Effect of Platelet Rich Plasma on Healing of Distracted Mandibular Segment

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Abstract

Introduction: Recent efforts to improve wound healing have focused on auto genus sources of bioactive mediators, such as platelet rich plasma (PRP), which offer the potential to enhance the bone healing, the aim of this work was to study the effect of platelet rich plasma on distraction osteogenesis.

Patients and Methods: Ten patients (7 females and 3 males), their ages ranged from 7 years to 23 years (with a mean of 14.45 years). They presented with bilateral mandibular hypoplasia. All patients were treated with bilateral mandibular distraction osteogenesis, using intra and extra-oral unidirectional distractors, platelet rich plasma was applied only at left site while the right site act as a control. The follow-up periods were 3 months, 6 month and one year using panoramic X-ray which was analyzed by special soft wares to determine the amounts of formed bone and its gray level also axial computerized tomography was used to measure bone density in Hounse field units.

Results: The gray level at the right site was 101/256±6.50 and that of left site was 108.7±7.30 with no significant difference p>.05.: The amount of formed bone at the right site was 294185 pexils±1.018, while that of the left site was 366921.5 pexils±1.70 with no significant difference p>.05 between the right and left sites. The CT density at the right site was 537.9 HU±35.32 and that of left site was 501HU±53.37 with no significant difference p>.05.

Conclusion: The platelet rich plasma has no significant role in distraction osteogenesis as regard amount of formed bone and its density.

Key Words: Distraction osteogenesis — Platelet rich plasma — Mandibular lengthening — Surgical correction of mandibular hypoplasia.

Introduction

MANDIBULAR deficiency is the most common category of dentofacial deformity, about 70% of patients with class 11 facial deformity have an associated skeletal discrepancy that’s commonly a result of a retrognathic mandible Nowadays mandibular skeletal deficiency can be corrected successfully by the mandibular distraction osteogenesis which has the potential to overcome the harzards associated with bilateral sagittal split osteotomy [1-3].

Distraction osteogenesis is the biologic process of new bone formation between bone segments gradually separated by incremental traction. This process begins when a distraction force is applied to the healing callus that joins the divided bone segments and continues as long as the tissue is stretched. Distraction osteogenesis provide higher stability with more preservation of inferior alveolar nerve than bilateral sagittal split osteotomy specially in cases required larger mandibular advancement [4,5].

Distraction force that is applied to bone also creates tension in the surrounding soft tissues, initialing a sequence of adaptive changes termed distraction histogenesis [6].

Studies had demonstrated that growth factors can stimulate bone formation and bone healing and these results encouraged many research workers to use them in maxillofacial surgical procedures [7]. Platelet-Rich Plasma (PRP) is a concentration of platelets that contains a group of growth factors proved to be actively secreted by platelets to initiate all wound healing. Many studies suggest that (PRP) play an important role in maxillofacial reconstruction because it has a favorable effect on human osteablast like cells, and acts on both enhancing bone regeneration and activating the wound healing [8,10]. Platelet-rich plasma (PRP) was used for vertical distraction of iliac bone graft used for
mandibular reconstruction and it is stated that application of (PRP) in distraction osteogenesis represents new biotechnology and still lacking a lot of research \[\text{ill.} \] Accordingly this study was designed to evaluate the efficacy of platelet-rich Plasma (PRP) on healing and consolidation of distracted bone in cases with mandibular skeletal deficiency.

**Patients and Methods**

Ten patients presented with skeletal mandibular deficiency indicated for bilateral distraction osteogenesis were included in this study. They were selected from the cases received at the Oral surgery Department, Faculty of Dentistry, Suez Canal University October 2007 to May 2011.

Patients included in this study were arranged for topical application of platelet rich plasma (PRP) in the left side of the distraction and the right side selected to be the control one. After admission to the Oral Surgery Department the selected cases of this study were arranged for general assessment and local maxillofacial examination with documentation of the finding in every patient file and including:

- Routine laboratory investigation.
- Facial appearance in posteroanterior and lateral side view.
- Mandibular micrognathia.
- Relation of the mandible to maxilla.
- Occlusion abnormality and oral hygiene.
- Study model.
- Panoramic X-ray films.
- Computerized tomography-lateral cephalometric.

