

# Effect of plasma rich in growth factors on alveolar osteitis

Department of Oral and Maxillofacial Surgery, School of Dentistry, Islamic Azad University, Dental Branch, <sup>1</sup>Trauma Research Center, Baqiyatallah Medical Sciences University, and OMFS Department Islamic Azad University of Medical Sciences, <sup>2</sup>Private Practice Dentistry, Tehran, Iran

Afshin Haraji, Eshagh Lassemi, Mohammad Hosein Kalantar Motamedi<sup>1</sup>, Maryam Alavi<sup>2</sup>, Saman Adibnejad<sup>2</sup>

## ABSTRACT

**Introduction:** The high prevalence of dry socket or alveolar osteitis (AO) is of concern in surgical removal of third molars. The aim of the present study was to assess the preventive effect of plasma rich in growth factors (PRGF) on AO and also its effect on pain management and healing acceleration in third molar extraction sockets of high-risk patients. **Materials and Methods:** This split-mouth, double-blind clinical trial included 40 bilateral third molar extractions (80 sockets) with at least one identified risk factor for AO. PRGF was obtained from patient's own blood, based on manufacturer's instruction, and blindly placed in one of the two bilateral sockets (PRGF group;  $n = 20$ ) of each patient. The contralateral socket was treated with a placebo (control group;  $n = 20$ ). Samples were evaluated for AO and pain incidence on days 2, 3 and 4 and healing and infection on days 3 and 7. Data were analyzed in SPSS v16 using Wilcoxon test. **Results:** There was a significant difference in dry socket and pain incidence and healing rate between the two groups. Intensity of pain and occurrence of dry socket in the study group was lower than the controls. Also the healing rate was higher ( $P < 0.05$ ) for the PRGF group. No sign of infection was seen in either group. **Conclusion:** The application of PRGF may significantly reduce the incidence of AO or its associated pain and may accelerate healing. The prophylactic use of PRGF following third molar extraction may be suggested especially in the patients at risk of AO.

**Key words:** Dry socket, plasma rich in growth factors, PRP, third molar extraction

**Address for correspondence:**  
Dr. Mohammad Hosein Kalantar  
Motamedi, Africa Expressway,  
Golestan St. Giti Blvd.  
No. 16 Tehran, 19667, Iran.  
E-mail: motamedical@lycos.com

## INTRODUCTION

The high prevalence (20% to 30%) of dry socket and its associated discomfort and complications remain one of the most important concerns of the dental profession.<sup>[1-6]</sup> The etiology of alveolar osteitis (AO) is not clear but increased fibrinolytic activity in the extraction socket has been shown to be associated with the clot lyses and exposure of the bone to the oral cavity.<sup>[4,7]</sup> The increased fibrinolysis is thought to be attributed to

surgery trauma, pathogenic fibrinolytics, enzymatic changes due to the inflammation, presence of high amounts of bacteria before and after surgery and other factors. The treatment is merely symptomatic and is limited to pain alleviation. Clinicians have attempted to observe preventive measures e.g. the administration of antifibrinolytics, antiseptics and antibiotics. These attempts, however, have not been uniformly successful due to the obscurity of the etiologic factors. Failure to prevent AO, on the other hand, will lead to clinical presentation of highly tender exposed bony surfaces, severe pain in the extraction site, moderate to severe dull headache with pain radiating to the ears in some instances, halitosis and altered taste.<sup>[7]</sup>

The present study was conducted to assess the effect of autogenous PRGF applied postoperatively in the prevention of AO.

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> www.njms.in
	<b>DOI:</b> 10.4103/0975-5950.102150

## MATERIALS AND METHODS

### Inclusion and exclusion criteria

Included were 40 patients with age range of 18 to 45 years. Bilateral (maxillary or mandibular) third molar extractions with similar scores of the Pederson scale of extraction difficulty and at least one AO risk factor (a history of pericoronitis, contraceptive uptake, smoking habits, bruxism or a history of AO) were chosen. Excluded were patients under antibiotic regimen or other interfering medications (e.g. steroids or antidepressants) at the time of the study. Also patients with complications during extraction, neurologic diseases, prophylactic needs, and lack of cooperation (e.g. patients who were not present for the follow-up sessions) were excluded. Impacted or partially impacted third molars were not excluded provided the difficulty of extraction was similar bilaterally. Venous blood samples were taken from patients prior to extraction.

