

EVALUATION OF AUTOLOGOUS PLATELET RICH PLASMA AND PLATELET RICH FIBRIN IN OSSEOUS REGENERATION USING CBCT AFTER SURGICAL REMOVAL OF IMPACTED BILATERAL MANDIBULAR THIRD MOLARS: A RANDOMIZED CONTROLLED TRIAL STUDY

Dentistry

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ABSTRACT

Introduction: Platelet rich plasma (PRP) and the new generation concentrate platelet-rich fibrin (PRF), are biomaterials which are known to contain platelet-derived growth factors. These GFs can accelerate the healing, thereby shortening postoperative recovery period. **Aim:** To evaluate and compare the effectiveness of platelet rich fibrin (PRF) with that of platelet rich plasma (PRP) on soft tissue healing and bone regeneration by using CBCT in Bilateral Mandibular third molars extraction socket. **Materials And Methods:** The present prospective study was conducted on 30 patients undergoing bilateral identical mandibular third molar extraction were randomly divided into two groups. Group A- In bilateral third molar, one side was included in study group where Platelet rich plasma (PRP) was placed while other side consider as control group, where extraction was done without placement of PRP. Group B - In bilateral third molars, one side was included in study group where Platelet rich fibrin (PRF) was placed and other group consider as a control group, where extraction was done without placement of PRF. Evaluation of pain and soft tissue healing was carried out on immediate postoperative and on the 2nd day, 4th day, and 8th day. Radiological bone density was assessed on the day of extraction, on the 3rd and 6th months postoperatively. **Results:** The postoperative mean pain index score on 8th day, there was no significant difference ($p > 0.05$) between Study side of Group A (PRP) and Study side of Group B (PRF) it was observed pain index score was similar in both study group (0.46 ± 0.51). The mean values of soft tissue healing index score on 8th day post-operative, for Study side of Group B (PRF) (4.95 ± 2.43) were significantly higher as compared to Study side of Group A (PRP) (4.83 ± 2.51) and the difference was found to be of highly statistical significance ($p < 0.05$). Postoperative mean bone density at the 6th months was higher in study side Group B (PRF) (717.33 ± 35.55 HU), which was highly statistically significant ($P < 0.001$). **Conclusion:** Our results showed a significant improvement in the soft tissue wound healing and increase in bone density in study side Group B (PRF) than study side of Group A (PRP). Although the postoperative pain scores was not statistically significant among the two groups.

KEYWORDS

Platelet rich plasma, Platelet rich fibrin, Cone beam computed tomography, Impacted mandibular third molar.

INTRODUCTION

Extraction of impacted mandibular third molars is the most frequent procedure performed by oral surgeons.¹ This procedure may be associated with considerable postoperative complications including pain, trismus, edema, surgical site infection as well as alveolar osteitis.² Various material has been described in literature which is used for socket preservation, reconstruction of alveolar defect such as Bone graft and their substitutes i.e. Autograft, Allograft, Xenograft and Alloplastic material. They are osteoconductive as well as osteostimulative. Autograft are considered as Gold standard for alveolar bone preservation. some grafts are immunogenic and highly expensive which is not cost effective for lower economic patients. So, Platelet rich plasma and Platelet rich Fibrin are more advantage as they are easy to manipulation, No additives, they contain more healing factors, more stems cells and no trauma to the soft and hard tissue during surgical procedure. In current time, one of the most promising innovation in the field of surgical dentistry is use of PRF and PRP. Used alone or as an additive with other biomaterials, it accelerates the healing mechanism of soft tissue and also help in osseous regeneration. Platelets contain important growth factors that, when secreted, are responsible for increasing cell mitosis, increasing collagen production, recruiting other cells to the site of injury, initiating vascular in-growth, and inducing cell differentiation.³