**Surgical procedures:**

All cases were managed surgically under general anesthesia and the following standard principles were applied in every case:

- Flap was designed in the lower vestibule 5mm below mucogingival line extending from 1st premolar to the last molar region then mucoperiosteal flap was reflected to expose the surgical site.
- Osteotomy was designed at the predetermined site using ossilating saw simultaneously with irrigation using normal saline, steotomy designed only through the buccal cortex.
- The intraoral distractor was applied and fixed in position using miniscrews, on using extraoral distractor trocar was used to retract the cheek and penetrate it for application of the self tapping pins in their positions.

- Lingual cortex osteotomy was completed using osteotome, the distractor activated to be sure that it acts efficiently then it is returned to its original position (Fig. 1).
- The flaps were sutured under water seal with resorbable suture. All the previous steps were done on both right and left mandibular sites except that the platelets rich plasma was only applied at the left surgical site while the right site was a control one.
- After the latency period, the distractors were activated 1mm daily at the rate of 0.5mm two times a day for a variable periods according the patients requirements.
- At the end of consolidation period the distractors were removed using local anesthesia for the extraoral distractors and general anesthesia for removal of the intraoral distractors.

The platelet rich plasma was prepared after aspiration of 60mm 3 of venous blood and prepared according to standard method \[12\].

Postoperative radiographs were obtained for each patient immediately post-activation period and at 3,6,12, months. Follow-up panoramic radiographs were used to document new bone formation by digital subtraction (Fig. 2) technique (using Image J soft ware available as a public domain) also panorama used to determine the new bone gray levelusing specially designed soft ware program (Fig. 3). Axial computerized tomography was used to determine new bone density in Hounsefield unite (Fig. 4).

**Results**

Ten patients sustained bilateral mandibular hypoplasia were included in this study, the ages of the studied patients were similar and ranged from 7.5 to 23 years with mean age 14 years, seven patients were females (70%) and the rest were males (30%) these findings. Mandibular hypoplasia was developmental in nine patients (90%) and was due to facial trauma followed by ankylosis in one patient (10%). All the patients were managed surgically under general anesthesia, and intraoral distractors were used in four patients (40%) and extraoral distractors were used in six patients (60%). Latency period ranged from 4 to 9 days and the mean of latency period was 6 days with standard deviation (SD)±1.49 the activation period was ranged from 7 to 23 days and its mean was 13.9 and SD±5.36 consolidation period ranged from 45 to 60 days and the mean of latency period was 54 days with standard deviation±7.74.
The width of distraction was ranged from 5mm to 12mm and its mean was 7.9 and SD±2.23. All the previous findings were illustrated in The mean of the base line platelets count was 272100/mm3 with SD±37513.09 and the mean of platelets count in platelets rich plasma (PRP) was 1150000/mm3 and SD±74907.35, and t-value was 15.365 and there is significant difference between the two counts p<0.001.

Every patient had regained facial symmetry, normal jaw movements and good healing at both right and left sites.

Gray level results:

As regards gray level determination through analysis of panorama films, it was 87.41/256±9.57 at right site and 79.27/256±6.71 at left site immediately post distraction, with no significant differencep>.05, while at the 3rd month postoperatively, gray level was 83.49/256±12.75 at right site and 113.28±8.58 at left site with no significant differencep>.05. At the sixth month postoperatively the gray level at the right was 102.77/256±7.68 while at left site gray level was 99.21±7.91 with no significant differencep>.05. After one year post operatively the gray level at the right site was 101/256±6.50 and that of left site was 108.7±7.30 with no significant differencep>.05. As shown in (Table 1).

