Original Article - Comparative Study

Comparison of platelet rich plasma and synthetic graft material for bone regeneration after third molar extraction

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ABSTRACT

Aims: To compare the efficacy of Platelet rich plasma and synthetic graft material for bone regeneration after bilateral third molar extraction. **Material and Methods:** This study was conducted in 10 patients visiting the outpatient department of Oral & Maxillofacial Surgery, Yenepoya Dental College & Hospital. Patients requiring extraction of bilateral mandibular third molars were taken for the study. Following extraction, PRP (Platelet Rich Plasma) was placed in one extraction socket and synthetic graft material in form granules [combination of Hydroxyapatite (HA) and Bioactive glass (BG)] in another extraction socket. The patients were assessed for postoperative pain and soft tissue healing. Radiological assessment of the extraction site was done at 8, 12 and 16 weeks interval to compare the change in bone density in both the sockets. **Results:** Pain was less on PRP site when compared to HA site. Soft tissue evaluation done using gingival healing index given by Landry et al showed better healing on PRP site when compared to HA site. The evaluation of bone density by radiological assessment showed the grey level values calculated at 4 months at the PRP site were comparatively higher than HA site. **Conclusion:** The study showed that the platelet rich plasma is a better graft material than synthetic graft material in terms of soft tissue and bone healing. However a more elaborate study with a larger number of clinical cases is very much essential to be more conclusive regarding the efficacy of both the materials.

Keywords: Bioactive glass, bone density, hydroxyapatite, mandibular third molar extraction, pain, platelet rich plasma

INTRODUCTION

Bone is often subjected to various damages leading to its regeneration or repair.[1] Repair restores the bone to its original form and function. In the case of extraction socket healing, there is resorption of alveolar bone leading to decrease in ridge volume and alteration of ridge contour that consequently impairs prosthetic rehabilitation.[2] Special attention should be given for healing of bone following third molar extraction as it is associated with periodontal defects on the distal surface of an adjacent second molar.[3] Several biocompatible graft materials have been used to combat above healing defects, which include allografts, alloplasts, autografts or xenografts.[4] All these materials are being researched to know their capability of improving clinical outcomes.[5]

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Synthetic graft materials mainly comprise of calcium phosphate ceramics, which have a composition similar to bone mineral.[6] Hydroxyapatites (HAs) were considered to be the most useful[7] until; Larry Hench developed a material using silica (glass) incorporated with calcium and phosphorous to fuse broken bones that came to be known as "bioactive glass"(BG). Both synthetic HA and BG are now combined to be known as "bioactive ceramics."[8] Both these materials have osteoconductive properties,[8,9] The major advantages of these grafts are their biocompatibility and potential to offer an unlimited supply of bone substitutes, the absence of donor site infection and decreased operative time.

Platelet-rich plasma (PRP) has been used and researched extensively for bone regeneration following a breakthrough study done by Marx *et al*.[10] PRP is an autologous concentration of human platelets in a small volume of plasma. Various growth factors are released by activated platelets which include angiopoietin-2, connective tissue-activating peptide III, epidermal growth factor, factor V, factor XI, factor XIII, fibrinogen, basic fibroblast growth factor, fibronectin, insulin-like growth factor-I, osteocalcin, P-selectin (also called GMP-140), platelet-derived endothelial cell growth factor (or thymidine phosphorylase), platelet-derived growth factor, serotonin, transforming growth factor-b1 (TGF-b1), thrombospondin-1, vascular endothelial growth factor, and von Willebrand factor.[1] All these factors contribute to improve soft- and hard-tissue healing; hence, PRP has been used for bone regeneration by various clinicians.[11-13]

Autologous grafts, demineralized bone matrix, synthetic grafts, and PRP have been used alone or in combination with earlier studies for bone regeneration.[5,14] Both HA and BG have been used in past synergistically with PRP for the treatment of intrabony defects.[15,16] The unique feature of this study is that efficacy of PRP and synthetic granules (50% HA and 50% BG) have been evaluated individually for bone regeneration after bilateral third molar extraction.

