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Evaluation of the Use of Plasma Rich in Growth Factors with Immediate Implant Placement into Fresh Extraction Sockets: A Controlled Prospective Study

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Abstract : *The purpose of this study was to evaluate the clinical and radiographic outcomes of using Plasma Rich in Growth Factors (PRGFs) with Immediate Implant Placement into Fresh Extraction sockets. Twelve patients were included in this study. Each patient received four implants placed immediately after extraction in the anterior regions of maxilla after treating two implants with Plasma Rich in Growth Factors (group I) while the others were not and served as a control (group II) . Implant success , plaque index PI, and bleeding index BI, probing pocket depth PPD, and marginal bone loss MBL were evaluated for both groups. Complete soft tissue healing had occurred in all patients and all the implants were successfully osseointegrated over 18 months. The results of the present study showed that at 18 months the mean PPD values were 4.14±0.45 mm at control site and 3..29±0.32 mm at test site; mean values of MBL were 1.33±0.21mm at control site and 1.18±0.13 mm at the test site, there were no statistical differences between the test and control group regarding, BI, PI, while there were statistical differences between the test and control regarding, PPD, MBL through follow- up periods. Using Plasma Rich in Growth Factors with immediate placement of dental implants into Fresh Extraction sockets reduces marginal bone loss around the implant*

Keywords: *Fresh extraction sockets, Immediate dental implants , Plasma Rich in Growth Factors*

I. Introduction

The placement of dental implants into fresh extraction sockets was introduced in the late 1970s [1]. Immediate postextraction implant placement is a well-accepted protocol due to the preservation of aesthetics, shorter total treatment time, maintenance of socket walls, reduced surgical time, and better actual implant placement [2]. Although the concept of immediate placement of dental implants after removal of a tooth with periapical pathology, was a matter of debate [3], Some studies reported that, the success in immediate implant placement for replacement of teeth with periapical lesions, can be achieved if certain preoperative and postoperative measures are followed, such as antibiotic administration, meticulous cleaning, and alveolar debridement, before surgical procedure [4-7]. Plasma Rich in Growth Factors (PRGFs) is derived from autologous blood by sequestering and concentrating the platelets by centrifugation [8]. It is advocated the platelet concentration can enhance oral wound healing by releasing abundant growth factors, including platelet-derived growth factor (PDGF), transforming growth factor- (TGF-), insulin-like growth factor (IGF) and epidermal growth factor [9]. Recently, (PRGFs) has been applied clinically to facilitate and improve bone and soft tissue healing [10]. Anitua in 1999 reported that the application of (PRGFs) inside the extraction sockets improved soft tissue repair and bone regeneration [8]. However there are little information available about the efficacy of using Plasma Rich in Growth Factors with Immediate Implant Placement into Fresh Extraction sockets . The aim of this study was to evaluate the clinical and radiographic outcomes of using PRGFs with Immediate Implant Placement into Fresh Extraction sockets

II. Material And Methods

This study was designed and performed as a prospective controlled study . All patients were asked to sign surgical consent forms. The study protocol was approved by an ethical committee of Al-Andalus University of Medical Sciences Twelve patients (7 females and 5 males) ranging in age 45-58 years with an endodontic failure, tooth fracture, or unrestorable carious tooth were included in this study. Each patient received four implants placed immediately after extraction in the anterior region of maxilla after treating two

implants with Plasma Rich in Growth Factors (group I) while the others were not and served as a control (group II). The test and control sides were switched according to the order of patients. All patients in this study were at physically able to tolerate the procedure, had to be in good health, with no chronic disease or smoking habits. Patients were excluded if any of the following were evident: periodontal disease; any disease, condition, or medication that might compromise healing or osseointegration; or inability or unwillingness to return for follow-up visits and if there was need for grafting the implant site . All implants in this study were Euroteknika implants (Euroteknika, Sal-lanches, France), which are compatible with the Astra system (Dentsply International, Waltham, MA, USA). The dimensions ranged from 10 to 12 mm in length and 4.1 mm in diameter. Primary stability (torque 25 N/cm) of the implants was achieved during the surgical procedure. Preliminary diagnostic procedures included a digital panoramic radiographic evaluation.

