Evaluation of immediately loaded dental implants placed in healed bony sites with or without addition of autologous platelet-rich plasma

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Abstract: The concept of immediate loading by using titanium one-piece implant can be preferred to the two stage technique due to the ability of the immediate loading to eliminate the need for the healing period to restore the implant. The aim of the present study was to evaluate the effect of adding platelet-rich plasma with immediately loaded self-tapping dental implant (OsteoCare™ Maxi-Z one piece) placed in healed bony sites (posterior maxillary area) on accelerating the rate of osseointegration or reducing the crestal bone resorption around these implants through the first three months follow-up period. **Materials and Methods:** The present study was conducted on 12 patients; 9 males (75%) and 3 females (25%) with a mean age of 37.5 years (28-55). Twenty four Maxi Z implants were used; each patient received two implants placed bilaterally in healed bony sites in the posterior maxillary area after the addition of platelet-rich plasma in one side while the other side was used as a positive control. All implants were immediately loaded after implant placement. **Results:** Complete soft tissue healing had occurred in all patients and all the implants were successfully osseointegrated over the twelve months follow-up period with a success rate of 100%. The results of the present study showed that there was no statistical difference between the two sides (test + control) regarding PD, MBI, MPI, implant mobility, crestal bone resorption and bone density through the twelve months. **Conclusion:** The Osteocare's Maxi Z one-piece, self-tapping self-drilling implant has shown high success rate regarding initial stability and successful osseointegration. However, within the limitations of the present study, 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 resorption "through first three months period" in immediately loaded dental implant placed in posterior maxillary area.

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1. Introduction:

Through a history of nearly 50 years, dental implants have gained a high reputation due to their high success rate, (***Buser et al 1997***). It was proposed according to ***Branemark et al (1985)*** that having successful tissue integration needs a two-stage surgical protocol and an undisturbed healing period of at least three to six months. The immediate loading protocol is being recognized as an alternative technique to the classical delayed loading approach. Immediate nonfunctional prosthetic restoration which does not seem to affect the process of osseointegration has proven to be more effective ***(Pillar et al 1986; Brunski 1992 and Nkenke et al 2005).***

PRP gel is an autologous modification of fibrin glue. It is formed by mixing PRP derived from centrifugation of autologous whole blood with thrombin and calcium chloride. PRP gel includes a high concentration of platelets and a native concentration of fibrinogen. When platelet concentrate is activated by the addition of thrombin and calcium chloride this results in the release of a cascade of growth factors from the platelet alpha granules, ***(Whitman et al 1997 and El-Sharqawy et al 2007).*** The osseointegration of dental implants arises from cell migration, differentiation, bone formation and bone remodeling along the implant surface, each of these processes is platelet-and blood clot- dependent. Therefore, PRP can be used to enhance osseointegration in patients whose osseointegration may be less predictable such as the elderly, individuals with osteoporosis, diabetics or

other forms of compromised regeneration, as well as, in the posterior maxillary area ***(Monov 2005).***

Kim et al 2002 assessed the efficacy of demineralized bone powder (DBP) alone or combined in a mixture with platelet-rich plasma to enhance osseointegration of dental implants in dogs. Histo-morphometric results revealed a higher percentage of bone contact with DBP and PRP compared with control and DBP alone. ***Zechner et al (2003)*** evaluated histologically and histo-morphometrically the effect of topical application of PRP during implant placement on local bone formation in 12 adult mini-pigs. Un-decalcified ground sections were prepared at 3, 6 and 12 weeks after PRP and implants placement and histo-morphometric results showed a significantly more bone-to-implant contact at the sites with topical PRP application during the early healing phase.

Duka et al (2008) tested the influence of PRP combined with bovine deproteinized bone BDB and resorptive membrane of bovine origin RBDM on the bone defect filling and level of bone resorption during early implant insertion in 10 dogs. Radiologic analyses were done immediately and 10 weeks after the insertion. Bone defect filling was measured by a graduated probe 10 weeks after the implant insertion**.** The results showed that the use of PRP combined with BDB and RBDM have a positive effect on increasing the bone defect filling and decreasing the level of bone resorption around early inserted dental implants. On the other hand, ***Nikolidakis et al (2006)*** evaluated the effect of local application of autologous platelet-rich plasma on bone healing around titanium implants with two different surface configurations. PRP fractions were obtained from venous blood sample of 6 goats and applied via dipping of the implant in PRP liquid before insertion. The evaluation of the bone mass close to implant surface indicated that all the groups induced a significant increase of the bone mass except the PRP gel groups. So, the additional use of PRP did not offer any significant effect on the bone response to the implants. The same was observed with ***Gurgel et al (2007)*** in experimental study on ten male adult mongrel dogs, who evaluated histometrically bone healing in surgically created dehiscence-type defects around titanium implants treated with an association of platelet-rich plasma and guided bone regeneration. Within the limit of this study it was concluded that PRP does not exert additional effects on the bone healing.