### PRGF preparation

Ten milliliters of blood was obtained from cephalic or basilic veins (due to their accessibility and sufficient diameter) using 19 gauge needle to avoid platelet rupture or activation in the lumen. Sampled blood was immediately transferred to a syringe containing anticoagulant (1 ml of 3.8% sodium citrate for 10 ml blood) and centrifuged in PRGF system (BTI, Vitoria, Spain), set for 460 G in 8 minutes, to sediment platelets. Three layers were isolated after centrifugation: Red blood cells (RBCs) at the bottom, white blood cells (WBCs) in the middle and plasma on the surface. The surface plasma itself contained three distinct layers [Figure 1]. Platelet poor in growth factors (PPGF) on the top (500  $\mu$ l), plasma growth factors (PGF) in the middle and PRGF at the bottom which contains the highest concentrations of platelets and growth factors accumulated right above the RBCs. PPGF and PGF were

separately retrieved using two 500  $\mu$ l pipettes.  $\text{CaCl}_2$  was then added to PRGF (0.05 ml per ml) and coagulation was obtained within 5 to 8 minutes. To decrease coagulation time, PRGF was placed on a thermal block prior to activation to reach body temperature (37°). Finally the formed gel was placed in the socket.<sup>[8,9]</sup>

### Study process

This split-mouth, double-blind clinical trial was peer reviewed and approved by the local board of medical ethics and the research committee of the school of dental medicine. All extractions were performed by a single surgeon in order to standardize the level of surgical trauma. PRGF was blindly placed in one of the two bilateral sockets of each patient. These sockets were considered as the PRGF group ( $n = 20$ ). The other socket in each patient was treated via placebo. These sockets were considered as the control group ( $n = 20$ ). Sockets were examined 2, 3 and 4 days postoperatively by a blinded examiner to detect possible development of AO and pain was recorded on visual analogue scale (VAS). The scoring was as follows: 0 = no pain, 1–3 = mild pain, 4–6 = moderate pain, 6–8 = severe pain and 9 = pain with the highest possible severity. Healing was assessed on the third and the seventh days based on healing scale. The scale had 4 stages as follows: clot degeneration, wound departure with pus or without pus and no healing.<sup>[10]</sup> Data were analyzed in SPSS v16 using the Wilcoxon test.

## RESULTS

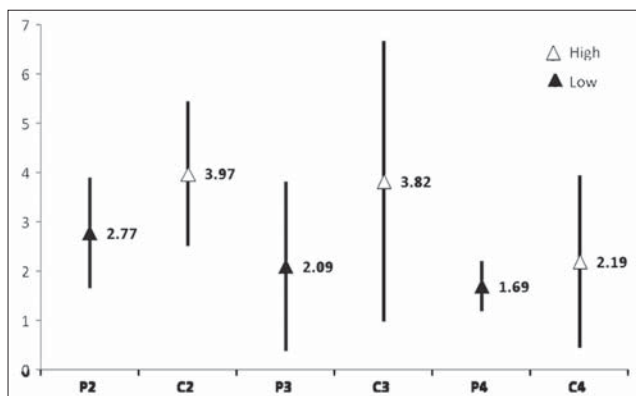
Patients were  $22.1 \pm 1.7$  years old. The extraction sites were maxillary in half of the cases (20 patients, 40 sockets) and mandibular in the other half (20 patients, 40 sockets). Based on our questionnaire, 18 patients were smokers, 20 patients were bruxers, 15 patients had a history of pericoronitis, 9 patients had a history of AO and 10 patients were using contraceptive drugs.

### Dry socket

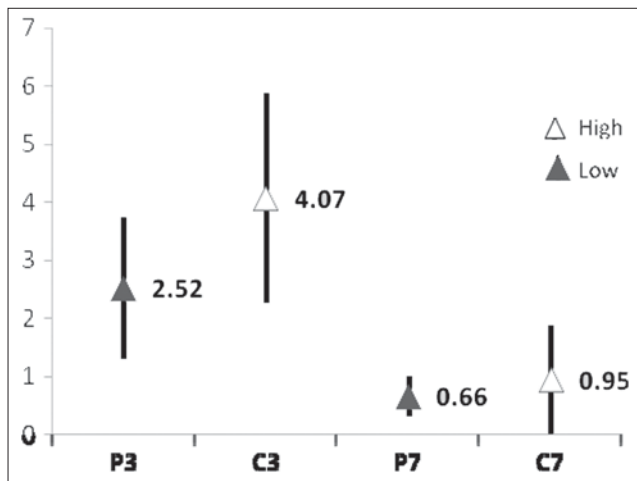
In the control group, 14 patients presented AO with no AO on the PRGF side. AO did not develop in the 22 patients on either side. Four patients developed AO on both sides. This was indicative of a statistically significant difference when PRGF was used ( $P < 0.05$ ).