2.1 Preparation of PRGFs:

Before surgery and the administration of local anesthesia, 10 ml of peripheral blood was drawn. The blood was deposited in laboratory glass tubes pre-treated with 3.8% trisodium citrate. The tubes were centrifuged at 270 rpm at room temperature for 7 min in a centrifuge unit specifically designed for use with this technique (PRGF System; BTI Biotechnology Institute, Vitoria-Gasteiz, Alava, Spain). This allows the separation of blood into distinct layers: a cellular layer at the bottom, PRP in the middle, and platelet-poor plasma at the top. The cellular components (mostly red blood cells and a thin layer of white blood cells) remain at the bottom of the tube, above which is the plasma component consisting of PRGFs and finally a layer of plasma poor in growth factors. The middle layer was collected and stored in a sterile glass container until use. Leukocytes were not collected in this preparation. At the time of the application, approximately 50 µl of 10% CaCl2 solution was added per 1 ml of PRGF concentrate to enable clot formation. A platelet cell count was done before and after centrifugation.

2.2 Surgical procedure:

One hour before surgical procedure, patients began a prophylactic regimen of 600 mg clindamycin. All procedures were performed after the administration 3.6-5.4 ml of combination consisting of a local anesthesia (Mepevacaine Hcl 2%) and a vasoconstrictor (Levonordefrin) at ratio of 1:20,000. Full-thickness mucosal flaps were raised, and then the teeth were gently extracted by extraction forceps, with minimum surgical trauma and without any damage to the adjacent hard tissues. The bony sockets were then carefully debrided with a sharp curette to remove any granulation or fibrous tissue present and irrigated with sterile saline. Integrity of the socket walls and socket depth from the alveolar crest of bone to the socket apex were checked with the osteotomy probe. Depth of the socket was measured to determine the drilling needed after the root apex. Osteotomies were performed via standard protocols in all cases, including, slow-speed sequential drills, and copious irrigation. Drilling extended at least 3-5 mm beyond the root apex. In the test sites, the prepared PRGFs was slowly injected at low pressure into the drill holes immediately before implant placement. In addition, the implants were dipped in PRGFs before seating . Implants were manually screwed into the prepared osteotomies at the crestal ridge. Implant stability was monitored and noted upon placement. Closure of the wound was obtained by coronal repositioning of the flap. "Fig1 "

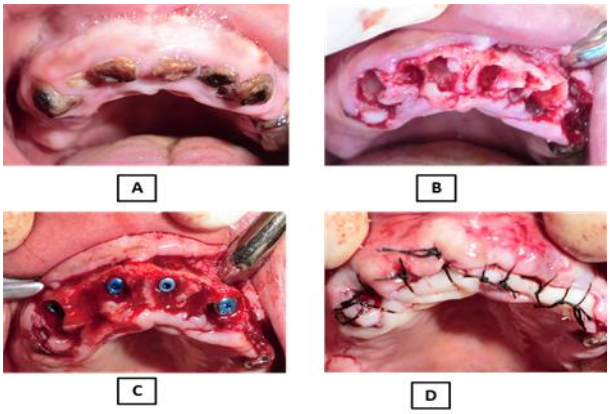

Fig. 1: (A) Before extraction. (B) After extraction. (C) implant placement . (D) suturing . (Test: right side; control: left side.).

2.3 Postoperative Phase:

Post-operative instructions were given to the patients, which included extra-oral ice packs application for 2 hours on the first day to minimize oedema, oral hygiene instructions including warm 0.2% Chlorhexidine

Hcl as an antiseptic mouthwash twice daily for 7 days, to continue the use of 300 mg clindamycin orally every 6 hours postoperatively for five days and to take ibuprofen 600 mg twice daily for 7-10 days. A direct digital panoramic radiograph was taken immediately after implants placement to evaluate the implants position. Patients were recalled after 1 week for the removal of sutures and to assess the presence of any pain, swelling, or infection. After a healing period of 6 months, the second-stage surgical procedure was performed with the placement of a healing abutment on the implant. Prosthetic rehabilitation started 2 weeks after the second stage surgical procedure, in which the prosthesis were cemented with temporary cement.

2.4 Follow-up Phase:

2.4.1 A-Clinical Evaluation:

All patients were examined immediately after surgery and during the first week to check if there was pain, discomfort, swelling, or infection. The plaque index PI and bleeding index BI were used for clinical evaluation at 12 and 18 months after implant placement. In accordance with Mombelli et al [11] the probing pocket depth around the implant was measured at the four aspects of the implant; facial, palatal and proximal surfaces, using the probe graduation in mm then the mean was calculated and also evaluated at12 and 18 month after implant placement.

