Mandibular Third Molar Extraction Wound Healing With and Without Platelet Rich Plasma: A Comparative Prospective Study

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Abstract

Aims To evaluate the efficacy of autologous platelet rich plasma (PRP) in regeneration of bone and to assess clinical compatibility of the material in mandibular third molar extraction socket.

Objective of the Study To compare the healing of mandibular third molar extraction wounds with and without PRP.
Materials and Methods Group A consists of the 30 patients where PRP will be placed in the extraction socket before closure of the socket. Group B consists of 30 patients who will be the control group where the extraction sockets will be closed without any intra socket medications. The patients would be allocated to the groups randomly.

Results Soft tissue healing was better in study site compared to control site. The result of the study shows rapid bone regeneration in the extraction socket treated with PRP when compared with the socket without PRP. Evaluation for bone blending and trabecular bone formation started earlier in PRP site compared to control, non PRP site. Also

there was less postoperative discomfort on the PRP treated side.

Conclusion Autologous PRP is biocompatible and has significant improved soft tissue healing, bone regeneration and increase in bone density in extraction sockets.

Keywords Bone density · Bone trabeculae · Mandibular third molar extraction socket · Platelet rich plasma · Soft tissue healing

Introduction

Platelet rich plasma (PRP) is a new and potentially useful adjunct in oral and maxillofacial bone reconstructive surgery. Platelets are very important in the wound healing process. They arrive quickly at the wound site and begin coagulation. They release multiple wound healing growth factors and cytokines, including platelet derived growth factor (PDGF), transforming growth factors (TGF)/ β 1 and β 2, vascular endothelial growth factor (VEGF), platelet derived endothelial cell growth factor (PDEGF), interleukin-1 (IL-1), basic fibroblast growth factor (bFGF), and platelet activating factor-4 (PAF-4). These growth factors are thought to contribute to bone regeneration and increased vascularity, vital features of a healing bone graft [1].

It is now well known that platelets have many functions beyond that of hemostasis. 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. These are all crucial steps in early wound healing. Using the concept that if a few are good, then a lot may be better, increasing the concentration of platelets at a wound may promote more

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rapid healing. It seems very logical that increasing the concentration of platelets in a bone graft, and therefore increasing the concentration of growth factors, may lead to a more rapid and denser regenerate [2].

Platelet rich plasma (PRP) was first introduced to the oral surgery community by Whitman et al. in their 1997 article entitled “Platelet Gel: An Autologous Alternative to Fibrin Glue With Applications in Oral and Maxillofacial Surgery.” The authors thought that “through activation of the platelets within the gel and the resultant release of growth factors, enhanced wound healing could be expected.” PRP enjoyed a great increase in popularity in the oral and maxillofacial surgery community after the publication of a landmark article by Marx et al. in 1998. Marx et al.’s [3] study showed that combining PRP with autogenous bone in mandibular continuity defects resulted in significantly faster radiographic maturation and a histomorphometrically denser bone regenerate. It certainly seemed as though a new age in bone grafting had begun.

Materials and Methods

The present study was undertaken at the department of oral and maxillofacial surgery, Vyas Dental College and Hospital Jodhpur, after obtaining ethical clearance. This study involved both male and female patients, who were referred to the department of oral and maxillofacial surgery for removal of mandibular 3rd molar.

Inclusion criteria:

1. Patients’ age between 18 and 50 years.
2. Patients who required mandibular 3rd molar extractions.

Exclusion criteria:

1. Patients with pericoronitis, periapical infection or lesions with respect to impacted 3rd molars.
2. Opposing traumatic occlusion or impinging upper 3rd molars.
3. Smokers, alcoholics and patients with any systemic diseases.
4. Female patients on oral contraceptives.
5. Those patients with incomplete follow up will be excluded from the study.

After obtaining the complete history, patients were examined clinically and were explained about the procedure, its complications and the follow up period involved in the study. The patients who were willing were enrolled for the study. Informed consent was taken.

Pre-operative radiographic investigation will consist of an OPG or an IOPA radiograph. Group A will consist of the patients where PRP will be placed in the extraction

socket before closure of the socket. Group B will be the control group where the extraction sockets will be closed without any intrasocket medicaments. The sample size in each group will consist of 30 patients. The patients would be allocated to the groups randomly. Patient of both the groups will be assessed on day 3, 7 and 14 for dry socket and soft tissue healing. Radiographic assessment for bone healing will be done at 3rd week, 2nd month and 4th month (Figs. 1, 2, 3).

Clinical Evaluation

- Soft tissue healing will be assessed based on the criteria given by Landry et al. [4].
- The presence or absence of dry socket will be diagnosed based on Blum’s criteria [5].
- Bone healing of the third molar socket will be assessed radiographically using an OPG. The criteria for bone healing and the scoring system will be based on a

Fig. 1 Case 1: **A** Radiograph (IOPA) at 3rd week post operatively, **B** radiograph (IOPA) at 2nd month post operatively, **C** radiograph (IOPA) at 4th month post operatively

Fig. 2 Case 2: **A** Radiograph (IOPA) at 3rd week post operatively, **B** radiograph (IOPA) at 2nd month post operatively, **C** radiograph (IOPA) at 4th month post operatively

modification of the Kelley's method as described by Olufemi et al. [6].