MATERIALS AND METHODS

Patient selection

The present study was undertaken at the Department of Oral and Maxillofacial, Surgery, Yenepoya Dental Hospital. Ethical Committee clearance was procured from University Ethics Committee. A total of 10 subjects requiring bilateral extraction of mandibular third molar were selected. The following criteria were followed in selecting the patients:

- Age group 18–40 years
- Male and female patients
- ASA grade 1 patient
- Subjects having vertical impaction of bilateral mandibular third molars
- Surgical site free from any active infection
- Cases where primary closure of the wound was possible.

An informed consent was taken from each subject.

Material 1

The synthetic biomaterial used in this study was a new generation composite bioactive material containing silica, calcium and phosphorus made through a nonconventional processing method - "the sol-gel process." It is an indigenously prepared, resorbable synthetic porous ceramic granular graft with a particle size in the range of 150–500 microns and a pore size range of 100–200 microns. These granules are made up of 50% BG and 50% HA mixture. The material was procured in sterile packs [Figure 1].

Material 2

Preparation of platelet rich plasma gel

Under all aseptic conditions, 10 ml of blood was drawn intravenously from the antecubital region of patients forearm using disposable syringes. The collected blood was transferred to plastic tubes containing 1 ml of 3.2% sodium citrate solution as an anticoagulant.

PRP was prepared by double centrifugation method using clinical table top centrifugation machine.[17] The whole blood was first centrifuged at 2400 r.p.m. for 10 min. The supernatant formed was platelet poor plasma (PPP) and buffy coat. This PPP and Buffy coat layer were then collected in a fresh tube using 10 ml syringe and centrifuged at 3600 r.p.m. for 15 min. The upper half of the supernatant was discarded, and the lower half was mixed thoroughly to yield PRP. This PRP obtained was in liquid form, so to make it a gel it was mixed with 0.5–1 cc of 10% calcium chloride ($CaCl_2$) [Figure 2].[18]

Surgical procedure

In this study, both the impacted teeth were removed at same operating day. Under all aseptic conditions and local anesthesia impacted third molars were removed by a single operator. After removal of both the teeth, PRP gel was placed in one socket and HA granules in another socket, which was selected randomly by lottery method. The wound was closed primarily with 3–0 black braided silk.

Follow-up

Patients were recalled on day 1, day 3, day 7, 8 weeks, 12 weeks, and 16 weeks postoperatively for follow-up study. The pain was evaluated at day 1, day 3, and day 7 using the visual analogue scale (VAS).[19]

Evaluation of soft-tissue healing was done at day 1, day 3, and day 7 by healing index given by Landry *et al*.[20] The scores were given on the basis of tissue color, bleeding on palpation, epithelialization of incision margins and presence or absence of suppuration.[21]

Intraoral periapical radiographs were taken and digitised using the standardized technique as advocated by Peretz *et al*.[22] Radiographs were obtained at baseline, and at 8th week, 12th week, 16th weeks postoperatively to assess and compare gray level histogram between PRP sites and HA site. X-ray machine was used at 65–70 kVp and 10 mA. These radiographs were placed on a light viewing box and digitalized using canon EOS 1000d camera (ISO 200, F = 8, shutter speed = 1/125). The camera images were taken at same radiograph camera distance with a camera holder jig. The gray level histograms were obtained with the help of ImageJ (National institute of Health) software.[23,24]

RESULTS

After analysis of the data the following observations were made: There were 9 (90%) male subjects and 1 (10%) female subjects who had participated in the study. The subjects who had participated in the study were in the age range from 18 years to 28 years, with a mean age of 22 years.

Assessment of pain

Assessment of pain by VAS on the 1st day showed mean pain score of 1.8 in PRP site and 2.7 in HA site, on 3rd day mean pain score was 1.1 in PRP site and 2 in HA site, on 7th day score was 0 in both PRP and HA site. By doing the Mann–Whitney U-test for comparison of PRP and HA it was found that there was a significant difference in pain on day 1 and day 3 with less pain in PRP site [Graph 1].

Assessment of healing index of soft-tissue

Assessment of soft-tissue healing by healing index showed the mean score on the 1st day of 3.4 in PRP site, 2.7 in HA site, on 3rd day 3.8 in PRP site and 3.1 in HA site, on 7th day mean score of 4.9 in PRP site and 4 in HA site. By doing the Mann–Whitney U-test for comparison of PRP and HA it was found that there was a significant difference in healing on day 1 and day 3 with better healing in PRP site [Graph 2].