2.4.2 B-Radiographic Evaluation:

Radiographic examinations with digital panoramic radiographs were performed directly after surgery (baseline) and at 6 ,12 and 18 months "Fig 2". An independent radiologist analyzed the radiographs without knowledge which implants were treated with PRGF. The reference for the measurements was the implant-abutment interface. The saved image was opened in Image J program. The scale was determined in reference to the known implant length. From "Analyze" command, "Set Scale" command was selected to convert pixels dimension to millimeters. A line was drawn from the implant apex to the implant shoulder. The length of the implant was measured and compared to the real implant length to determine the magnification factor in the image. The distance from the implant apex to the first seen point of Bone Implant Contact was measured. The difference between it and the implant length represents vertical marginal bone defect. The measurements were noted mesially and distally and the mean was calculated in mm according to the magnification factor of the image. All the measurements were taken three times then the mean was calculated.

In accordance with Buser et al, [12] an implant was classified as having survived if the following parameters were met: (1) absence of recurring peri-implant infection with suppuration; (2) absence of persistent subjective complaints such as pain, foreign body sensation, and/or dysesthesia; (3) absence of a continuous radiolucency around the implant; and (4) absence of any detectable implant mobility.

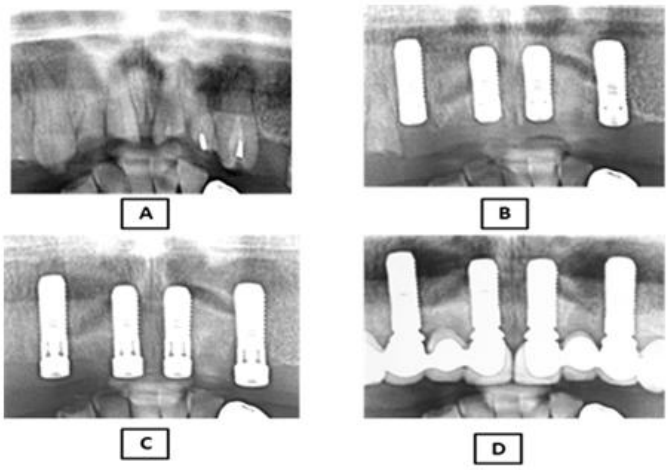

Fig. 2: Radiographic evaluation. (A) Before extraction. (B) Immediately after implant placement. (C) After 6 months. (D) After 18 months. (Test: right side; control: left side.).

2.5 Data analyses:

The statistical analyses were performed using SPSS version 17 software (SPSS Inc., Chicago, IL, USA). Comparison between quantitative variables were carried out by Student t-test of two independent samples. The results were considered to be significant at P- values less than 0.05.

III. Results

All patients showed good compliance and the healing period was uneventful for both treatment groups without infection or complications. The survival rate was 100% in two groups and none of the implants lost osseointegration through follow up periods . Baseline analysis of marginal bone loss showed no significant differences between group I and group II , thus allowing post-treatment results to be compared .

3.1 Plaque Index (PI):

There were no significant differences between control and test groups at 12 and 18 months, at 5% level (P>0.05), "Table 1" , mean plaque index values were 0.65±0.23at control site, 0.76± 0.22at test site at 12 months ,and they were 0.98±0.45at control site, 0.98±0.27 at test site at 18 month.

1.2 Bleeding index MBI :

There were no significant differences between control and test groups at 12 and 18 months, at 5% level (P>0.05), "Table 1" , mean Bleeding index values were 0.55±0.345 at control site, 0.60±0.36 at test site at 12 months ,and they were 0.67±0.48control site, 0.56±0.47at test site at 18 months.

Table. 1: Mean± SD and t test of plaque index (PI) ,bleeding index (BI) in the tested groups (I and II) during different observation periods.

	PI			BI		
	I	II	P value	I	II	P value
12mo.	0.76±0.22	0.65±0.23	0.122	0.60±0.36	0.55±0.34	0.612
18mo.	0.98±0.27	0.98±0.45	1.00	0.56±0.47	0.67±0.48	0.881

3.3 Probing Depth (PD):

There were significant differences between control and test groups at 12 and 18 months, at 5% level (P<0.05), "Table 2" , mean Probing Depth values were 3.50±0.29at control site, 2.66±0.38 at test site at 12 ,and they were 4.14±0.45control site, 3.29±0.32at test site at 18 months.