In a human study by ***Mannai (2006)*** who studied the re-construction of the maxilla in ninety-seven consecutive patients with the simultaneous placement of implants combined with a small amount of intraoral autogenous bone providing the necessary viable stem cells and a larger amount of xenogenic bone used as a scaffold and a purely autologous platelet concentrate for optimal bone formation. A total of 314 implants, sand blasted acid-etched type were placed simultaneously in the anterior, posterior or both parts of the maxilla. 97.8% of all cases healed uneventfully with excellent hard and soft tissues healing. Bone maturation was excellent at 3 months as seen on x-rays and CAT scans. The same with ***Lee et al (2008)*** who evaluated dental implant survival rates using the concept of a nonfunctional, immediate loading protocol with non splinted dental implants in the grafted maxillary sinus during a 52-week period. Random histo-morphological analysis was completed to evaluate the early healing effect of platelet-rich plasma and 50% autogenous bone combined with three different substitute graft materials in a 50:50 composite ratio. During the 52-weeks observation period, no implants were lost. Between 4 to 8 months of graft healing time, histological and histo-morphometrical analysis revealed formation of new vital bone in different graft specimens ranging from 77% to 100%. The results of this clinical study indicate that immediate nonfunctional loading with the use of PRP combined with bone graft is a predictable protocol.

On the other hand, a randomized prospective controlled study was done by ***Schaaf et al (2008)*** to verify the effect of adding platelet-rich plasma on bone density in the maxilla after sinus floor elevation in combination with autologous bone. Bone biopsy was performed 4 months after augmentation. The results of histo-morphometric evaluation of the biopsies showed that the topical use of PRP did not improve the maxillary bone volume either clinically or statistically when compared with the conventionally treated patients.

2. MATERIALS AND METHODS:

2.1. Materials:

2.1.1. Subjects:

The present study was conducted on 12 patients; 9 males (75%) and 3 females (25%) with a mean age of 37.5 years (28-55). All patients were in acceptable general health having no systemic disease that contraindicates surgery. patients had favorable oral hygiene and motivation to provide a reasonable

prognosis for long-term benefit from the implant and each patient had bilateral posterior (premolar or molar) maxillary edentulous area suitable for implant placement.

The study was performed according to the split-mouth design. The posterior area of the upper arch of each patient was divided into:

Experimental side(A): Implant placed in healed bony site with the addition of PRP.

Control side (B): Implant placed in healed bony site without PRP. One side was randomized to be the control side while the contralateral site served as the experimental one. The implants were non-functionally immediately loaded.

2.1.2. Preparation of platelet-rich plasma PRP:

Adequate amount of blood was drawn from each patient by veni-puncture of the anticubital vein. Blood was collected into glass test tubes that contained 10% trisodium citrate solution as an anticoagulant. The blood containing glass tubes were centrifuged at 2,500 rpm for 10 minutes, which resulted in the separation of three basic components: Platelet poor plasma PPP in the top, PRP in the middle and then RBC layer in the base of the test tube. The PPP layer was aspirated and discarded. Then the remaining plasma was collected and a second centrifugation (15 minutes at 3600 rpm) was performed to concentrate the platelets. At the time of the application, a sterile syringe was used to aspirate 1cm3 of PRP, 1cm3 of sterile saline solution containing 10% calcium chloride (a citrate inhibitor that allows the plasma to coagulate) and 100 U/mL of sterile human thrombin and 1cm3 of air. Adequate mixing was done to initiate the coagulation process. Then the needle was removed and the PRP gel was slowly injected. Cell count for the platelet cells was done before and after centrifugation