PRP has become a valuable adjunct to promote healing in many procedures in dental and oral surgery. They include: ablative surgical procedures, mandibular reconstruction and surgical repair of the alveolar cleft, treatment of infrabony periodontal defects and periodontal plastic surgery, as well as procedures relating to the placement of osseointegrated implants. In such procedures, the adhesive nature of PRP facilitates the easier handling of graft material, with more predictable flap adaptation and hemostasis, and a more predictable seal than is the case with primary closure alone. PRF was first described by Choukroun et al. for specific use in Oral and Maxillofacial Surgery.⁴ PRF is nothing but a centrifuged blood that contains fibrin clot, where growth factors and cytokines are trapped in fibrin meshwork. PRF accelerates and enhanced the body's natural wound mechanisms. PRF has been extensively used during tooth avulsion or extraction, mucogingival surgery during implant

placement (particularly as surface treatment for the stimulation of osseointegration), the treatment of peri-implant bone defects (after peri-implantitis, during implantation in an insufficient bone volume or during immediate postextraction or post-avulsion implantation), the sinus lift procedures and various complex implant supported treatments.^{5,6}

According to Choukroun et al. platelet rich fibrin (PRF), an autologous fibrin Product belonging to a new generation of platelet concentrates, is a slowly and naturally polymerizing fibrin matrix in which growth factors (PDGF- β , TGF β -1, VEGF, and insulin-like growth factor-1), leukocytic cells, and their cytokines (interleukin [IL]-1 β , IL-6, IL-4, and tumor necrosis factor- β) are enmeshed. After the use of PRF as a membrane in conjunction with bone graft or alone as a fibrin matrix, the favourable effects of this agent on the soft tissue and bone healing has been demonstrated. According to reports, PRF can promote wound epithelialization, bone filling of residual cyst cavities, and bone maturation after sinus lifting operations.⁶ The stimulatory effects of fibrin sealants and platelet concentrate; alone or in combination with bone grafts, on soft tissue healing has also been well documented. However, their direct effect on bone regeneration is controversial. Following tooth extraction, a cascade of inflammatory reactions immediately begins, and the extraction socket is temporarily closed by clotting blood. Epithelial tissue proliferation and migration start within the first week and tissue integrity is quickly restored. Histological evidence of active bone formation in the extraction socket is seen as early as 2 weeks following extraction. The socket is filled with newly formed bone in about 6 months. If a clinically acceptable method existed to consistently decrease healing time, both patients and clinicians would benefit.⁷

The present study was designed to comparatively evaluate the efficacy of PRF and PRP in osseous regeneration and soft tissue healing after surgical removal of Bilateral mandibular 3rd molars and compares it with healing of extraction sockets without use of PRF.

MATERIALS AND METHODS:

Patients visiting the out-patient Department of Oral and Maxillofacial Surgery, after obtaining ethical clearance. A sample size of 30 patients

aged 18 to 45 yrs both male and female patient who were referred to our Department of Oral and Maxillofacial Surgery for impacted Bilateral third molar surgery were included in the present study and randomly divided into two Groups;

Group A: Patients having bilateral Mandibular impacted 3rd molars, where in one side of tooth socket, Platelet rich plasma (PRP) was placed while extraction of the other side was done without placement of PRP.

Group B: Patients having bilateral Mandibular impacted 3rd molars, where in one side of tooth socket, Platelet rich fibrin (PRF) was placed while extraction of the other side was done without placement of PRF. The patients were followed post operatively on 2nd, 4th, and 8th days as well as on 3rd, and 6th postoperative months.

Inclusion Criteria:-

- 1) Patient age in between 18 yrs to 45 yrs.
- 2) Patient who required bilateral mandibular third molar extraction.
- 3) Patient who is medically fit for minor surgery
- 4) Patient who gave informed consent regarding blood sample collection.
- 5) Patient who gave consent for surgical treatment and post-operative follow-up

Exclusion Criteria:-

- 1) Patient not medically fit for surgery or who did not consent for the procedure.
- 2) Medically compromised patients having history of any bleeding disorder.
- 3) Patient who unable to sustain or did not consent for the procedures.
- 4) Patient who expresses inability to come for subsequent follow ups.