3.4 Marginal bone loss MBL:

There were significant differences between control and test groups at 6,12 and 18 months, at 5% level (P<0.05), "Table 2" , mean Marginal bone loss were 0.87±0.19 at control site, 0.42±.0.13at test site at 6 months, 1.02±0.17at control site, 0.93±0.09 at test site at 12 ,and they were 1.33±0.21control site, 1.18±0.13 at test site at 18 months. The difference in means of marginal bone loss between 6,12 months were 0.51±0.094 mm in test group and 0.29±0.15 mm in control group with significant differences(P<0.05) . The difference in means of marginal bone loss between 12,18 months were 0.24±.128 mm in test group and 0.95±.128 mm in control group with no significant differences(P>0.05). "Table 3"

Table. 2: Mean± SD and t test of marginal bone loss (MBL), and probing pocket depth (PPD) (in mm) in the tested groups (I and II) during different observation periods.

	MBL			PPD		
	I	II	P value	I	II	P value
Baseline	0.15±.0.24	0.12±0.22	0.733			
6mo.	0.42±.0.13	0.71±0.11	.000			
12mo.	0.93±0.09	1.02±0.17	.036	2.66±0.38	3.50±0.29	0.00
18mo.	1.18±0.13	1.33±0.21	.005	3.29±0.32	4.14±0.45	0.00

Table. 3: Mean± SD and t test of the differences of marginal bone loss (MBL).

	MBL		
	I	II	P value
Between 6, 12mo.	0.51±0.094	0.29±0.15	.000
Between 12, 18mo.	0.24±.128	0.95±.128	.200

IV. Discussion

The purpose of this study was to evaluate the clinical and radiographic outcomes of using Plasma Rich in Growth Factors (PRGFs) with Immediate Implant Placement into Fresh Extraction sockets . In this study, Soft tissue healing was uneventful in all patients included, none of the patients suffered from pain or periimplant infection, all implants were found to be successfully osseointegrated without any signs of peri-implantitis through follow-up periods.

Plaque index, bleeding index, probing pocket depth were evaluated to rule out the effect of peri-implant tissues inflammation on the marginal bone loss, and the results showed that there were no statistically significant

differences between means of (BI), (PI) at test and control sides at 12 and 18 months follow up periods. Mean probing depth values were 4.14±0.45 mm at control site and 3.29±0.32 mm at test site at 18 months, although there were significant differences between control and test groups , These values are within the normal limits of the Probing pocket depth around dental implants [13].

There were statistical differences between the test and control groups regarding marginal bone loss through follow- up periods. At 18 months follow-up period, the mean values of Marginal bone loss in this study were 1.33±0.21 mm at control site and 1.18±0.13 mm at the test site. There was statistical difference between test and control groups regarding the difference in marginal bone loss between 6,12 months but there was no statistical differences between 12,18 months, this shows that using PRGFS didn't effect on marginal bone loss after six month of functional loading of the implants.

The difference in bone loss between the two groups in this study after one year of function was 0.15 mm and according to the criteria of Alberktsson et al, [14] the implant was considered success if MBL less than 1.5 mm in the first year so the difference of less than 1 mm over one year is unlikely to have any clinical relevance for implant success .The same positive effect of using PRGFs on reducing marginal bone loss is demonstrated in our previous study [15] which aimed to evaluate the clinical and radiographic outcomes of the use of PRGFs with immediate implant placement in periodontally compromised extraction sites. Marginal bone loss was 0.41 mm At 1 year of function in the study of Massimo et al, [16] in their Single-Cohort Study which evaluated the clinical outcome of implants immediately placed into fresh extraction sockets of teeth affected by chronic periapical pathologic findings, using plasma rich in growth factors (PRGFs) as an adjunct during the surgical procedure. and they concluded that The use of PRGFs combined with an immediate implant placement procedure can be considered a safe, effective, and predictable treatment option for the rehabilitation of fresh postextraction infected sockets.

Recently, PRGFs have been used in the field of oral surgery for pregrafting future implant sites [17,18]. The interaction of PRP with the surface of the titanium implants with an acid-etched surface was examined by environmental scanning electron microscopy in previous experimental studies [10,19] . Histomorphometric analysis of the bone-implant interface performed after 8 weeks in goats showed that the implant surface adsorbed the protein-rich material, and osseointegration was enhanced when the surface was covered with PRGFs [20] .

