Evaluation of Role of Autologous Platelet Rich Fibrin in Wound Healing and Bone Regeneration after Mandibular Third Molar Surgery: A Prospective Study

Authors
Dr Aditya Harsh¹, Dr Bindu Bhardwaj², Dr Vikas Singh³, Dr Ruchika Tiwari⁴, Dr Rajesh Tak⁵, Dr Vidhi Verma⁶

¹,⁵,⁶Final year P.G. Resident, Department of Oral & Maxillofacial Surgery, MGDCH, Jaipur
²Professor & HOD, Department of Oral & Maxillofacial Surgery, MGDCH, Jaipur
³,⁴Professor, Department of Oral & Maxillofacial Surgery, MGDCH, Jaipur, India

Abstract
Background: Bony cavities filled with PRF showed healing in the half the time as compared to the time required for physiological healing. Thereby the aim of this study is to evaluate the role of autologous platelet rich fibrin in healing and bone regeneration in mandibular third molar extraction sockets.

Material & Methods: All the selected patients were explained about the procedure, its related complications and the follow-up period involved in the study. The study subjects were carried out in the Department of Oral And Maxillofacial Surgery, Mahatma Gandhi College and Hospital, Jaipur with bilateral impacted mandibular 3rd molars. The subjects were evaluated for pain, swelling and pocket depth on 3rd, 7th and 30th day post-operatively. Pocket depth was measured by using William’s Graduated Probe. 10-Level Visual analog scale was used to evaluate pain.

Results: Our study showed that the pain scores were measured by using VAS. There were no statistically significant differences observed between groups and swelling also statistically significant differences were observed in third days, seventh days and after one month between PRF and control side (p < 0.05). The degree of inflammation which was more on the 3rd post-PRF placement day was also significantly decreased by the after one month (P < 0.05).

Conclusion: We concluded that PRF could be used for control swelling after third molar extraction surgery. Studies with a larger sample that will need a bilateral third molar removal that will be extracted in different sessions with a longer follow-up is warranted to obtain a more statistically meaningful results with respect to bone regeneration.

Keywords: Platelet rich fibrin, impacted third molar, pain, bone regeneration, swelling.

Introduction
One of the greatest challenges of clinical research has been the development of bioactive surgical additives, which help to regulate inflammation and increase the speed of healing process.¹ Maxillofacial reconstruction, oral implants, regenerative procedures etc. are highly dependent on successful regeneration and healing. Healing in tissues is mediated by a variety of signaling proteins. Understanding of this process at
microcellular level is still not complete, but its proven fact that platelets do play an important role in wound healing.

Platelet rich fibrin (PRF) was first developed by a French Doctor Joseph Choukron for specific use in oral and maxillofacial surgery. PRF is an immune and platelet concentrate collecting on a single fibrin membrane, containing all the constituents of a blood favorable for healing and immunity.  

Three key factors in healing and soft tissue maturation are angiogenesis, immunity and epithelial cover. PRF is able to simultaneously support the development of these three phenomena. PRF also imparts the desirable additive features of a pliable, suitable fibrin mesh. Bony cavities filled with PRF showed healing in the half the time as compared to the time required for physiological healing. Very few studies have been done which authenticate the role of PRF in accelerating the rate of bone formation in extraction sockets. Thereby the aim of this study is to evaluate the role of autologous platelet rich fibrin in healing and bone regeneration in mandibular third molar extraction sockets.

**Material & Methods**

The study subjects were carried out in the Department of Oral And Maxillofacial Surgery, Mahatma Gandhi College and Hospital, Jaipur with bilateral impacted mandibular 3rd molars.

**Inclusion criteria**

1. Patients aged between 18-35 years.
2. Patients requiring bilateral mandibular 3rd molar extraction. Patient is willing for the same either in one sitting or in two sitting.
3. ASA grade I

**Exclusion criteria**

1. Very difficult extraction(Pederson’s Score 7-10)
2. Patient with uncontrolled diabetes, hypertension or other systemic diseases.
3. Patient with history of bleeding disorders.
4. Patient is a smoker and alcoholic.

**Methodology**

All the selected patients were explained about the procedure, its related complications and the follow-up period involved in the study. Patient who are willing to be part of the study were enrolled and written consent were obtained from them. Prophylactic antibiotics Inj Mox 1gm and Inj Dexona 8mg followed by analgesics/anti-inflammatory for 3 days were prescribed to the patient.

Procedure was performed under local anesthesia with all the necessary aseptic precautions and the side of control and test were decided randomly. 10ml of blood sample were taken without adding anti-coagulants in 10ml sterile test tubes and was centrifuged immediately at 3000 rpm for 10mins. After processing, 3 distinct sample layers was seen as mentioned below

- PRP : the uppermost layer representing acellular plasma
- PRF: platelets trapped in the fibrin meshes forming intermediate layer.
- RBCs: will be at the bottom.

The surgical procedure was consist of an incision, reflection of the mucoperiosteum, minimal bone removal with bur and hand piece under copious normal saline irrigation, tooth sectioning (if required), elevation of the impacted tooth, debridement of wound. PRF clot obtained were placed in one of the socket and primary closure were achieved using 3-0 BBS in both the sockets.