2.1.3. Implant System:

Twenty four Osteo Care™ Maxi Z one-piece implants (Osteo Care™ Implant System, London, United Kingdom) were placed in twelve patients who participated in this study. They were tapered self-tapping self-drilling implants and available with diameters of 3.30, 3.75, 4.50 and 5.50 mm and lengths of 11, 13, 15 and 17mm. Maxi Z one-piece implant was designed to allow immediate loading in healed bone sites and allows simultaneous expansion and compression of the bone in a process thus called "Comp-Ex procedure" which in turn improves bone quality and overall width. The Maxi Z one-piece were placed with a minimally invasive trans-mucosal flapless procedure and had a tapered pointed tip. The Maxi Z one-piece implant was machined from titanium alloy of 6AL-4V ELI (Extra Low Interstitial) to provide maximum strength and incorporates both the implant body and the abutment in a single component. The surface treatment of the implant is GBA (Grit-Blasted and Acid Etching) to create macro and micro roughness enhancing the osseo integration and improving the bone to implant contact. Also presented with a unique "Buttress" thread design that allows a maximum bone to implant contact and achieving higher initial stability even in poor bone quality. The Maxi-Z one piece also had an anatomical abutment design with double flat facets to minimize the time needed for the preparation and to improve the retention of the provisional as well as the final restoration.

2.2. Methods:

2.2.1. Preoperative measures:

All patients received instructions in self-performed plaque control measures and were subjected to a series of full mouth scaling and root planning using curettes and ultrasonic instrumentation. Pre-surgical radiographic evaluation was performed by obtaining panoramic radiographs and periapical radiograph on the area of interest. The preoperative radiographs were used to confirm the diagnosis and estimate the implant length using the radiographic stents. The ridge width was evaluated using the diagnostic casts, ridge mapping or directly in the patient's mouth using bone calipers**.**

2.2.2. Surgical Technique:
(Flapless Trans-mucosal Technique)

Osteotomy preparation: Implant surgery were performed under local anesthesia Ultra-caine D-S forte containing 1:200000(0.5mg/ml) epinephrine. In each patient site preparation and implant placement was done bilaterally in two healed bony sites. No incisions or flap was made. Osteotomy preparation was carried out through free hand flapless trans-mucosal drilling. Osteotomy preparation was done sequentially using 1.3mm profile pilot drill, 2.2mm drill and 2.75mm drill. The drills were mounted on a low speed reducing hand piece and saline was used for irrigation. One piece implant was used in both test sites (implant with PRP) and control sites (implant without PRP). In the test sites, the prepared PRP was slowly injected at low pressure into the drill holes

immediately before implant placement. In addition, the implant was dipped in PRP before seating.

Implant placement: The implant was removed from its protective pouch and held using the attached plastic carrier then placed into the prepared site. The implant was rotated clock wise for several revolutions until a resistance was met. The plastic carrier was removed and the ratchet wrench with the 2.4mm overhex driver was used for complete seating of the implant into its final position (the coronal part of the collar of the implant was flush or below the cestal bone of the alveolar ridge). After that, the initial stability was checked using the 30N/cm torque wrench. Attaining primary stability of over 30N/cm was considered crucial with all the placed implants to allow for the immediate loading protocol. Finally, a periapical radiograph was taken to check the final implant position and to estimate the initial bone level around the implant.

2.2.3. Abutment preparation and provisional restoration: Immediately after implant placement, the abutment was prepared using carbide burs with copious water irrigation to avoid overheating. Then, a temporary crown of either acrylic resin, composite or readymade acrylic temporary crown was fabricated. The provisional crown was cemented to the prepared abutment of the Implant and adjusted to be completely out of functional occlusion in centric and eccentric position. The patients were instructed to eat soft food for 2 months and to avoid direct biting on the provisional restoration.

2.2.4. Post-operative care: Oral antibiotic regimen of Augmentin 1 gm (Glaxo Wellcome Smith Kline Beecham)was given every 12 hours for five days following the procedure. NSAIDs were prescribed for one week to prevent post-surgical pain.

Final restoration: The provisional acrylic resin restorations were removed after a healing period of 6 months. The prepared abutments were treated as a normal crown and bridge case; full-arch rubber base impressions were made using the conventional impression technique. The final porcelain-fused-to-metal restorations were constructed and then delivered after few days and cemented permanently using zinc phosphate cement after being checked for shade matching, marginal fitness and occlusion.

