality assessment in the present study using NHLBI quality assessment tool

Sl.no.	*Factors evaluated*	*Unakalkar et al.*[3]	*Bhujbal et al.*[4]	*Amol NV et al.*[5]	*Yelamali T and Saikrishna*[6]	*Dutta et al.*[7]	*Satish and Baliga*[8]
1	Research question	1	1	1	1	1	1
2	Study's goal	1	1	1	1	1	1
3	Sample size rationale	1	1	1	1	1	1
4	Controls chosen or enlisted from the same	1	1	1	1	1	1
5	Methods for identifying or choosing cases and controls	1	1	1	1	1	1
6	Distinguish the cases from the controls with clarity	1	1	1	1	1	1
7	100% of eligible cases and/or controls were chosen	1	1	1	1	1	1
8	Concurrent controls used	1	1	1	1	1	1
9	Verify that the danger or exposure took place before the occurrence of the circumstance	1	1	1	1	1	1
10	Identical exposure/risk measurements that were well-defined, valid, dependable, and applied throughout the same time period	1	1	1	1	1	1
11	Risk/exposure assessors have blind spots regarding the participant's case or control status	2	2	2	2	2	2
12	Important possible confounding factors assessed and statistically corrected throughout the analysis process	2	2	2	2	2	2

L-"PRF" and HA could provide a synergistic effect, promoting both soft tissue and bone healing more effectively.

Bhujbal et al.,[4] Yelamali and Saikrishna,[6] Doiphode et al.,[10] Dutta et al.,[7] and Satish and Baliga[8] studies consistently show that "PRF" is more effective than "PRP" in promoting osteoblastic activity and bone healing. "PRF"'s three-dimensional fibrin network not only provides a scaffold for bone cell migration and attachment but also facilitates the sustained release of osteogenic growth factors, which enhances bone regeneration.

Afat et al.[11] the results demonstrate that L-"PRF" considerably increases bone density and quality, particularly when paired with HA. HA acts as a bone graft material that enhances the effects of L-"PRF", suggesting that combined therapies might offer superior outcomes in bone healing. Yousef et al.[12] and Rodrigues et al.[13] studies showed, overall, "PRF" shows promise for improving recovery after third molar extractions. Ye L et al.[14] and Selvam LM et al.,[15] also found A-"PRF" did significantly improve wound healing compared to the control group.

Furthermore, the current review also presented some limitations; the number of studies included for some parameter analysis was small, which might lessen the statistical power. Further research should focus on: Exploring the combined use of "PRF" with other therapeutic agents (like ozone gel) to maximize postoperative outcomes. Conducting larger-scale, multicenter trials to validate these findings across diverse patient populations. Investigating the molecular mechanisms underlying the differences in healing between "PRP" and "PRF" to develop optimized treatment protocols.

Conclusion

In conclusion, the literature consistently supports "PRF" over "PRP" in promoting better overall healing post-mandibular third molar extraction, particularly in terms of soft tissue regeneration and bone healing. PRF has superior handling properties due to its direct conversion into usable form. It has the potential to heal defects in bones. PRF is cost-effective because it does not require anticoagulants or chelating agents for preparation. This evidence provides a robust basis for clinical decision-making and optimizing patient outcomes in oral surgery.

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