After taking detailed history, patients were examined clinically and radiographically and were explained about procedure, complications and follow up period involved in the study. The patients who were willing to consent were enrolled for the study. Informed written consent was taken from each participant.

Pre-Operative Evaluation:

Radiographic evaluation (CBCT) was done for all the patients with same CBCT machine, Standardized patients position, exposure and film processing parameters.

Blood Investigation:

For all patients following investigation were carried out; CBC, Clotting Time (CT), Bleeding Time (BT), Biomarkers (HIV & HBsAg).



Fig.1: PRP Prepared

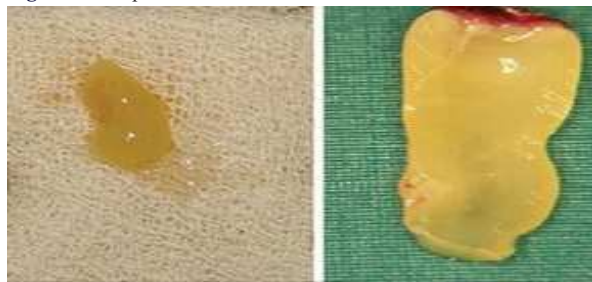


Fig.2: PRF membrane prepared

Method For Preparation Of PRP/PRF

Preparation of Platelet Rich Plasma gel (Group A) – (Fig. 1)

Under all aseptic techniques, 10 ml of blood was drawn intravenously from the antecubital region of patient's forearm using syringe (10ml). This was transferred to centrifugal vials containing 1ml of sodium

citrate (3.2%) dextrose anticoagulant. The tube were thoroughly shaken to ensure mixture of anti-coagulant with the drawn blood. The whole blood was then centrifuged at 2,400 rpm for 10 min. The supernatant formed was platelet poor plasma (PPP) and buffy coat. PPP and buffy coat [upper 1 mm red blood corpuscles (RBC)] layer was collected in a fresh tube and again centrifuged at 3,600 rpm for 10 min. The upper half of the supernatant (PPP) 80% was discarded and the lower half was mixed thoroughly to yield PRP. Activation of the PRP was done with addition of calcium chloride to form PRP gel.

Preparation of Platelet Rich Fibrin (PRF) Group B (Fig.2) :

In PRF protocol, a blood sample was taken without anticoagulant in 10 ml glass test tubes which are immediately centrifuged at 3000 rpm (approximately 400 g) for 10 minutes. The absence of anticoagulant implies the activation in a few minutes of most platelets of the blood sample in contact with the tube walls and the release of the coagulation cascades. A fibrin clot is then obtained in the middle of the tube, just between the red corpuscles at the bottom and acellular plasma at the top. The success of this technique entirely depends on the speed of blood collection and transfer to the centrifugation. Quick handling is the only way to obtain a clinically usable PRF clot. If the duration required to collect blood and launch centrifugation is delayed, failure will occur.

Surgical techniques: All the surgeries were performed by qualified and experienced Oral and Maxillofacial Surgeons under complete aseptic condition after standard painting and draping protocol. Inferior alveolar nerve block, lingual nerve block and long buccal nerve block were administered using 2 % lignocaine hydrochloride with 1: 80,000 adrenaline. Standard or modified ward's incision will be given as per the requirement with the help of 15 no. BP blade. Full thickness mucoperiosteal flap was raised to expose sufficient bone on lateral and distal aspect of the impacted molar. cautious guttering of the bone was achieved with stainless steel bur (rose head bur no -8, straight fissure burs no-701 or 702 both as per requirement) mounted on low speed micromotor (Marathon M3 spectrum clinical Micromotor, Max speed: 35,000 Rpm, Torque: 2.9N-cm) straight hand piece. Constant irrigation was done with normal saline while removing bone to prevent thermal necrosis. As per the requirement sectioning of tooth was done. Elevators and forceps were used to remove the tooth in pieces or in toto. Surrounding bone was smoothened using bone file and wound was gently irrigated with 10 ml of normal saline.