A recent retrospective study by Anitua et al, [21] of BTI implants used in conjunction with PRGFs, with up to 5 years of follow-up, showed overall implant survival rates of 99.2% for 5,787 implants placed in 1,060 patients. One half of the failures occurred within the first year of loading, and 70% of patients who experienced an implant failure had presented with chronic or aggressive periodontitis. Another retrospective study by Anitua et al, [22] with up to 5 years of follow-up reported a 99.3% implant survival rate for 1,139 immediately loaded implants bioactivated with PRGFs in 241 patients. Even though the sample size of these studies was quite large, their retrospective design could undermine the power of the conclusions. Anand U et al, [23] assessed clinically and radiographically the soft and hard tissue changes around the immediately loaded single tooth implants bioactivated with platelet-rich plasma (PRP), placed in the mandibular posterior region and they found that The use of platelet-rich plasma may lead to improved early bone apposition around the implant; and thus, results in increased rate of osseointegration. However, contradictory results were reported in study by EL-Marssafy,L et al, [24] who investigated the effect of adding platelet-rich plasma with immediately loaded self-tapping dental implant placed in healed bony sites on accelerating the rate of osseointegration or reducing the crestal bone resorption around these implants and they concluded that local application of autologous platelet-rich plasma into the prepared drill holes immediately before implant placement didn't accelerate the rate of osseointegration or decrease the crestal bone resorptoin. . Casati M. Z et al, [25] in animal study investigated the influence of platelet-rich plasma (PRP) on bone regeneration in dehiscence-type bone defects around dental implants They demonstrated that that platelet-rich plasma alone did not enhance bone regeneration for peri-implant defects. Also Sanchez et al, [26] found that the addition of PRP to xenogenic bone grafts did not significantly alter bone mineral density or graft maturity levels in their study that assessed the bone mineral density changes after bone regeneration therapy using xenogeneic demineralized freeze-dried bone graft plus platelet-rich plasma in 3-wall peri-implant defects in dogs However Nikolidakis D et al, [27] have shown that the additional use of PRP in gel form did not offer any significant effect on the bone response to the CaP-coated implants, whereas PRP in a liquid form showed a significant effect on bone apposition to roughened titanium implants during the early post-implantation healing phase in their study that investigated the effect of local application of autologous platelet-rich plasma (PRP) on bone healing in combination with the use of titanium implants in goats.

V. Conclusion

Within the limits of the present study Using Plasma Rich in Growth Factors with immediate placement of dental implants into Fresh Extraction sockets reduces marginal bone resorption around the implant . The results of our study however, need to be confirmed in the long term and with a larger sample of patients.

References

[1] W. Schulte, H. Kleineikenscheidt, K. Lindner, R. Schareyka, The Tübingen immediate implant in clinical studies, Dtsch Zahnarztl Z, 33(5), 1978, 348-59

[2] R.J. Lazzara, Immediate Implant Placement into Extraction Sites: Surgical and Restorative Advantages, Int J Periodontics Restorative Dent ,Vol.9, 1989, 332-43.

[3] JA. Lindeboom, Y. Tjiook, FH. Kroon, Immediate placement of implants in periapical infected sites: a prospective randomized study in 50 patient, Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 101(6), 2006 , 705-10.

[4] AB Jr. Novaes, AB. Novaes, Immediate implants placed into infected sites: a clinical report, Int J Oral Maxillofac Implants, 10(5), 1995, 609-13.

[5] AB. Novaes Jr, GM. Vidigal Júnior, AB. Novaes, MF. Grisi, Polloni S, A. Rosa, Immediate implants placed into infected sites: a histomorphometric study in dogs, Int J Oral Maxillofac Implants, 13(3), 1998, 422-7.

[6] N. Casap, C. Zeltser, A. Wexler, E.Tarazi, R. Zeltser, Immediate Placement of Dental Implants Into Debrided Infected Dentoalveolar Sockets, Journal of Oral and Maxillofacial Surgery, 65 (3), 2007, 384-392.

[7] R. Crespi, P. Capparè, E. Gherlone, Fresh-socket implants in periapical infected sites in humans, J Periodontol, 81(3), 2010, 378-83.

[8] E. Anitua, Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants, Int J Oral Maxillofac Implants, 14(4), 1999, 529-35.

[9] RE. Marx, Platelet-rich plasma: evidence to support its use, J Oral Maxillofac Surg, 62(4), 2004, 489-96.

[10] E. Anitua, M. Sánchez, G. Orive, I, Andía, The potential impact of the preparation rich in growth factors (PRGF) in different medical fields, Biomaterials, 28(31), 2007, 4551-60.