2.2.5. Post operative measures and evaluations:

2.2.5.1. Clinical records:

- Peri-implant soft tissue health according to ***Mombelli et al 1987*** was measured by the following parameters which were recorded for each implant in each patient at 6 months and 12 months post operatively: Modified bleeding index (MBI), Modified plaque index (MPI) and Peri-implant probing depth (PD).
- Implant mobility was tested using the Periotest M (Medizintechnik Gulden, Bensheim, Germany), records were taken immediately post operatively then at three, six and twelve months post operatively.

2.2.5.2. Radiographic evaluation: Stadardized periapical x-rays films were taken immediately after implant insertion, three, six and twelve months post operatively to detect: 1) Marginal bone level. 2) Change in bone density around the implant.

2.2.5.3. Statistical evaluation: Analysis of data was performed using SPSS 17 ® (Statistical Package for Scientific Studies) for Windows. Description of variables was presented as follows: - Description of quantitative variables was in the form of mean, standard deviation (SD). Data were explored for normality using Kolmogorov-Smirnov test of normality. The results of Kolmogorov-Smirnov test indicated that most of data were normally distributed (parametric data) so parametric tests were used for the comparisons. - Comparison between quantitative variables was carried out by student T-test of two independent samples. As well as paired T-test for dependent samples. Results were expressed in the form P-values. The significance of the results was in the form of P-value that was differentiated into: * Non-significant when P-value > 0.05 *, significant when P-value ≤ 0.05 * and highly significant when P-value ≤ 0.01.

3. Results:

3.1. Complete soft tissue healing had occurred in all patients without any postoperative inconvenience during the study period.

3.2. Six patients experienced no postoperative pain, five patients had mild pain while only one patient had moderate pain. Minimum need for analgesics was reported for all patients.

® SPSS, Inc., Chicago, IL, USA.

3.3. The 24 Maxi Z implants were successfully osseointegrated as revealed by the clinical and radiographic examinations.

3.4.**Clinically:**

The statistical analysis comparing test and control sites at 6 and 12 months revealed no significant differences between them regarding any of the following clinical parameters : Modified bleeding index, Modified plaque index and Peri-implant probing depth.

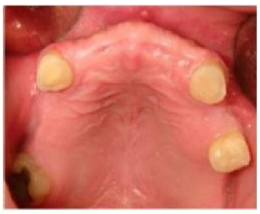

Fig. (1): Pre-operative clinical photograph

Fig. (2): PRP gel.

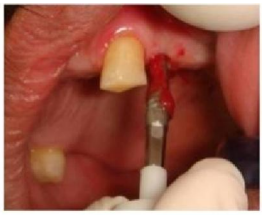

Fig. (3): Manual placement of the implant (test side).

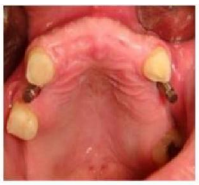

Fig. (4): Clinical photograph showing the implants at both sides immediately after placement.

Immediately post-operative, the mean and standard deviation values of PTMV were -2.23±0.62 at the PRP site and -2.14±0.52 at the control site. There was no statistically significant difference between the means of PTMV at the two sites (P-value = 0.699). ***At 3 months follow-up period,*** the mean and standard deviation values of PTMV were -2.91±0.62 at PRP site and -2.80±0.60 at the control site. There was no statistical significant difference between the means of PTMV at the two sites (P-value = 0.669). ***At 6 months follow-up period,*** the mean and standard deviation values of PTMV were -3.51±0.57 at PRP site and -3.44±0.38 at the control site. There was no statistically significant difference between the means of PTMV at the two sites (P-value = 0.740). ***At 12 months follow-up period,*** the mean and standard deviation values of PTMV were -4.04±0.74 at PRP site and -3.89±0.55 at the control site. There was no statistically significant difference between the means of PTMV at the two sites (P-value = 0.580).