Fig.3: PRP Being Placed In The Right Third Molar Socket



Fig.4: PRF being placed in the left third molar socket

Placement of PRP/PRF: (Fig:3 & 4)

Group A - In bilateral third molar, one side was included in study group where Platelet rich plasma (PRP) was placed while other side consider as control group, where extraction was done without placement of PRP.

Group B - In bilateral third molars, one side was included in study group where Platelet rich fibrin (PRF) was placed and other group consider as a control group, where extraction was done without placement of PRF. The irregular margins of the wound were trimmed and wound was closed with interrupted sutures with 3-0 Black surgical

silk wire. Pressure pack was given.

Post-Operative Instructions:

Standard printed post operative instructions was given to the patients.
1) To keep the pressure pack for 45 minutes. 2) Avoid vigorous rinsing for 24 hours. 3) Not to have spicy, hot and hard food for 24-48 hours. 4) Warm saline rinse after 48 hours. 5) Be gentle while brushing the tooth. 6) To take the prescribed medicines as per the instructions 7) Suture removal will be done after 7 days.

Medication prescribed :

1) Cap. Amoxicilin 500mg + Potassium Clavunate 125 mg BD * 5 Days 2) Tab. Diclofenac sodium + Paracetamol BD * 5 Days 3) Tab. Ranitidine Hydrochloride 150 mg BD * 5 day

METHOD FOR ASSESSMENT OF PARAMETERS

All patients were recalled on 2nd day 4th day and 8th day for Pain and Soft tissue healing assessment, as well as on 3rd months, and 6th months for Bone density assessment postoperatively.

Pain Assessment:

Pain assessment was done by using Visual Analog Scale on 2nd, 4th, and 8th day postoperatively.

Soft Tissue Healing:

Soft tissue healing and Assessment was done with Landry, Turnbel and Howley Index on 2nd, 4th, and 8th day postoperatively.

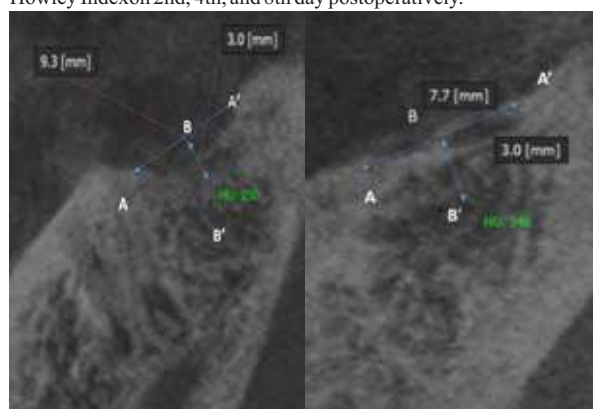


Fig.(A)

Fig.(B)

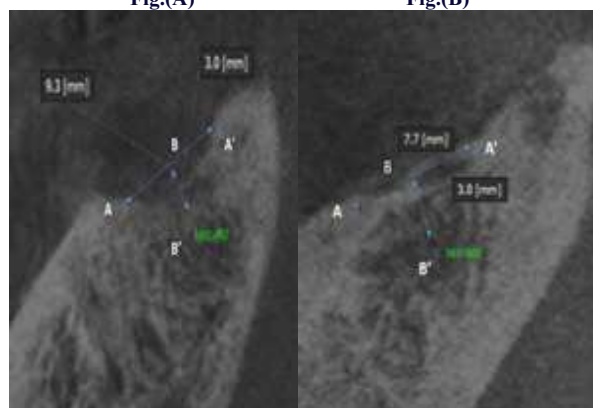


Fig.(C)

Fig.(D)

Radiographic assessment (CBCT): (Fig:5) Bone density measured on CBCT by "Hounsfield" unit on postoperative 1st day and after 6 months between Control Group of Group A (PRP) and control Group of Group B (PRF) at different time intervals

A- Bone density measured on 1st postoperative day without placement of PRP;

B- Bone density measured on 1st postoperative day without placement of PRF;

C- Bone density measured on CBCT 6th months postoperatively without placement of PRP;

D- Bone density measured on CBCT 6 months postoperatively without placement of PRF.