### Pain and healing

The intensity of pain though second, third and fourth postoperative days is presented in Figure 1. The intensity of post-extraction pain was significantly less in PRGF group compared to control group in ( $P < 0.00$  for each post-extraction day). Figure 2 represents the healing scores of the study group. The healing was significantly better in the PRGF group ( $P < 0.00$  for both assessment days).



**Figure 1:** The comparative illustration of the pain intensity (mean  $\pm$  standard deviation) felt by the patients (scored on VAS) on the second, the third and the fourth days following the third molar extraction. P2: PRGF group in the second day. C4: control group in the fourth day. Gray triangles represent PRGF group and the white ones represent control group



**Figure 2:** The comparative illustration of the healing scores (mean  $\pm$  standard deviation) on the third and the seventh days following the third molar extraction. P3: PRGF group in the second day. C7: control group in the fourth day. Gray triangles represent PRGF group and the white ones represent control group

## DISCUSSION

The present study included 40 candidates of bilateral intra-arch third molar extraction (80 sockets). Included were cases with similar scores of the Pederson scale of difficulty of extraction and at least one AO predisposing factor.

Studies have shown that 0.2 ml of plasma located right above the red blood cells contains the highest concentrations of platelets, growth factors and fibrinogen.<sup>[11]</sup> The application of PRGF in the extraction socket was associated with decreased occurrence of AO, decreased pain and discomfort and enhanced healing. Authors have reported the contributing effect of PRGF in healing after periodontal surgical or non-surgical managements.<sup>[12]</sup> Consistent to the findings of the present study, Amitua *et al.*<sup>[8]</sup> studied the application of PRGF in different oral surgeries and reported remarkable outcomes in terms of epithelial proliferation, wound healing and bone regeneration in periodontal defects which were candidates for implant therapy. In another study, decreased epithelialization time, decreased bone regeneration time and improved bone regeneration were observed when PRGF was applied in the extraction socket of third molar. Also no pain, infection or AO was observed with the application of PRGF.<sup>[13]</sup> This was also in accordance to the results of the present study. Several studies have assessed the effect of PRP, on the healing and regeneration of the soft and hard tissues in different surgeries.<sup>[12-14]</sup> The coagulative effect of PRGF was most important. PRGF and PRP have the same platelet concentration which is the least concentration needed for clinical effects. (The PRP platelet concentration is 4–7 times more than the peripheral blood platelet concentration (200,000) and the PRGF platelet concentration is 8 times more than the

peripheral blood in 0.5 cc above the RBCs and 4 times greater in the next layer.)<sup>[9,15]</sup>

Rutkowski *et al.*<sup>[16]</sup> studied the effect of PRP on the prevention of AO after the extraction of 904 mandibular extractions. They claimed that the application of PRP decreases the occurrence of AO up to 60% seen in the high-risk patients. This value was 77% in the present study which is thought to be attributed to a higher efficacy of PRGF compared to PRP. The study of Rutkowski *et al.* did not include matched cases and was not case-control but the study population in the present split-mouth study was matched according to gender, age and difficulty of extraction.

Jerome *et al.*<sup>[17]</sup> studied the preventive effect of PRP on AO following surgical removal of mandibular third molars of 117 patients. In their study, AO occurred in 3.4% of the PRP group and 12.8% of the control group. Also they noticed faster tissue healing, enhanced homeostasis and less swelling with the application of PRP.

PRGF does not need bovine or human thrombin for coagulation. Apart from the growth factors restored in the platelets, PRGF includes plasma proteins and coagulative factors and is then more advantageous compared to PRP.<sup>[18]</sup> The pain relief and the healing rate increase due to the application of PRGF may be due to the inclusion of signaling proteins and platelet granules, which are immediately released with the activation of platelets and the initiation of coagulative cascade to form the clot. These factors are either synthesized by megakaryocytes or stored within the platelet granules or stored plasma proteins by endocytosis while circulating in blood cycle, because platelets do not have a nucleus and do not possess required elements for the production of these factors (insulin like growth factors, vascular endothelial growth factor, epidermal growth factor, nerve growth factor, transforming growth factor rho, cytokines like angiopoietin II and interleukin I).<sup>[19]</sup>

These factors trigger differentiation, increase collagen synthesis, increase chemotaxis and other immune system cells to the surgery site and initiate angiogenesis. It also induces fibroblast proliferation, bone formation and bone regeneration.<sup>[20]</sup> The application of PRGF may significantly prevent AO and its complications due to long-term angiogenic effect and increased regenerability. Patients with bruxism are highly susceptible to AO because of high bone density and the consequent decreased blood supply. The angiogenic effect of PRGF may reduce these complications in bruxers.<sup>[16]</sup> Patients with a history of pericoronitis may be predisposed to AO.