The results of digital subtraction:

As regards subtraction results through analysis of panorama films, it was 334870 pexils±1.190 when right site (immediately postdistraction) subtracted from right site at 3rd month post operatively (R2-R1), and results was 5915861.5 pexils±4.921 at left site (L2-L1) with no significant results between right and left sites p>.05. The subtraction results when right site (3rd h month postoperatively) subtracted from right site at 6th month postoperatively (R3-R2) was 347110 pexils±1.34 while the subtraction results at left site (L3-L2) was 417335 pexils±2.02. While the result when right site at 6th
month subtracted from the right site one year postoperatively (R4-R3) was 294185 pexils±1.018, while that of the left site (L4-L3) was 366921.5 pexils±1.70 with no significant difference p>.05 between the right and left sites (Table 2). Window of the soft-ware and the images which were distracted and the resultant subtraction image located in between, also there is window to reveal the subtraction result.

Computerized tomography density results:

As regards CT density in Hounsefield unie (HU) through analysis of computerized tomography films, it was 105.6 HU±32.59 at right site and 139.78 HU±26.49 at left site immediately post distraction, with no significant difference p>0.05, while at the 3rd month postoperatively .CT density was 353.38 HU±34.44 at right site and 366.24 HU±32.34 at left site with no significant difference p>.05. At the sixth month postoperatively the CT density at the right side was 403.12±36.34 while at left site CT density was 487.66 HU±63.27 with no significant difference p>.05. After one year post operatively the CT density at the right site was 537.9 HU±35.32 and that of left site was 501 HU±53.37 with no significant difference p>.05. as shown in (Table 3).

Table (1): Gray level of both right site (R) and left site (L) throught follow-up periods.

<table>
<thead>
<tr>
<th>Gray level of cases</th>
<th>Mean±SD</th>
<th>t-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post distraction</td>
<td>R 87.41±9.57</td>
<td>1.023</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>L 79.27±6.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 month post operative</td>
<td>R 83.49±12.75</td>
<td>2.232</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>L 113.28±8.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 month post operative</td>
<td>R 102.77±7.68</td>
<td>0.450</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>L 99.21±7.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year post operative</td>
<td>R 101.05±6.50</td>
<td>1.164</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>L 108.7±7.30</td>
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</tbody>
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Table (2): Subtraction results of both right sites (R) and left sites (L) throught follow-up periods.

<table>
<thead>
<tr>
<th>Digital subtraction in pexils</th>
<th>Mean±SD</th>
<th>t-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>R2-R1</td>
<td>334870±1,190</td>
<td>1,821</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>L2-L1</td>
<td>591586.5±4,921</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R3-R2</td>
<td>347110±1,34</td>
<td>1,758</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>L3-L2</td>
<td>417335±2,02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R4-L3</td>
<td>294185±1,018</td>
<td>1,045</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>L4-L3</td>
<td>366921.5±1,70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R1 : Right site inmediatly postdistraction.  
R2 : Right site 3rd month postoperatively.  
R3 : Right 6th month postoperatively.  
R4 : Right site one year postoperatively.  
L1 : Left site inmediatly postdistraction.  
L2 : Left site 3rd month postoperatively.  
L3 : Left site 6th month postoperatively.  
L4 : Left site one year postoperatively.

Discussion

Tissue healing and bone regeneration is one of the ultimate goals of any clinician to provide the optimum care for their patients’. Any technique or material may provide a positive effect to expedite healing should always be considered. The use of platelet-rich plasma (PRP) to enhance bone regeneration and soft tissue maturation has increased in the fields of orthopedics, maxillofacial surgery, and plastic surgery, while some authors have reported significant increases in bone formation and maturation rate [13,14] others did not observe any improvement [15,16].

Growth factors have showed the ability to promote cells proliferation and differentiation. Platelet derived growth factor (PDGF), transseforming growth factor (TFG-J3), vascular endothelial growth factor (VEGF), and platelet activating factor are highly concentrated in platelets granules. These factors have strong angiogenic, mitogenic, and capillary growth. PDGF enhances and initiate connective tissue healing and bone regeneration. TFG-J3 acts on connective tissue repair, enhances cells differentiation favoring bone formation. Both of these factors enhance bone regeneration by triggering adjacent cells, such as preosteoblast, via chemotaxis, which undergo mitosis, and also favoring their differentiation, enhancing bone remodeling, initiation and mineralization [9,17].