Radiographic Evaluation- (Fig:5)

CBCT was taken using XELIS software- ORTHOPHOS SL H 325

14.4s 85KV 6Ma. Bone density was measured by Housefield unit (HU) using CBCT. CBCT was taken immediate and post operatively, 3rd month and 6th month. Housfield unit (HU) was measure using constat reference point as below:

A = Highest point at alveolar crest just mesial to 3rd molars.

A' = Highest point at alveolar crest just distal to the 3rd molars.

B = Mid point of line drawn from A to A'.

B' = Perpendicular line upto 3mm point B'' is drawn. This point is considered as reference point to check Housfield unit (HU)

RESULTS:

The sample was composed of 30 patients were randomly divided into Group A and Group B. 12 patients were among the age group of 15-24 years, 8 patients were between the age group of 25-34 years, 10 patients were between the age group of 35-44 years. The mean age in our study Group A and B was 36 ± 9.99 and 32 ± 8.99 years, respectively. Among the 30 patients, 15 patients were male and 15 were female. Results were evaluated based on the clinical observations and radiographic analysis (CBCT).

Assessment Of Pain:

Postoperative pain was measured using Visual Analog Scale (VAS) on 2nd, 4th, and 8th day postoperatively. The pain scores were similar in both study group (0.46 ± 0.51) (Table1).

Soft Tissue Healing:

Soft tissue healing and Assessment was done with Landry, Turnbel and Howley Index on 2nd, 4th, and 8th day postoperatively. The mean healing index score on 8th post-operative day between Study side of Group A (PRP) and Study side of Group B (PRF), it was observed that healing index score was higher in Study side B (4.95 ± 2.43) as compared to Study side A (4.83 ± 2.51) and the difference was found to be of highly statistical significance ($p < 0.05$) (Table 2).

Table 1 Comparative Evaluation Of MEAN PAIN INDEX at 2nd, 4th and 8th postoperative Day Between Group A (PRP) and Group B (PRF)

MEAN PAIN INDEX									
2 nd day post-op				4 th day post-op			8 th day post-op		
	Study Group	Control Group	p-value	Study Group	Control Group	p-value	Study Group	Control Group	p-value
Group A (PRP)	6.06 (0.88)	6.2 (0.67)	0.816	4.6 (0.63)	4.4 (0.5)	0.347	0.46 (0.51)	0.4 (0.5)	0.724
Group B (PRF)	6.2 (0.67)	6.13 (0.63)	0.784	4.73 (0.59)	4.53 (0.51)	0.333	0.46 (0.51)	0.4 (0.5)	0.724
p-value	0.646			0.556			1.000		

Table 2 Comparative Evaluation Of MEAN HEALING INDEX at 2nd, 4th and 8th Postoperative Day Between Group A (PRP) And Group B (PRF)

MEAN HEALING INDEX									
	2 nd day post-op			4 th day post-op			8 th day post-op		
	Study Group	Control Group	p-value	Study Group	Control Group	p-value	Study Group	Control Group	p-value
Group A (PRP)	1.6 (0.5)	1.46 (0.51)	0.481	3.97 (1.27)	2.53 (0.51)	0.021 *	4.83 (2.51)	3.58 (1.84)	0.045 *
Group B (PRF)	1.6 (0.5)	1.46 (0.51)	0.481	4.21 (1.62)	2.53 (1.78)	0.001 **	4.95 (2.43)	3.43 (1.34)	0.007 *
p-value	0.481			0.041 *			0.031 *		

Radiographic Evaluation:

On 6th postoperative month, mean bone density score between Study side of Group A (PRP) and Study side of Group B (PRF), it was observed that bone density score was lower in study side of Group A (561.33 ± 52.35 HU) as compared to Study side of Group B (717.33 ± 35.55 HU) and the difference was found to be of highly statistical significance ($p < 0.001$) (Table 3).

