Platelet rich plasma effect on tissue healing after mandibular third molar surgery

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ABSTRACT

The purpose of this investigation was to assess the effect of platelet rich plasma (PRP) on soft tissue healing after mandibular third molar surgery. In this semi-blinded clinical trial study, 30 patients requiring surgical extraction of soft tissue impacted mandibular third molar and who indicated a willingness to return for recall visits were recruited. Patients were divided into test and control groups. In the test group, PRP was placed in the extracted socket, whereas the control group had no PRP. The mean postoperative pain score (Visual Analog Scale) and the amount of wound dehiscence were lower for the test group and it was statistically significant. Although the mean bleeding time was lower in the test group, this difference was not significant. The dry socket incidence and the mean intrinsical mouth opening were not significant between both groups. The PRP in the test group reduced pain and better soft tissue healing compared with in the control group. This study showed that topical application of PRP had a beneficial effect in enhancing socket healing after third molar surgery.

Keywords: Platelet rich plasma (PRP), impacted the third molar, wound healing
INTRODUCTION
Research in dental and oral surgery often contains materials and procedures which are capable of recovering clinical outcomes in terms of percentages of progress. This research describes the PRP biological mechanism of function, the in-office method for attracting PRP, its application and expected materials in procedures such as implant placement, periodontal bone and soft tissue surgery, sinus lifts, jaw reconstructions, soft tissue facial augmentations, and facial cosmetic surgeries. Platelet rich plasma (PRP) is an autologous blood derived production that has an increased concentration of platelets that are rich in growth factors and has the potential to enhance the healing of tissue at the cellular level via the recruitment, proliferation, and differentiation of cells involved in tissue regeneration [1]. Platelet rich plasma is defined as a portion of the plasma fraction of autologous blood having a platelet concentration above baseline [2, 3]. It contains a high level of platelets and a full complement of clotting and growth factors [2]. In addition to use in the treatment of chronic skin and soft tissue ulcerations [9-11], last study showed that the use of PRP in periodontal and oral surgery [10], maxillofacial surgery [9, 4] orthopedic and trauma surgery [5,12,13].

MECHANISM OF PLATELET-RICH PLASMA ACTION
PRP gel contains a high concentration of platelets and a local concentration of fibrinogen [2, 3]. In the course of wound healing, platelets are the first cells to react at a wound site, being critical to the initiation of this process. Also, platelets are a rich source of important growth factors, such as platelet derived growth factor (PDGF), transforming growth factor-b (TGF-b), and vascular endothelial growth factor (VEGF); all of them involved in the angiogenic cascade which assists in hard and soft tissues wound healing [3, 4, 16]. PRP may control cytokine release and inflammation, interacting with macrophages to progress tissue healing and regeneration [24], advancement of new capillary growth [6, 25], and epithelialization in chronic wounds [18]. Platelets in PRP also play an important role in host protection mechanism at the wound site. In a two-stage process, whole blood from the patient is centrifuged to break up the plasma from packed red blood cells and then further centrifuged to break up PRP from platelet poor plasma [27]. The obtained fraction then activated with the addition of thrombin or calcium [24,28], resulting in a gelatinous platelet gel [28].

Tooth extraction is a prevalent dental method which initiates severely rotten, periodontally affected, not restorable or impacted teeth. These
methods would be related to considerable postoperative pain, exclusively when third impacted molars are extracted. Also, protracted bleeding can be experienced by patients, particularly by those undergoing anticoagulant therapy [29]. The purpose of this investigation was to assess the effect of platelet rich plasma (PRP) on soft tissue healing after mandibular third molar surgery.

MATERIALS AND METHODS
This study had been conducted in the Department of Oral Surgery in Azad University of Esfahan (Khorasan), between July 24 and August 9 on 2016, which blood samples were collected from 30 healthy donors (similar in terms of age and sex) aged from 19 to 38 years (35 ± 10 years). All healthy people with bilateral mandibular third molar impactions were included in the study. Elected patients were screened for any infection in the region of lower third molars, any somatic diseases, oral habits, allergy or hypersensitivity to local anesthetics. Platelet counting checked to ascertain its normal [31]. PRP was produced by serial centrifugation of pristine autologous blood, generating plasma with an approximately threefold increase in the condensation of spotless platelets.

GROUP 1: The socket in which platele rich plasma was placed after surgical removal of impacted teeth.
GROUP 2: Socket without platelet rich plasma.
In both groups, the patients were summoned on seventh-day postoperatively to assess wound healing. The clinical evaluations were included the measurement of the probing depth distal to the third molar preoperatively, 7 days postoperatively. For clinical evaluations certain landmarks were used. In both groups, the elicitation socket was estimated. In the 7th postoperative day for any wound dehiscence. The clinical evaluation contained the comparison of the probing depth distal to the third molar preoperatively, 7 days postoperatively. The consideration for wound dehiscence was recorded.