[11] A. Mombelli, MA. vab Oosten, E Jr. Schurch, NP. Lang, The microbiota associated with successful or failing osseointegrated titanium implants, Oral Microbiol Immunol, 2(4),1987, 145-51.

[12] D. Buser, HP. Weber, U. Braegger, The treatment of partially edentulous patients with ITI hollow-screw implants: presurgical evaluation and surgical procedures, Int J Oral Maxillofac Implants, 5, 1990, 165-74.

[13] U. Lekholm, R. Adell, J. Lindhe, et al, Marginal tissue reactions at osseointegrated titanium fixtures, II. A cross-section retrospective study, Int J Oral Maxillofac Surg, 15, 1986, 53-61.

[14] T. Alberktsson, G. Zarb, P. Worthington, RA. Eriksson, The long-term Efficacy of currently Used Dental Imlants, A review and proposed criteria of success, Int J Oral Maxillofac Implants, 1(1), 1986, 11-25.

[15] A. Al Nashar, H. Yakoob, Evaluation of the use of plasma rich in growth factors with immediate implant placement in periodontally compromised extraction sites: a controlled prospective study, Int. J. Oral Maxillofac. Surg, 44, 2015, 507–512.

[16] M. Del Fabbro, C. Boggian, S, Taschieri, Immediate implant placement into fresh extraction sites with chronic periapical pathologic features combined with plasma rich in growth factors: preliminary results of single-cohort study, J Oral Maxillofac Surg, 67(11), 2009, 2476-84.

[17] E. Anitua, I. Andia, B, Ardanza, P, Nurden, AT, Nurden, Autologous platelets as a source of proteins for healing and tissue regeneration, Thromb Haemost, 91(1), 2004, 4-15.

[18] E. Anitua, M. Sánchez, AT. Nurden, P. Nurden, G. Orive, I. Andía, New insights into and novel applications for platelet-rich fibrin therapies, Trends Biotechnol, 24(5), 2006, 227-34.

[19] E. Anitua, Enhancement of osseointegration by generating a dynamic implant surface, J Oral Implantol, 32(2), 2006, 72-6.

[20] E. Anitua, G. Orive, R. Pla, P. Roman, V. Serrano, I. Andía, The effects of PRGF on bone regeneration and on titanium implant osseointegration in goats: a histologic and histomorphometric study, J Biomed Mater Res A, 91(1), 2009, 158-65

[21] E. Anitua, G. Orive, JJ. Aguirre, B. Ardanza, I. Andía, 5-year clinical experience with BTI dental implants: risk factors for implant failure, J Clin Periodontol, 35(8), 2008, 724-32.

[22] E. Anitua, G. Orive, JJ. Aguirre, I. Andía, Clinical outcome of immediately loaded dental implants bioactivated with plasma rich in growth factors: a 5-year retrospective study, J Periodontol, 79(7), 2008, 1168-76.

[23] U. Anand, and D.S. Mehta, Evaluation of immediately loaded dental implants bioactivated with platelet-rich plasma placed in the mandibular posterior region: A clinico-radiographic study, J Indian Soc Periodontol, 16(1), 2012, 89–95.

[24] L.EL-marssafy, O. Aboul-dahab, Z. Zahran, M. Shoib, Evaluation of Immediately Loaded Dental Implants Placed in Healed Bony Sites with or without Addition of Autologous Platelet-Rich Plasma, Journal of American Science, 7(3), 2011, 633-643.

[25] MZ. Casati, BC. de Vasconcelos Gurgel, PF. Gonçalves, SP. Pimentel, G. da Rocha Nogueira Filho, FH. Nociti, EA. Sallum, Platelet-rich plasma does not improve bone regeneration around peri-implant bone defects--a pilot study in dogs, Int J Oral Maxillofac Surg, 36(2), 2007, 132-6.

[26] A.R. Sanchez, S.E. Eckert, PH.J. Sheridan, A.L. WEAVER, Influence of Platelet –Rich Plasma Added to Xenogenic Bone Grafts on Bone Mineral Density Associated with Dental Implants, Int J Oral MaxillofacImplant , 20, 2005, 526-532.

[27] D. Nikolidakis, J. van den Dolder, J. G. C. Wolke, P. J. W. Stoelinga, and J. A. Jansen, The effect of platelet-rich plasma on the bone healing around calcium phosphate-coated and non-coated oral implants in trabecular bone, Tissue Engineering, 12,(9), 2006, 2555–2563.