Evaluation of Soft Tissue Healing by Landry et al. and Gonshor [4, 7]

Healing Index 1: Very poor (has 2 or more of the following)

- Tissue color: ≥ 50 % of gingiva red
- Response to palpation: bleeding
- Granulation tissue: present
- Incision margin: not epithelialized, with loss of epithelium beyond incision margin
- Suppuration present

Healing Index 2: Poor

- Tissue color: ≥ 50 % of gingiva red
- Response to palpation: bleeding
- Granulation tissue: present
- Incision margin: not epithelialized, with connective tissue exposed

Fig. 3 Case 3: **A** Radiograph (IOPA) at 3rd week post operatively, **B** radiograph (IOPA) at 2nd month post operatively, **C** radiograph (IOPA) at 4th month post operatively

Healing Index 3: Good

- Tissue color: ≥ 25 and < 50 % of gingiva red
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed

Healing Index 4: Very good

- Tissue color: < 25 % of gingiva red
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed

Healing Index 5: Excellent

- Tissue color: all tissues pink
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed

Criteria for Dry Socket Assessment Based on Blum's Criteria [5]

1. Post operative pain in and around extraction site.

2. Partially or totally disintegrated blood clot.
3. With or without halitosis.
4. With or without necrotic debris.
5. Denuded socket.
6. Exudates or pus in the socket.

Mean Radiographic Score for Assessment of Bone Healing at Different Time Points Between Groups [6]

Lamina dura

- +2 Lamina dura essentially absent, may be present in isolated areas
- +1 Lamina dura substantially thinned, missing in some areas
- 0 Within normal limits
- 1 Portions of lamina dura thickened, milder degrees
- 2 Entire lamina dura substantially thickened

Overall density

- +2 Severe increase in radiographic density
- +1 Mild to moderate increase in radiographic density
- 0 Within normal limits
- 1 Mild to moderate decrease in radiographic density
- 2 Severe decrease in radiographic density

Trabecular pattern

- +2 All trabeculae substantially coarser
- +1 Some coarser trabeculae; milder degrees
- 0 Within normal limits
- 1 Delicate finely meshed trabeculations
- 2 Granular, nearly homogenous patterns; individual trabeculations essentially absent

Preparation of PRP Gel [8–12]

1st STEP: Collection of blood (Figs. 4, 5)

Under all aseptic techniques 5 ml of venous blood will be collected from the antecubital region. 3.6 ml of the collected blood will be placed in a vial containing 0.4 ml CPDA (Citrate Phosphate Dextrose Adenin) anticoagulant solution. The blood will be gently mixed with the anticoagulant. The vials will be thoroughly shaken to ensure mixture of anti coagulant with the drawn blood.

2nd STEP: Preparation of PRP (Figs. 6, 7, 8)

1. The tube will be placed in a lab centrifuge machine and counter balanced. The first centrifuge cycle will be done at 2,000 rpm for 15 min. The result will be separation of the whole blood into a lower red blood cell region and upper straw coloured plasma. This

Fig. 4 Drawing of blood

Fig. 5 Drawn blood in test tube

Fig. 6 Cellular layers separation after 1st spin

Fig. 7 Cellular layers separation after 2nd spin

Fig. 8 PPP layers separation after 2nd spin

plasma contains relatively low concentration of platelets (platelet poor plasma) in the uppermost region and higher concentration of platelets and WBC in the boundary layer often called as 'Buffy coat'.

2. With a micropipette the PPP and the buffy coat layer including 1 mm below the boundary layer will be collected in a sterile test tube and centrifuged at 3,000 rpm for 10 min. After the second centrifuge the upper half will be discarded and the lower half will be used as PRP.

3rd STEP: PRP GEL Preparation (Figs. 9, 10, 11, 12)

The PRP will be activated with CaCl_2 to form a PRP gel.

Results

After analysis of the data the following observations were made:

In case group there were 30 patients (males 13 and females 17). In control group also there were 30 patients

Fig. 9 PRP before activation

Fig. 10 PRP activated with CaCl_2

Fig. 11 PRP gel

(males 16 and females 14). The patients who had participated in the study were in the age range of 18–50 years, in the study group 33.83 years and in control group 35.30 years (Table 1).

Fig. 12 PRP gel placement in extraction socket

Table 1 Test statistics of age

	Mean	SD	$P > .05$	Interpretation
Case group	33.83	8.867	.604	No difference
Control group	35.30	10.590		

Results of Clinical Assessment

Clinical Assessment

Test statistic—Pearson Chi Square test

Assessment of healing index of soft tissue:

Assessment of soft tissue healing by 3rd day for case group showed a mean score of 2.50 and for control group 1.87 ($P > 0.002$). After 7th day for case group mean score was 3.53 and for control group 2.87 ($P > 0.001$). After 14th day for case group mean score was 4.53 and for control group 3.90 ($P > 0.003$) (Table 2).