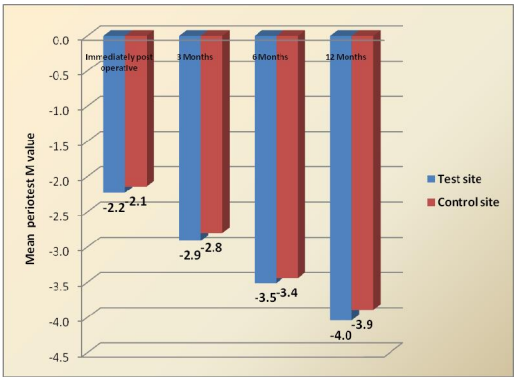

Figure (5): Mean periotest M value of both sites

3.5. Radiographic evaluation:

Results revealed that ***at 3 months follow-up period,*** the mean and standard deviation values of crestal bone resorption were 0.57±0.29 mm at the PRP site and 0.60±0.30 at the control site. There was no statistically significant difference between the means of crestal bone resorption at the two sites (P-value = 0.839). ***At 6 months follow-up period,*** the mean and standard deviation values of crestal bone resorption were 0.68±0.29 mm at PRP site and 0.69+_0.30 mm at the control site. There was no statistically significant difference between the means of crestal bone resorption at the two sites (P-value = 0.913). ***At 12 months follow-up period,*** the means and standard deviation values of crestal bone resorption were 0.70±0.30 mm at PRP site and 0.72±0.30 mm at the control site. There was no statistically significant difference between the means of crestal bone resorption at the two sites (P-value = 0.866).

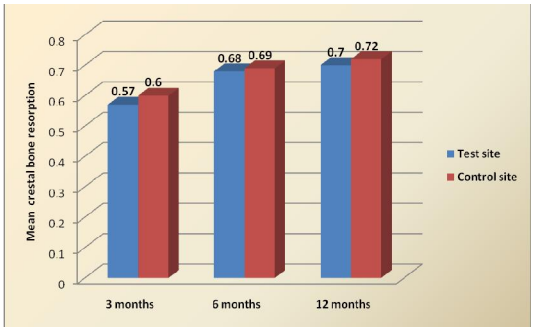

Figure (6): Mean crestal bone resorption scores of both sites

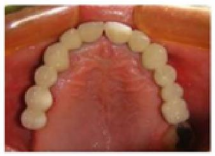

Fig. (7): Final ceramo metal restoration.

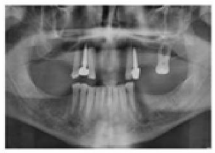

Fig. (8): Immediate post-operative panoramic x-ray.

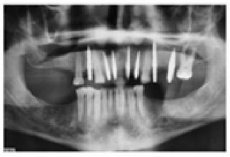

Fig. (9): 6 months post-operative panoramic x-ray.

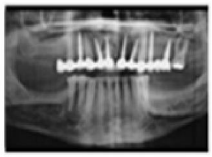

Fig. (10): 12 months post-operative panoramic radiograph

Immediately post-operative, the mean and standard deviation values of bone density were 88.36±5.02 at the PRP site and 88.42±4.92 at the control site. There was no statistically significant difference between the means of bone density at the two sites (P-value = 0.978). ***At 3 months follow-up period,*** the mean and standard deviation values of bone density were 75.61±4.26 at PRP site and 75.95±4.32 at the control site. There was no statistically significant difference between the means of bone density at the two sites (P-value = 0.847). ***At 6 months follow-up period,*** the mean and standard deviation values of bone density were 78.44±3.76 at the PRP site and 77.35±4.12 at the control site. There was no statistically significant difference between the means of bone density at the two sites (P-value = 0.507). ***At 12 months follow-up period,*** the mean and standard deviation values of bone density were 81.84±4.56 at PRP site and 80.73±4.21 at the control site. There was no statistically significant difference between the means of bone density at the two sites (P-value = 0.544).

Discussion:

In implant dentistry it was proposed according to ***Branemark et al (1985)*** that having successful tissue integration needs a two-stage surgical protocol and an undisturbed healing period of at least three to six months. The rationale for this recommendation was that premature loading may prevent direct bone apposition and may lead to fibrous tissue encapsulation and clinical failure. The immediate loading protocol is being recognized as an alternative technique to the classical delayed loading approach. Immediate nonfunctional prosthetic restoration which does not seem to affect the process of osseointegration has proven to be more effective ***(Pillar et al(1986); Brunski (1992) ; Nkenke et al(2005).***Immediate loading protocol has obvious advantages for the patient by decreasing the treatment time and reducing the number of surgical interventions. Both function and esthetics can be immediately restored with the temporary restoration ***(Fischer 2008).***