The subjects were evaluated for pain, swelling and pocket depth on 3rd, 7th and 30th day post-operatively. Pocket depth was measured by using William’s Graduated Probe. 10-Level Visual analog scale was used to evaluate pain.

**Results**

Our study showed that the pain scores were measured by using VAS. There were no statistically significant differences observed between groups (table 1) and swelling also statistically significant differences were observed in third days, seventh days and after one month between PRF and control side (p < 0.05)
(Table 2). The degree of inflammation which was more on the 3rd post-PRF placement day was also significantly decreased by the after one month ($P < 0.05$).

**Table 1:** Results of Postoperative pain

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PRF Side</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd postoperative day</td>
<td>26.4±30.36</td>
<td>25.50±29.95</td>
<td>0.296</td>
</tr>
<tr>
<td>7th postoperative day</td>
<td>9.41±16.57</td>
<td>10.21±19.75</td>
<td>0.503</td>
</tr>
<tr>
<td>30th postoperative day</td>
<td>6.32±8.20</td>
<td>5.27±2.33</td>
<td>0.06</td>
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</tbody>
</table>

**Table 2:** Results of Swelling

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PRF Side</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd postoperative day</td>
<td>4.62±6.42</td>
<td>3.42±6.55</td>
<td>0.042</td>
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<tr>
<td>7th postoperative day</td>
<td>1.28±3.95</td>
<td>0.82±3.81</td>
<td>0.040</td>
</tr>
<tr>
<td>30th postoperative day</td>
<td>0.76±1.81</td>
<td>0.55±1.21</td>
<td>0.045</td>
</tr>
</tbody>
</table>

**Table 3:** Wound Healing

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PRF Side</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd postoperative day</td>
<td>1.25±0.57</td>
<td>1.03±0.17</td>
<td>0.187</td>
</tr>
<tr>
<td>7th postoperative day</td>
<td>0.98±0.43</td>
<td>0.85±0.11</td>
<td>0.623</td>
</tr>
<tr>
<td>30th postoperative day</td>
<td>0.78±0.57</td>
<td>0.38±0.08</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Discussion**

The surgical removal of impacted third molars cause trauma of the soft tissue and bony structures in the oral cavity. The postoperative signs and symptoms of pain, edema and limited mouth opening due to muscle spasm might occur.\(^3,4\)

PRF described by Choukrouns is prepared naturally without addition of thrombin, and it is hypothesized that PRF has a natural fibrin framework and can protect growth factors from proteolysis.\(^5\) PRF releases high quantities of three main growth factors transforming growth factor \(\beta\)-1 (TGF beta-1), platelet-derived growth factor AB (PDGF-AB), vascular endothelial growth factor (VEGF), and an important coagulation matricellular glycoprotein (thrombospondin-1, TSP-1) during 7 days. Apart from these PRF also secrete EGF, FGF, and three important proinflammatory cytokines- IL-1b, IL-6, and TNF-\(\alpha\) which obtained with a simple centrifugation procedure, to stimulate several biological functions such as chemotaxis, angiogenesis, proliferation, differentiation, modulation, thereby representing a possible therapeutic device for a more rapid and effective regeneration of hard and soft tissues\(^6,7\). Platelets also play a role in host defense mechanisms at the wound site, by delivering signaling peptides which attract macrophage cells. Platelet concentrates may contain small amounts of leukocytes that synthesize interleukins involved in the non-specific immune reaction\(^8\).

Recently some studies evaluated the effect of platelet rich plasma (PRP) to the extraction sockets healing and postoperative complications\(^9,10\). Several studies showing animal experiments and clinical trials showed that PRF might affect the regeneration of soft and hard tissue, healing and reduce the side effects\(^8,11\).

Mozatti et al\(^9\) evaluated that the effects of PRP on inflammation process, wound healing, pain and swelling after third molar extraction. They reported that PRP was more effective on wound healing in the extraction socket. Our results supported that PRF was more effective on the swelling in the third day after third molar surgery. Alissa et al\(^10\) evaluated the influence of PRP on healing of extraction sockets. They reported that PRP may have some benefits in reducing complications such as alveolar osteitis, swelling, pain and improving healing of soft tissue.

Kumar et al\(^7\) investigated the effect of platelet-rich fibrin (PRF) on postoperative pain, swelling, trismus, periodontal healing they concluded that case group had less pain, swelling, and trismus on the first postoperative day compared with the control group. Their results also showed increased and faster periodontal healing in the case group.

The present study found no significant difference between PRF and control sides in terms of pain which is similar to Singh et al\(^6\), but different from Kumar et al\(^7\) study where the control and PRF groups consisted of different patients. As the results of the study the null hypothesis was partially rejected since there was no positive effect of PRF seen on the pain.

There are some limits to our study; the present study was conducted on bilaterally removed third molars at the same session the results of pain might have been influenced by the control side.
Conclusion
We concluded that PRF could be used for control swelling after third molar extraction surgery. Studies with a larger sample that will need a bilateral third molar removal that will be extracted in different sessions with a longer follow-up is warranted to obtain a more statistically meaningful results with respect to bone regeneration.

References