Platelet rich plasma contains fibrin, fibronectin and vitronectin which are known to act as cell adhesion molecules for osteoinduction and as a matrix for bone connective tissue and epithelial migration [18].

It is concluded that the use of platelet rich plasma in distraction osteogenesis seems to be effective in restoring the seyver atrophic mandible. Also PRP was used for vertical distraction of iliac bone graft used for mandibular reconstruction and
they stated that application of (PRP) in distraction Osteogenesis represent a new biotechnology and still lacking a lot of research [11,19].

Despite the theoretical benefits of the osteogenic growth factors within PRP, the results of the present study did not show a statistically significant difference in total bone formation and bone density when PRP and non PRP sites were compared by the aid of digital subtraction (for determination of bone formation) and computerized tomography with gray level detector program (for detection of bone density). These results are consistent with previous studies investigating the effect of the PRP in different maxillofacial works. Where Gurbuzer et al. [20] investigated the effect of PRP on osteoblastic activity during the healing process of impacted mandibular third molar extraction sockets by means of bone scintigraphy, and they concluded that the application of PRP alone into the extraction sockets failed to increase the osteoblastic activity in comparison to non PRP treated sockets.

Also our study was in accordance to that of Farrel et al. [21] where they found no enhanced bone formation when inferior border mandibular defects were treated with PRP, Also Aghalo et al. [22] similarly showed no benefit for the use of PRP alone in cranial defects according to radiographic and histomorphometric findings in postoperative 1st, 2nd, 3rd and 4th months.

Shanaman et al. [15] similarly concluded from histologic material obtained from three patients that PRP did not enhance the quantity or quality of bone formation for ridge augmentation.

Platelets rich plasma is not with out absolute benefits, it acts as a biological adhesive material that aids for good adaptation of the flap to the bone surface also it acts as a protective cover for the surgical site and permits good haemostasis.

It is stated that when PRP used along with bone graft it holds the bone particles together thereby making manipulation of the graft material much easier [23].

However the study of Butterfield et al. [24] failed to find a direct stimulatory effect of PRP on healing of autogenously bone grafts using computerized tomography and histomorphometric analysis.

Swelling after any surgery and subsequent fluids washout seems to be a challenging role for PRP to maintain its concentration, also periostium elevation leads to the death of the preosteoblasts in the periosteum which delay the healing. The lack of increased osteoblastic activity within the distracted gap might be simply because PRP was not osteoinductive.

Digital subtraction technique was used through this work for the study of bone formation at the distraction sites because the healing process progresses slowly, so it cannot be easily evaluated quantitatively using plane X-ray because the structural noise produces visual confusion and limits the detection of small structural changes, and this was in accordance to the study of Tsiklakis, et al. [25] that was stated that digital subtraction is a method that can resolve these problems and increase diagnostic accuracy, with digital subtraction techniques superimposed structures are eliminated and the area of change is more clearly observed.

Recently, there has been a trend toward the use of computerized tomography CT in assessing the process of bone healing in maxillofacial region [26].

On comparison between CT and conventional radiography it was found that CT offers better accuracy without anatomic superimposition in addition to improving the image quality [27] so this technique was used through our study and the axial sections obtained with some modification where X-ray beam adjusted to be parallel to the base of the mandible instead of being perpendicular to the axial plane of the skull to obtain symmetrical plane for the right and left site of the mandible.

Distraction osteogenesis is a good procedure for management of mandibular deficiency, and effect of platelet rich plasma requires more research work.

**Conclusion:**
- There is no significant deference between right distracted segment (without using PRP) and that of left site (with the use of PRP) as regards the formed amount of distracted callus and its density.
- Panorama X-ray film along with gray level detection and digital subtraction techniques is valuable method for evaluation of distraction osteogenesis.
- Computed tomography provides a good means for determination of bone density but it is expensive and patients exposed to more radiation.
- Further studies are required to confirm the role of platelet rich plasma in different maxillofacial procedures.

**References**