Table 3 Comparative evaluation of MEAN BONE DENSITY at post operatively on the day of extraction, 3rd month and 6th month between Group A (PRP) and Group B (PRF) $p \leq 0.05$ (significant)

MEAN BONE DENSITY									
On the day of extraction				Third month		Sixth month			
	Study Group	Control Group	p- value	Study Group	Control Group	p- value	Study Group	Control Group	p- value
Group A (PRP)	449.67 (28.18)	451.47 (26.21)	0.858	498.0 (15.67)	476.33 (16.95)	0.001*	561.33 (52.35)	504.0 (28.48)	0.001*
Group B (PRF)	495.53 (27.34)	487.47 (24.93)	0.406	595.13 (41.17)	541.53 (40.94)	0.001*	717.33 (35.55)	637.33 (33.05)	0.001**
p-value	0.602			0.001**			0.001**		

DISCUSSION

Healing is a complex biological process which involves participation of many cells and growth factors. Platelet-derived growth factor have a strong chemotactic effect on osteoblasts and other connective tissue cells, and may act to recruit mesenchymal cells during bone development and remodeling. The platelets are activated by coagulation cascade, particularly thrombin and subendothelial collagen. These platelets contain several growth factors, which stimulates biological functions such as chemotaxis, angiogenesis, proliferation, differentiation, and modulation, which affects the wound healing and regeneration. The application of autologous PRP in oral and maxillofacial surgery was popularized by Marx.⁸

PRP and PRF are the autologous concentrates of platelets predominately used in oral and maxillofacial surgery and periodontology to enhance the healing process and to minimize the potential postoperative complications.⁹

Growth factors are the realistic way in enhancing soft and hard tissue healing. Since a long it has been known that the platelets are rich in certain growth factors and cytokines which are gradually released.

Platelet-derived growth factor have a strong chemotactic effect on osteoblasts and other connective tissue cells, and may act to recruit mesenchymal cells during bone development and remodeling. Insulin-like growth factors increase proliferation and play a major role in stimulating mature osteoblast function. The major effects of insulin-like growth factors (IGF) are to promote the late-stage differentiation and activity of osteoblasts. Vascular endothelial growth factors (VEGF) is the most critical mediators of angiogenesis stimulating endothelial cells Proliferation, differentiation, and vasculogenesis. VEGF plays an important role in the mobilisation and recruitment of endothelial progenitor cells (EPC), endothelial cells differentiation and proliferation as well as recruitment and survival of osteoblasts and osteoclasts.¹⁰⁻¹² Sumanth Unakalkar et al.¹³ in their prospective study we able to identify certain advantages of PRF over PRP as follows:

- No need of anticoagulant and chelating agent.
- PRF has better consistency and can be easily carried to extraction socket.
- PRF converts directly to usable form whereas PRP needs to be converted to gel form so that it can be placed inside the socket.

This prospective study evaluate the Efficacy of use of PRP as well as PRF in osseous regeneration in a fresh third molar extraction socket. Third molar extractions are often used as a measurement tool for comparing treatments because they are usually performed electively on a younger populations that do not present with multiple confounding factors (e.g. Systemic pathologies, multiple medications) therefore, this study is relevant for healthy 15 to 45 yrs old patients.

In our present study, pain was evaluated using 10 point Visual Analog scale (VAS) on 2nd, 4th and 8th postoperative day in both Group A and Group B respectively and there was no statistically significant ($P=0.646$) difference between Group A and Group B.

Accordance with study carried out by Alissa et al.¹⁴ who noticed that pain level was less in PRP side compared to control side. There was no statistical significance on 1st, 3rd, and 7th postoperative day.

Another study conducted by Abhishek Singh et al.¹⁵ who noticed that though pain was less in PRF side compared to control side there was no statistically significant difference between both sides on 1st, 3rd day and 7th day.