Radiographic assessment

At 8 weeks: Blending of bone margins in three patients in PRP site and four patients in HA site [Figure 3a and b] Chi-square test showed *P* value of 0.033. The trabecular bone formation was seen in nine patients at PRP site and nine patients at HA site.

At 12 weeks: Blending of bone margins was seen in all the 10 patients in both PRP and HA sites [Figure 4a and b]. The trabecular bone formation was seen in all 10 patients in PRP site and HA site.

At 16 weeks: Blending of bone seen in all 10 patients in both PRP site and HA site [Figure 5a and b]. The trabecular bone formation was seen in all 10 patients in both the sites.

Assessment of gray level value at 16 weeks showed that the average gray scale value for PRP site was 144.29 and for HA site it was 138.04 [Graph 3].

DISCUSSION

Autogenous bone is regarded as the gold standard for the repair of bony defects in the maxillofacial region[25] as it is the most biocompatible and osteoinductive material. However, the quantity of autogenous bone that can be harvested is limited[26] and so in large defects, synthetic graft materials do the needful. There are numerable autologous and alloplastic materials available, but PRP and synthetic granules (50% HA and 50% BG) were used individually in this study because both materials increase TGF-beta expression that leads to the rapid bone formation.[1,27]

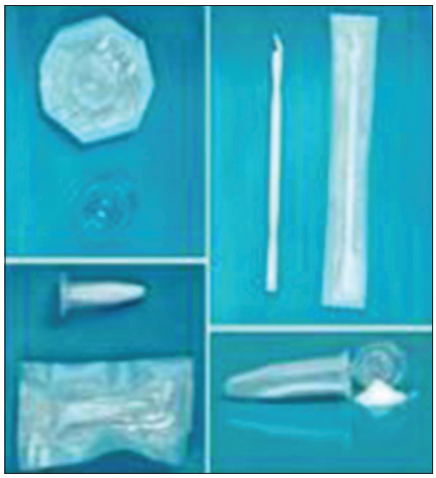


Figure 1: Synthetic granules (50% hydroxyapatite and 50% bioactive glass)

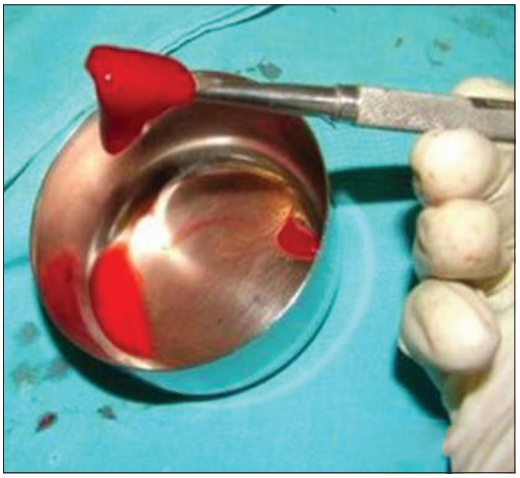


Figure 2: Platelet-rich plasma gel

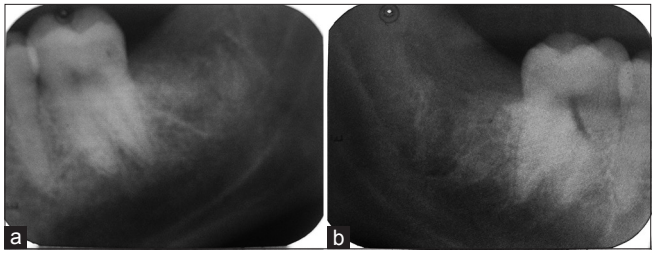


Figure 3: (a) Radiograph (intraoral periapical) at 8 weeks postoperatively-hydroxyapatite site. (b) Radiograph (intraoral periapical) at 8 weeks postoperatively-platelet rich plasma site