Table 2 Test statistics of soft tissue healing index

	Group	Mean	SD	$P < .05$	Interpretation
Soft Tissue Healing index 3rd day	Case group	2.50	.572	.002	Difference significant
	Control group	1.87	.819		
Soft Tissue Healing index 7th day	Case group	3.53	.571	.001	Difference significant
	Control group	2.87	.819		
Soft Tissue Healing index 14th day	Case group	4.53	.571	.003	Difference significant
	Control group	3.90	.845		

Table 3 Test statistics of bone healing lamina dura

	Group	Mean	SD	$P > .05$	Interpretation
Bone healing lamina dura 3rd week	Case group	-.13	.346	.000	Difference significant
	Control group	-1.73	.450		
Bone healing lamina dura 2nd month	Case group	.87	.346	.000	Difference significant
	Control group	-.67	.606		
Bone healing lamina dura 4th month	Case group	1.87	.346	.000	Difference significant
	Control group	.33	.606		

Test statistic—Mann–Whitney U test, Wilcoxon W test, Z test.

Radiographic Assessment:

Radiographic assessment at bone healing lamina dura 3rd week for case group showed a mean score of -0.13 and for control group -1.73 ($P > 0.000$). After 2nd month for case group mean score was 0.87 and control group -0.67 ($P > 0.000$). After 4th month for case group mean score was 1.87 and control group -0.33 ($P > 0.000$) (Table 3).

Bone healing overall density 3rd week for case group showed a mean score of -0.10 and for control group -1.60 ($P > 0.000$). Bone healing overall density 2nd month for case group the mean score was -0.90 and for control group -0.67 ($P > 0.000$). Bone healing overall density 4th month for case group the mean score was 1.90 and for control group 0.27 ($P > 0.000$) (Table 4).

Bone healing trabecular pattern 3rd week for case group showed a mean score of -0.17 and for control group -1.63 ($P > 0.000$). Bone healing trabecular pattern 2nd month for case group the mean score was 0.83 and for control group -0.77 ($P > 0.000$). Bone healing trabecular pattern 4th month for case group the mean score was 1.83 and for control group -0.10 ($P > 0.000$) (Table 5).

Discussion

During the last decade, there have been several in vivo animal studies, which have used biological mediators such as polypeptide growth factors to expedite soft tissue and bony healing. It is therefore a reasonable hypothesis that increasing the concentration of platelets in bone defects

Table 4 Test statistics of bone healing overall density

	Group	Mean	SD	$P > .05$	Interpretation
Bone healing overall density 3rd week	Case group	−.10	.305	.000	Difference significant
	Control group	−1.60	.770		
Bone healing overall density 2nd month	Case group	.90	.305	.000	Difference significant
	Control group	−.67	.606		
Bone healing overall density 4th month	Case group	1.90	.305	.000	Difference significant
	Control group	.27	.640		

Table 5 Test statistics of bone healing trabecular pattern

	Group	Mean	SD	$P > .05$	Interpretation
Bone healing trabecular pattern 3rd week	Case group	−.17	.379	.000	Difference significant
	Control group	−1.63	.809		
Bone healing trabecular pattern 2nd month	Case group	.83	.379	.000	Difference significant
	Control group	−.77	.430		
Bone healing trabecular pattern 4th month	Case group	1.83	.379	.000	Difference significant
	Control group	.10	.481		

may lead to improved, faster healing and stimulate new bone formation [13].

Surgical sites enhanced with PRP have been shown to heal at two to three times that of normal surgical sites. PRP can be a great adjunct to many surgical procedures [14], and PRP accelerates wound maturity and epithelialization, hence decreased scar formation. PDGF and epidermal growth factor (EGF) are the main growth factors involved in fibroblast migration, proliferation, and collagen synthesis. Increased concentrations of these growth factors is a likely reason for the accelerated soft tissue wound healing [15].

The PRP is activated to form PRP gel thus causing degranulation of α -granules present in the platelets and releasing the growth factors. The various agents for the activation reported in literature include CaCl_2 alone, CaCl_2 plus bovine thrombin, human thrombin, autologous bone or whole blood which contains thrombin [16].

In our technique CaCl_2 alone was mixed with PRP to form an autologous platelet gel. This platelet gel was free of eliciting any antigen–antibody reaction as it was prepared from patients' own blood.

Conclusion

The study clearly indicates a definite improvement in the soft tissue healing and faster regeneration of bone after third molar surgery in cases treated with PRP as compared to the control group post operatively. This improvement in the wound healing, decrease in pain, and increase in the bone density signifies and highlights the use of PRP, certainly as a valid method in inducing and accelerating soft and hard tissue regeneration. An added benefit of PRP noted in the present study is its ability to form a biologic

gel that provided clot stability and functions as an adhesive. The procedure of PRP preparation is simple, cost effective and has demonstrated good results.

The present study was done with a follow up of 4 months, further clinical trials with longer duration follow up with larger sample size should be done to get more affirmative and conclusive result.

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