Method of Preparation of PRP gel
Blood Sampling
Under all antiseptic situations, 16 ml of blood was withdrawn from the antecubital region of the patient lower arm using vacationer needle and vacationers containing 4 ml of anti-coagulant Citrate Phosphate Dextrose Adenine (CPDA).

Preparation of cPRP
The vacationers were thoroughly shaken to vouch for phlegm of anti-coagulant with the drawn blood. All the tubes were located in the centrifuge machine (Digital Centrifugation Machine REMI Motors Ltd.) which was counterbalanced. The first centrifuge cycle was done at 1200 rpm for 10 min. The result obtained from differentiation of the whole blood into a lower red blood cell zone and upper straw-colored plasma (The obtained supernatant is PRP). This plasma includes the relatively low concentration of platelets (platelet poor plasma) in the upper region, Buffy coat (higher condensation of platelet in the border) and upper is collected in a fresh vacationer after second centrifugation. The tubes were located in a rack with their top uncovered and measurement of growth factor levels.

**PRP gel Preparation**

6 ml of PRP and 1 ml of thrombin at 370°C for 3 min leads to the formation of PRP gel. The PRP samples were stored in Eppendorf tubes at 78°C. All the patients were measured for pain and swelling on the 7th postoperative day. Visual Analogue Scale (VAS) was used as a subjective method to measure the pain. All the impacted teeth were removed surgically by an alone operator under local anesthesia. PRP gel was located in the experimental extraction site before closure of the lesion. All the patients were measured for pain and swelling on the 7th postoperative day. VAS was used as a subjective method to measure the pain [31].

**Statistical Analysis**

All quantitative mensuration have been explained using summary statistics (n, mean, and standard deviation, median, minimum, maximum, and other counties) for statistical significance using student t-test.

**RESULTS**

The results were analyzed based on clinical observation. Following the completion of the clinical study on the patients, the mensuration and data taken from all the patients were organized for statistical studies and after the analysis of data following observation was made. There were 14 (46.7%) male patients and 16 (53.3%) female patients who participated in this study. The patients who participated in the study were about 18 to 50 years old with mean age of 38 years. Both groups were quite similar regarding sex (Table 1).
Platelet healing

Table 1. Assessment of sex differences in the two groups

<table>
<thead>
<tr>
<th>%</th>
<th>Group 2 (n=15)</th>
<th>Group 1 (n=15)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.7</td>
<td>7</td>
<td>7</td>
<td>Male</td>
</tr>
<tr>
<td>53.3</td>
<td>8</td>
<td>8</td>
<td>female</td>
</tr>
<tr>
<td>100</td>
<td>15</td>
<td>15</td>
<td>sum</td>
</tr>
</tbody>
</table>

Table 2. Assessment of the age of both groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=15)</th>
<th>Group 2 (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>26.3</td>
<td>25.3</td>
</tr>
<tr>
<td>SD</td>
<td>2.7</td>
<td>3.8</td>
</tr>
</tbody>
</table>

Results of Clinical Assessment

Assessment of pain was a visual analog scale of the third day showed a mean pain score of 3 in study group and 6.7 in the control group. The pain was less in the study group compared to the control group. There was statistically significant difference between the study and the control groups on the third day (P=0.005).

Table 3. Assessment of pain using VAS post-operative

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=15)</th>
<th>Group 2 (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3</td>
<td>6.7</td>
</tr>
<tr>
<td>SD</td>
<td>2</td>
<td>1.8</td>
</tr>
</tbody>
</table>
Assessment of wound dehiscence

Assessment of wound dehiscence was a visual analog scale of the 7th day showed a mean wound dehiscence score of 20 in study group and 86.7 in the control group. Wound dehiscence was less on the study group compared to control group. There was statistically significant difference between the study and control groups on the 7th day (P<0.001).

<table>
<thead>
<tr>
<th>P-value</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Statistical significant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>13</td>
<td>86.7</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Wound dehiscence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>6.7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dry socket</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Assessment of the color mucosal was a visual analog scale of the 3rd day showed a mean color maximal score of 3 in study group and 6.7 in the control group. Color mucosal was less on the study group compared to control group. There was a statistically significant difference between

<table>
<thead>
<tr>
<th>P-value</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Color tissue</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>12</td>
<td>80</td>
<td>Willing</td>
<td>3rd day after</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reddish</td>
<td>Surgery</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>20</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>6.7</td>
<td>Willing</td>
<td>7th day after</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reddish</td>
<td>Surgery</td>
</tr>
<tr>
<td>0.5</td>
<td>14</td>
<td>93.3</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>
the study and control groups on the 3rd day (P=0.001) though the pain was less in study group compared to control group. There was no statistically significant difference between the study and control groups on the 7th day (P= 0.5).