PRGF also accelerates the bone and tissue healing rate.<sup>[20]</sup>

## CONCLUSION

Our study shows that the application of PRGF will help prevent the AO formation especially in susceptible patients.

## ACKNOWLEDGMENT

This work was supported by the Research Department of Faculty of Dentistry.

## REFERENCES

- Torres-Lagares D, Serrera-Figallo MA, Romero-Ruiz MM, Infante-Cossio P, García-Calderón M, Gutiérrez-Pérez JL. Update on dry socket. *Med Oral Patol Oral Cir Bucal*. 2005 Jan-Feb;10(1):81-5; 77-81.
- Jaffar N, Nor GM. The prevalence of post-extraction complications in an outpatient dental clinic in Kuala Lumpur Malaysia. *Singapore Dent J* 2000;23:24-8.
- Simon E, Matte M. Post –extraction complications seen at a referral dental clinic Dar Es Salaam, Tanzania. *Int Dent J* 2001;51:273-6.
- Blum IR. Contemporary views on dry socket (alveolar osteitis): A clinical appraisal of standardization, aetiopathogenesis and management: A critical review. *Int J Oral Maxillofac Surg* 2002;31:309-17.
- Fridrich KL, Raj O. Alveolar osteitis following removal of mandibular third molars. *Anesth prog* 1990;37:32-41.
- Lilly GE, Osborn DB. Alveolar osteitis associated with mandibular third molar extractions. *J Am Dent Assoc* 1974;88:802-6.
- Peterson LJ. Contemporary oral and maxillofacial surgery. (W.B. Saunders Co., Philadelphia)4<sup>th</sup> ed. 2003;9. p. 290.
- Anitua E, Sánchez M, Orive G, Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials*. 2007 Nov;28(31):4551-60. Epub 2007 Jul 30.
- Anitua E, Sánchez M, Orive G, Andia I. Delivering growth factors for therapeutics. *Trends Pharmacol Sci*. 2008 Jan;29(1):37-41. Epub 2007 Nov 26. Review.
- Fernando S, Hili C. M, Walker R. A randomized double blind comparative study of low level laser therapy following surgical extraction of lower mandibular third molars teeth. *Br J Oral Maxillofac Surg* 1993;31:170-2
- Anitua E, Sánchez M, Orive G. The importance of understanding what is platelet-rich growth factor (PRGF) and what is not. *J Shoulder Elbow Surg*. 2011 Jan;20(1):e23-4; author reply e24. Epub 2010 Nov 3.
- Sammartino G, Tia M. Use of autologous PRP in periodontal defect treatment after extraction of impacted mandibular third molars. *J Oral Maxillofac Surg* 2005;63:766-72.
- Simon D. Potential of osseous regeneration of PRP: A comparative study in mandibular third molar sockets. *Indian J Dent Res* 2004;15:133-6.
- Weibrich G, Hansen T. Effect of platelet concentration in PRP on peri implant bone regeneration. *Bone* 2004;34:665-7.
- Marx RE. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg*. 2004 Apr;62(4):489-96.
- Rutkowski JL, Fenell JW. Inhibition of alveolar osteitis in mandibular tooth extraction sites using platelet rich plasma. *J Oral Implantol* 2007;33:116-21.
- Sammartino G, Tia M, Gentile E, Marenzi G, Claudio PP. Platelet-rich plasma and resorbable membrane for prevention of periodontal defects after deeply impacted lower third molar extraction. *J Oral Maxillofac Surg*. 2009 Nov;67(11):2369-73.
- Anitua E. Plasma rich in growth factors: Preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants* 1999;14:529-35.
- Caplan AL. Mesenchymal stem cells and gene therapy. *Clin orthop* 2000;379(suppl):s67-70.
- Clunn GF, Refson JS, Lymn JS, Hughes AD. Platelet-derived growth factor beta-receptors can both promote and inhibit chemotaxis in human vascular smooth muscle cells. *Arterioscler Thromb Vasc Biol* 1997;17:2622-9.

**How to cite this article:** Haraji A, Lassemi E, Motamedi MK, Alavi M, Adibnejad S. Effect of plasma rich in growth factors on alveolar osteitis. *Natl J Maxillofac Surg* 2012;3:38-41.

**Source of Support:** This work was supported by the Research Department of Faculty of Dentistry. **Conflict of Interest:** None declared.