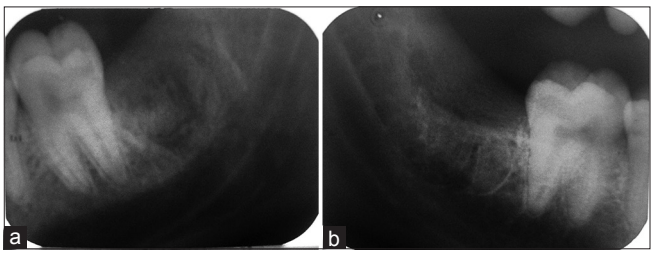


Figure 4: (a) Radiograph (intraoral periapical) at 12 weeks postoperatively-hydroxyapatite site. (b) Radiograph (intraoral periapical) at 12 weeks postoperatively-platelet rich plasma site

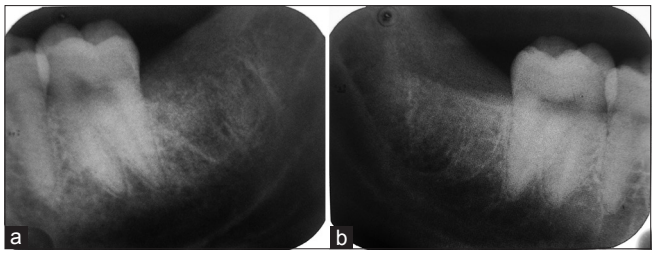
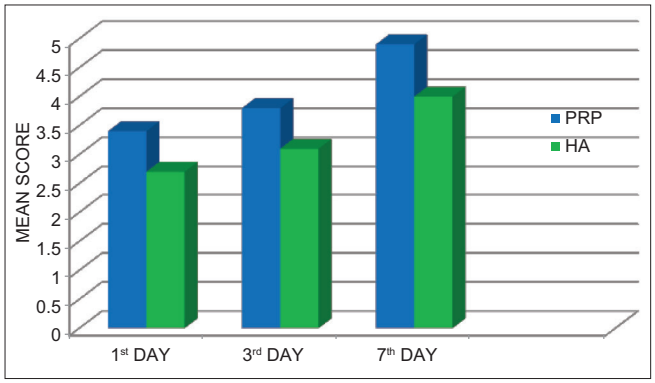


Figure 5: (a) Radiograph (intraoral periapical) at 16 weeks postoperatively-hydroxyapatite site. (b) Radiograph (intraoral periapical) at 16 weeks postoperatively-platelet rich plasma site

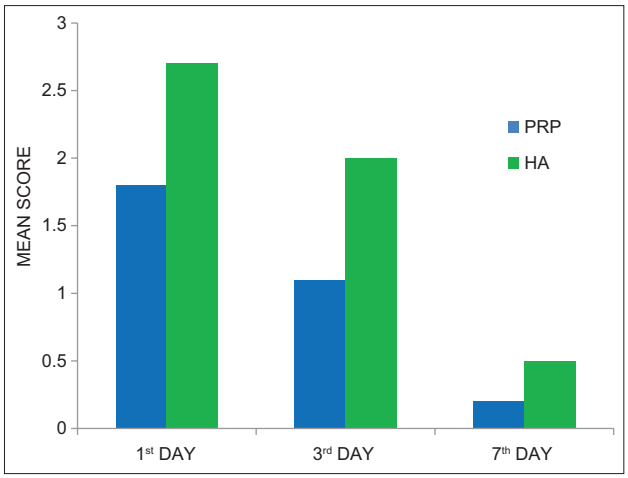


Graph 2: Assessment of healing index

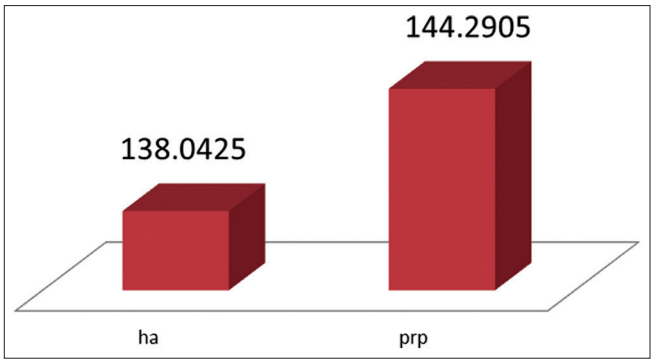
PRP is an autologous concentration of human platelets in a small volume of plasma also known as autologous platelet gel.[28] PRP can be prepared by two methods; one using single centrifugation protocol and the other using double centrifugation protocol. Nagata *et al*. concluded in their study that double centrifugation protocol resulted in higher platelet concentrations, and so it was used in this study.[17] Activation of PRP leads to the release of various growth factors that promote soft-tissue and bone healing.[1] This activation can be done by various agents such as $CaCl_2$ alone, $CaCl_2$ along with bovine thrombin or human thrombin as reported in the literature. Tsay *et al*. reported the use of synthetic peptide known as peptide-6 SFLLRN (thrombin receptor activating peptide) for activation of PRP.[29] Some studies indicate the bovine thrombin may cause the development of antibodies to clotting factors V, XI, and thrombin results in the risk of life-threatening coagulopathies.[30] Thus, $CaCl_2$ alone was mixed with PRP to prepare platelet gel.