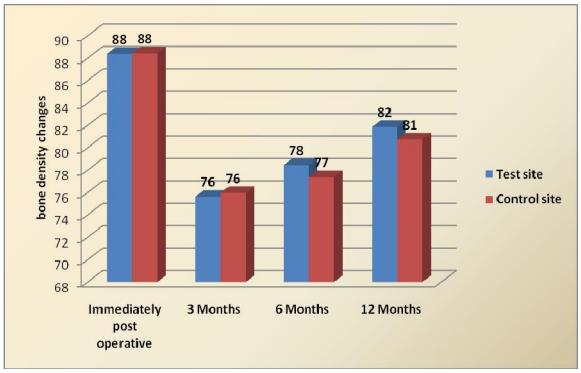

Figure (11): Mean bone density changes of both sites

The drawbacks of the two-piece implants system that was reported by ***Hahn (2005)*** included the structural weakness at the implant abutment junction and the need to remove the healing abutment to replace it with the final one which adds complexity to the procedure and affect the already healed gingival tissues. All these were avoided in the present study by using the one-piece implant. No complications were reported with the use of one-stage surgical technique which corresponds well with other reports on similar treatments as ***Ericsson et al (1994)***.

Platelet-rich plasma (PRP) is an autologous source of high platelet concentrate and native fibrinogen to support bone and soft- tissue healing. It is obtained by sequestering and concentrating platelets using gradient density centrifugation. A blood clot is the centre focus of initiating any soft tissue healing and bone regeneration. In all natural wound, a blood clot forms and starts the healing process. PRP is a simple strategy to concentrate platelets or enrich natural blood clot which forms in normal surgical wounds to initiate a more rapid and complete healing process

Raja and Naidu (2008). Activation of the PRP is done by mixing it with thrombin and calcium chloride which results in the release of a cascade of growth factors from the platelet alpha granules. The growth factors are a diverse group of polypeptides that have important roles in the regulation of growth and development of a variety of tissues. They seem to signal the local mesenchymal and epithelial cells to migrate, divide and increase collagen and matrix formation (***Kim et al 2002 ; Sanchez et al 2003)***.

The present study was conducted to evaluate the effect of injecting platelet-rich plasma into the prepared drill holes "immediately before implant placement" on accelerating the rate of osseointegration or reducing the crestal bone resorption in immediately loaded dental implants placed in healed bony sites (posterior maxillary area). Twenty four implants were placed in twelve patients. Each patient received two implants (the test side with PRP and the control without) immediately loaded with a non-functional fixed temporary restoration for 6 months and left to integrate with the surrounding bone then replaced with Porcelain Fused to Metal final restorations. All the implants were successfully osseointegrated over the twelve months follow-up period with a success rate of 100%. Implants used in this study were Maxi Z one-piece (Osteo Care implant system, London, United Kingdom) self tapping, self drilling tapered dental implants with GBA (Grit-Blasted and Acid-etched) surface treatment to create macro and micro irregularities to enhance and fasten the process of osseointegration and to improve the bone to implant contact. Also the implant is presented with a unique "Buttress" thread design that allows a maximum bone to implant contact to achieve higher initial stability even in poor bone quality. The Maxi Z one-piece implant is designed to allow for immediate loading in healed bone sites as well as in immediate post extraction cases. It is placed in under-sized osteotomy and modifies the quality of bone by condensation thus enhancing the process of osseointegration ***(Zahran et al 2010).***