### Table 6. Assessment of the mouth opening

<table>
<thead>
<tr>
<th>P-value</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>0.77</td>
<td>27.1</td>
<td>11</td>
<td>28.3</td>
</tr>
<tr>
<td>0.36</td>
<td>36.1</td>
<td>6.5</td>
<td>38.5</td>
</tr>
<tr>
<td>0.302</td>
<td>39.7</td>
<td>4.6</td>
<td>41.9</td>
</tr>
</tbody>
</table>

**Assessment of mouth opening**

Assessment of mouth opening was a visual analog scale of the 3rd day showed a mean score of 11.7 in study group and 11 in the control group. On seventh day mouth opening was 7.5 in the control and 6.5 in the study group (P= 0.77). Mouth opening was less on the study group compared to control group. There was no statistically significant difference between the study and control groups on 7th day (P= 0.36). Assessment of level of inflammation was a visual analog scale of the 3rd day showed a mean score of 0.3 in study group and 0.2 in the control group. There was no statistically significant difference between the study and control groups on 7th day (P= 0.02).

### Table 7. Assessment of level of inflammation

<table>
<thead>
<tr>
<th>P-value</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>0.02</td>
<td>0.2</td>
<td>0.3</td>
<td>1.5</td>
</tr>
</tbody>
</table>
### Table 8. Assessment of bleeding times

<table>
<thead>
<tr>
<th>P-value</th>
<th>Group 2</th>
<th>Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>0.02</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>0.1</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**DISCUSSION**

For the first time was explained the positive effects of PRP on tissue regeneration, maxillofacial surgery and bone regenerate in 1998. Extensive application of PRP, a growing number of human clinical studies, have detailed the use of growth factors in reconstructive oral and maxillofacial surgery [34,35] periodontology [36-38], implantology [39,40], pre- prosthetic surgeries [45] sinus grafting [40] distraction osteogenesis [40,41], alveolar bone grafting [42], and plastic surgery [43]. The aim of this study is tissue reconstruction and restore tissue function after surgery. Complications of surgery can affect the patient life. Elaborated characteristics of PRP provided as: It provides adhesiveness and tensile strength for clot stabilization, is biologically acceptable to the root surface, containing important growth factors such as PDGF and TGF-b released by platelets, promotes angiogenesis, containing a dense fibrin network that is highly osteo-conductive, has hemostatic properties, improves wound healing and is an affordable treatment modality [44,45].

In the present study, the mean pain intensity, dry socket, wound dehiscence, the severity of inflammation, mouth opening, color mucus surgery were evaluated for both groups (with PRP and without PRP) on 1st, 2nd and the 7th postoperative day. Also, mean pain intensity,
wound dehiscence was less than the control group. Statistically significant in PRP group difference was seen on the 3rd postoperative day (P<0.001). Anitua reported improved epithelialization and bone density when PRP was placed in the extraction sockets [39]. All subjects of both the groups had Color mucosa, but a statistically significant intergroup difference was not seen on the 3rd postoperative day (P=0.001). In this study mean pain intensity, dry socket, wound dehiscence was assessed for both the Groups. The group I showed significant (P<0.001) decrease in mean pain intensity, dry socket, wound dehiscence than group II. Our findings were supported by Deepti Simon et al. [46]. Also, the mouth opening was evaluated for both groups. Statistically significant in PRP group difference was not seen on the 3rd postoperative day (P>0.05). We evaluated soft tissue healing and gingival attachment by measuring the wound dehiscence and bleeding time, inflammation level was measured by evaluating the alveolar bone level and bone density distal to mandibular third molar Group I (extraction socket with PRP) showed no sign of dehiscence on a 2nd postoperative day while group II showed positive sign of dehiscence. This showed a better soft tissue healing of extracting socket with PRP as compared to the socket without PRP. On the 7th day, none of the patients had wound dehiscence. Mancuso in his study also reported a decrease in alveolar osteitis; objectively faster soft tissue flap healing and less edema 7 days post-surgically in PRP-treated sockets. Marx [47,48] also supported the presence of growth factor in high concentration in PRP which is responsible for its effect in accelerating both soft and hard tissue healing.

CONCLUSION

This study was performed to measure the special efficacy of PRP in soft tissue and special efficacy regeneration distal to mandibular third molar after elimination of impacted third molar. This study attempted to use autologous PRP to promote wound healing and osseous instruction in human third molar extraction sites. It clearly demonstrates decisive recovery, in soft tissue healing and faster regeneration of bone after 3rd molar surgery in cases treated with PRP as compared to control group postoperatively. PRP is an affordable and widely accessible modality to minimize postoperative complication and enhance both hard and soft tissue healing potentials. However, this autologous product removes turbulence about immunogenic reaction and disease transmission. The advantageous outcomes of PRP in a dental clinic, including reducing in bleeding and rapid wound healing hold commitment for further methods. PRP is a new application in tissue technology and develop for clinician and researchers. The restriction of
this study was that the postoperative follow up is a short term (7 day) to get at a conclusive conclusion on the efficacy of PRP in perfect bone regeneration process, but suitable enough to appraise the effect of PRP in initiating and enhancing both hard and soft tissues healing.

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