The granules used in this study are made up of 50% BG and 50% HA mixture. The glassy part (BG) is 17% silicon, 53% calcium (as CaO) and 30% P_2O_5. The glass is composited with an equal quantity (50%) of synthetic HA. The mixture is processed in the form of porous granules so as to have the desired *in vivo* bioactivity.[31] Salms *et al*. and Froum *et al*. have concluded through their studies that both HA and BG have positive effect on socket healing.[27,32]

We carried out a clinical trial to compare the effectiveness of PRP and synthetic granules in terms of better soft-tissue healing and bone regeneration. Several factors affect bone healing that may vary from cases to cases, and so to avoid such bias both materials were placed in different extraction sockets of a single individual in the same sitting. Soft-tissue healing was evaluated using gingival healing index by Landry *et al*., which showed better soft-tissue healing of extraction sockets with PRP as compared



Graph 1: Assessment of pain using visual analogue scale



Graph 3: Assessment of bone density on postoperative radiographs

to HA sockets. This finding is supported by the authors who in their study reported that there was decreased the rate of alveolar osteitis, objectively faster soft-tissue flap healing and decreased swelling in the extraction sockets treated with PRP.[13,33]

All the procedures were done comfortably under local anesthesia on an outpatient basis. Both the materials not only fill and obliterate the extraction socket defect but also help in gaining height of the alveolar bone. It was observed that both the materials were biocompatible and did not show any exaggerative tissue reaction or any postoperative infection. These findings were in accordance with earlier studies done by Matsui *et al*. and Shapoff *et al*.[34,35]

Bone density can be measured by calculating the gray level value on the radiograph. All the radiographs were taken and digitalized using the standardised technique as stated by Peretz *et al*.[22] Gray level values can be measured with the help of different software available such as ImageJ (National Institute of Health), and Adobe Photoshop software (Adobe Systems).[3,24,36] The radiological assessment in the follow-up period of 4 months showed radiological evidence of osseous ingrowths into both the extraction socket defect. The evaluation of bone density was done by ImageJ software. The radiological assessment showed the grey level values calculated at 4 months at the PRP site 144.29 were comparatively higher than the HA site 138.04.

When comparing, PRP is safer as it is autologous source than homologous like HA. PRP takes care of soft-tissue healing along

with bone regeneration that may be the reason that there was no opening of socket margins as seen in this study. However, in cases of HA a proper closure is mandatory, if failed to do so, there might be exfoliation of the material as seen in three of our cases. PRP contains various factors as mentioned earlier, so this could explain the better soft-tissue and bone healing in PRP as seen in our study. PRP is cost-effective than HA.

The limitation of this study was that the sample size was small consisting of 10 patients and 4 months postoperative follow-up is a short duration, as has been reported in the literature where a long-term follow-up of 2–5 years has been done. Hence, a more elaborate study of the materials with a larger number of clinical cases and long-term follow-up is very much essential to be more conclusive regarding the biocompatibility and efficacy of the material in bone regeneration. A further histological sampling following clinical study would be useful to study the nature of the regenerated bone.

CONCLUSION

In our study, PRP gave better results than synthetic biomaterial in terms of soft-tissue and bone healing. However, for the success of the procedure, a perfect soft-tissue closure and avoidance of infection are mandatory. Both the materials accelerate bone regeneration in the extraction sockets. PRP is safe, cost-effective when compared to the synthetic biomaterial.

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Conflicts of interest

There are no conflicts of interest.

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