In the present study Soft tissue healing was generally uneventful in all patients included in this study. At six and twelve months follow-up period none of the patients suffered from pain or peri-implant infection, all implants were found to be successfully osseointegrated without any signs of peri-implantitis. Clinical parameters were measured at 6 months and 12 months at both sides in each patient. There was no statistically significant difference between means of (MBI), (MPI) and (PD) at test and control sides. The mobility of all implants in this study was measured using the Periotest M. It proved to be a valuable gadget for the numerical evaluation of the initial stability of the implants at the time of insertion as well as for assessment of osseointegration at the follow-up times. It could replace the torque wrench as a tool of measuring the initial stability which is not available in the surgical kits of many implant systems. The Periotest M gave more precise readings than the classical Periotest as it measures in a decimal number. This apparatus is widely used to assess implant outcome and provides a measurement of the implant reaction to a defined impact load which is used for the assessment of primary stability, ***(Tricia et al 1995;Fischer 2008 ; Alsaadi 2008).*** During the study period none of the implants showed any signs of clinical mobility and Periotest measurements were taken immediately after placement (baseline) and then at 3, 6 and 12 months postoperatively. Periotest mean values for the test sides (PRP) were immediately post-operatively -2.23, -2.91 at 3 months, 3.51 at 6 months and -4.04 at 12 months. At the control sides the Periotest mean values were -2.14 immediately post-operative, -2.80 at 3 months, -3.44 at 6 months and -3.89 at 12 months. There was no significant difference between the mean Periotest values for both the test and control sides at the base line, 3 months, 6 months and at 12 months follow up period.

The radiographic parameters in this study included measuring the crestal bone loss and bone density changes around the implants. Regarding the bone loss, on initial examination at the third month postoperatively (baseline readings) the mean radiographic bone loss for the test sites was 0.57 then at the sixth month 0.68 and at the twelfth month 0.70. While in the control sites the mean radiographic bone loss at the third month postoperatively was 0.60 and then at the sixth month 0.69 and at the twelfth month the mean radiographic bone loss was 0.72. There was no statistically significant difference between mean crestal bone resorption scores around implants in both test and control sides at 3 months or at 6 and 12 months postoperatively. However, the increase in the crestal bone resorption from the baseline till twelve months in both the test and control sides of all implants throughout the study was considered normal and met with the results of many studies done by ***Drago and Lazzara (2004) ;and Jaffin et al (2007); Andersen et al(2002)*** reported 100% success of immediately loaded implants with mean crestal bone level 0.53 mm over 12 months period. The results of

this study also coincide with the results of ***Thor et al (2005)*** as they found no significant difference in the marginal bone level measurements and clinical function of dental implants after one year of loading their implants in the maxilla whether or not PRP is added. An overall survival rates of 98.7% was obtained in this study. According to ***Olsson et al (1995)*** the self-tapping implant is a design modification that is specifically designed to be used in poor bone quality (as the posterior maxillary area). When the self-tapping implant is inserted the denser cortical bone is compressed leading to the increase in primary stability. Primary stability is a prerequisite and indicator for having adequate osseointegration ***(Adell et al 1981; Meredith 1998 ;Friberg et al 1999a)***.

In the current study, all implants attained high initial stability over 30N/cm which may be due to their tapered design, buttress threads and under-dimensioned drilling. It was reported by ***O'Sullivan et al(2000) ; Sakoh et al (2006)*** that tapered implant design in combination with undersized drilling could lead to higher initial stability than conventional implants. ***Monov et al (2005)*** concluded that if the primary stability is high, it seems that the healing process has only little influence on future implant stability, so even the instillation of PRP into the drill holes of the fixtures will not show any additional effect. This was in agreement with our present study as there was no significant difference in the bone densities changes around the implants at both sides (the test and the control sides). Immediately post-operatively the mean bone density measurement around implants at the test sites measured 88.36 then at three months post-operatively it was 75.61 then at six months post-operatively it was 78.44 and finally at twelve months post-operatively it was 81.84. At the same time the mean bone density measurement around implants at the control sites measured 88.42 immediately postoperatively, then it was 75.95 at three months postoperatively. At six months postoperatively the mean bone density measured 77.35 and finally at twelve months postoperatively it was 80.73. The addition of PRP into the drill holes immediately before implant placement did not fasten the rate of osseointegration during the first three months period. At the same time the level of crestal bone resorption was the same in the test and control sides.These results were in agreement with ***Froum et al (2002) ; Thor et al(2005)*** as they evaluated the efficacy of platelet-rich plasma on bone growth and osseointegration and found no positive effect after adding PRP.