The measurement of soft tissue healing was done using Laundry, Turnbull and Howley¹⁶ index. Intragroup comparison of soft tissue

healing index between Study Side and Control side of Group A shows no statistical significance ($p=0.481$) on 2nd postoperative day but on 4th and 8th postoperative day difference was found to be highly statistical significance ($p<0.05$). this data was in accordance with Alissa et al.,¹⁴ Abhishek singh et al.¹⁵ Yelamali et al.¹⁷

On assessment of radiographic parameters bone density was measured using Hounsfield unit using CBCT XELIS software- ORTHOPHOS SL H 325 14.4s 85KV 6mA. Tannaz Shapurian et al.¹⁸ state that the Hounsfield index is a standardized and accepted scale for reporting and displaying reconstructed CT values. It is the measure of x-ray attenuation and varies according to the density of the tissues. The denser the tissue, the higher the HU number, which ranges from -1000 HU (air) to 1000 HU (dense bone). Since the values are directly related to the tissue attenuation coefficients. Hence, we undertaken Housfield unit using CBCT as a measurement tool for bone density.

On intragroup comparison of mean bone density between study side and control side of group A undertaken on the day of extraction, 3rd and 6th postoperative month shows statistical significance on the 3rd and 6th postoperative month. ($p<0.05$).

This finding is in accordance with Davis VL et al.¹⁹ who examined the effect of PRP on bone healing after removal of bilateral third molars. PRP treated sites demonstrated early and significant increased radiographic density over baseline measurements following tooth removal. They observed that it requires 6 weeks for control extraction sites to reach bone density comparable to that of PRP treated sites at week 1. Similar findings were seen in studies done by Alissa et al.¹⁴

On intragroup comparison of mean bone density between study side and control side of group B undertaken on the day of extraction, 3rd and 6th postoperative month shows statistical significance on the 3rd and 6th postoperative month. ($p<0.05$).

Baratam Srinivas et al.²⁰ evaluated bone density with use of PRF by using CBCT within the period of 24 hrs and 3rd postoperative month. He concluded that extraction sockets grafted with PRF showed statistically significant difference in wound healing and bone density whereas not much difference was seen in alveolar bone height in the two groups.

Intergroup comparison of mean bone density between study Group of Group A as well as study Group of Group B on the day of extraction, 3rd and 6th postoperative month. We concluded that no significant difference found on the day of extraction between study Group of group A and study group of group B. Highly statistical difference was found on 3rd and 6th postoperative month between study group of Group A and Group B.

Tejesh yelamali et al.¹⁷ evaluated the role of Platelet rich fibrin and Platelet rich plasma in wound healing of extracted third molar sockets. They evaluated the bone density using Gray scale values with the help of Histogram tools of adobe photoshop CS on 4th postoperative month. They concluded that the mean values of bone density for PRF groups were significantly higher as compared to PRP groups.

Malhotra A et al.²¹ concluded that PRF significantly helped in bone regeneration distal to second molar. It was also seen that use of PRF accelerated healing of bone and soft tissue distal to second molar thereby minimizing the possibility of periodontal problems seen after third molar surgery.

The advantage of our study is that it's the first study as per our knowledge which compared and evaluated osseous regeneration and soft tissue healing with first generation PRP with second generation

PRF by using CBCT after surgical removal of impacted third molar. As per this study PRF is having advantages over PRP in osseous regeneration. The sample size is determined by considering the sensitivity as the main outcome in the study. The sensitivity of diagnostic criteria is 80% and the power of study is 80%, so the required sample size was 30 and in this study 30 subjects were included.

CONCLUSION

In this present study, the results obtained from sample size of 30 patients with follow up periods of 6 months was critically evaluated & thus, concluded that PRF leads to faster osseous regeneration by quality as well as quantity at the end of 6 months than PRP.

Limitations:

Considering all the advantages of present study, still some limitations should be taken into consideration.

Firstly, the sample size was less i.e. 30 patients. Secondly, Our follow up period was up to 6th month which is of short duration. In future, greater sample size and longer duration of follow up is needed to evaluate the role of PRF and PRP in promoting osseous regeneration. However, this duration of time was adequate enough to evaluate the effects of PRF and PRP in enhancing both the hard and soft tissue healing.

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Conflicts Of Interest: There are no conflicts of interest

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