On the other hand, the results of our study were in contrast to the finding of ***Lynch et al (1991) ; Zechner et al (2003)*** who found that the growth factors presented in PRP have a statistically significant positive effect on bone regeneration and implant-to-bone contacts. Also the clinical studies by ***Marx et al (1998); Anitua (1999) ;Sykaras et al (2001)*** have shown that the local application of PRP increased the amount of peri-implant newly formed bone and its density.The same positive effect of using PRP occurred in a clinical study by ***Lee et al (2008)*** using immediate nonfunctional loading implants in the maxilla during a 52-weeks period. There high implant survival rate 77% to 100% was due to the early formation of large percentages of new vital bone with the help of PRP addition as confirmed by using histologic and histo-morphometric analysis. The appropriate concentration of platelets in PRP is an important issue that must be analyzed. The platelet counts of PRP in the present study were in the expected range and correspond to the values described by ***Weibrich et al (2004)*** who added- PRP in peri-implant bone defects and concluded that a concentration of 1 million platelets/ ML is the most productive concentration for bone healing. This concentration was confirmed by other studies who found that the most regenerative concentration of platelets in PRP in both humans and animals is 1 million platelets/ ML and a viable platelet concentrate levels of 400% to 600% above baseline is necessary to achieve optimal bone and soft tissue healing, ***(Marx et al 2002; Kim et al 2002b).*** In the current study, the mean donor platelet counts from whole blood had a value of 224.000-+ 35.653 / ML, this value was in comparable with the mean value of 260.300 / ML from the ***Weibrich et al (2002)*** study. Platelet counts in the PRPs had a mean value of 1025.000 -+ 58.547/ ML, which is comparable with the mean value of 908.500/ML found by the same study**.** At the same time the mean platelet count increased in this study by 4.58 folds after centrifugation which was within the range obtained by other several studies ***(Marx 2001; Marx et al 2002 ; Rodriguez et al 2003).*** It was found that if the platelet concentration in the PRP is lower than 4-6 folds of the baseline, the effect of PRP is suboptimal, while higher concentration might have inhibitory effect ***(Floege et al 1991 ; Pollard 2001).*** However, recently ***Smith et al (2009)*** found that using the triple spin technique to gain platelets concentrate of 23 times the baseline is more effective to increase the bone height and quality for optimum endosseous implant placement.

The explanation for our results and for the absence of significant changes in bone density or crestal bone resorption after the addition of PRP may be attributed to the simultaneous effect of bone trabeclua compression that occurred around both the test and control sides implants with the use of self-tapping, self-drilling implants or due to the fact concluded by ***Nazaroglou et al (2009)*** who found it truly difficult to predict the final concentration of platelets into the surgical region because of the bleeding from the bone. Bleeding from the gap might dilute the PRP and consequently the actual concentration of platelets would be less than what was expected. Furthermore, as the regenerative potency of PRP undoubtedly depends on its growth factors levels, it must be taken into consideration that the appropriate GF levels are not known yet. Recent studies observed differences in GF levels even in PRP samples with the same concentration of platelets, ***(Lartineau et al 2004 ; Frechette et al 2005).*** At the same time, the addition of PRP might have positive effect in bone with compromised healing capacity as in patients with diabetes or osteoporosis ***,Schaaf et al (2008)***. The strict case selection and using simple not complicated cases might hide the benefit effect from adding PRP. Another characteristic of PRP is the influential time in which its growth factors would exert their effect. Some scientists found that this influential time is up to 2 months, while others concluded that the effect of PRP lasts only for a few days. Taking into consideration that the main part of osteogenesis takes place in the first month after surgical procedure and bone is removed and formed with more fast rate for the first 6-7 months, it is obvious that if the effect of PRP can be prolonged, its use can be considered as serviceable. Reversely, if PRP action lasts for only a few days, it can be concluded that this technique is not as beneficial as many believe ***(Marx et al 1998; Butterfield et al 2005;Raghoebar et al 2005; Gerard et al 2006 ;Thor et al 2007).*** The potential of PRP to promote soft and hard tissue healing is accepted without doubt due to the biological characteristics of the released growth factors and their effect on human tissues (haemostasis, creation of new vascularity, production of collagen matrix, migration, proliferation and differentiation of epithelial and osteoproductive cells) ,***Schaaf et al (2007).*** However, it is obvious that more studies are needed on the physical, biological and biochemical features of platelets, optimal concentration of PRP and growth factors levels, interactions between the growth factors and to find the actual duration of PRP's effect which simultaneously indicates the duration of the regenerative potency of platelet's growth factors necessary to enhance bone formation around endosseous dental implants.

Conclusion

Within its limits, the present study has shown that the 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 resorption "through first three months period" in immediately loaded dental implant placed in posterior maxillary area.

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