Bone density and implant stability with advanced platelet-rich fibrin in immediately loaded-implant assisted mandibular overdentures

Densidade óssea e estabilidade dos implantes com fibrina rica em plaquetas avançada em overdentures mandibulares com carga imediata

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ABSTRACT

Objective: The aim of this study is to determine the effect of Advanced Platelet-Rich Fibrin on bone density and implant stability in immediately loaded-implant-assisted mandibular overdentures (Split-mouth study).

Material and Methods: Ten completely edentulous patients received two implants in the mandibular canine region and locator attachments were used to retain immediately loaded-implant mandibular overdentures. Each patient served in two Groups, one Group for each side. One side of the mandible received an implant with topical application of Advanced Platelet-Rich Fibrin in the implant osteotomy site (Group I) and the other site received an implant without application of Advanced platelet-rich fibrin (Group II). Each patient was examined clinically for implant stability using Osstell Mentor device and radiographically by ultra-low dose CT scan to measure bone density around the implant at baseline, three, six months, and one year. Results: There were no statistically significant differences (P>.05) in bone density and implant stability among the studied Groups during one year follow-up period. Conclusion: Advanced Platelet-Rich Fibrin has no effect on bone density and implant stability in immediately loaded implant-assisted mandibular overdenture.

KEYWORDS

Advanced platelet-rich fibrin; Bone density; Immediately loaded implant; Implant stability; Locator attachment; Mandibular overdentures.

RESUMO

Objetivo: O objetivo deste estudo é determinar o efeito da Fibrina Rica em Plaquetas Avançada na densidade óssea e estabilidade dos implantes em Overdentures mandibulares com carga imediata (estudo de boca dividida).

Material e Métodos: Dez pacientes edêntulos foram submetidos à instalação de dois implantes mandibulares na região dos caninos e pilares locator foram utilizados como sistema de retenção para as overdentures mandibulares com carga imediata. Cada paciente participou nos dois grupos, sendo um grupo para cada lado. Um lado da mandíbula recebeu implante com aplicação tópica de Fibrina Rica em Plaquetas Avançada no local do sítio cirúrgico do implante (Grupo I) e o outro local recebeu implante sem aplicação de Fibrina Rica em Plaquetas Avançada (Grupo II). Cada paciente foi examinado clinicamente quanto à estabilidade do implante usando o dispositivo Osstell Mentor e radiograficamente por tomografia computadorizada de ultrabaixa dose para medir a densidade óssea ao redor do implante no início do estudo, três, seis meses e um ano. Resultados: Não houve diferenças estatisticamente significativas (P>0,05) na densidade óssea e na estabilidade do implante entre os
INTRODUCTION

Mandibular dentures pose challenges related to poor stability and retention [1]. Dental implants have greatly improved outcomes of treatment in an edentulous patient. In many developed countries, the two-implant for the mandibular overdenture is considered a minimum standard of care [2]. Mandibular implant overdenture has many benefits such as; improving stability, retention, chewing ability, speaking, and decreasing the resorption of the residual ridge [3].

Various loading protocols for dental implants have been studied. Immediate loading protocol may reduce some patient burdens such as multiple visits, costs, waiting for the final restoration, inconvenience, and morbidity related to multiple surgical phases [4,5]. Many attachments were used according to inter-arch space. Locator attachments were indicated in cases of limited inter-arch space and provided an adequate means of retention in such cases [6]. Besides, the common challenges of immediate loading, the repeated removal of overdenture may be detrimental to early osseointegration. The healing phase after implant installation is a critical phase for immediate loading protocol so it must be carefully monitored [7].

The Osseointegration of dental implants is defined as the apparent direct attachment or the connection of osseous tissue to an inert, alloplastic material without intervening fibrous connective tissue [8]. The biological fixation of the implant is an early formation of peri-implant bone trabeculae, which confirms tissue anchorage. Biological fixation is different from primary stability. Implant primary stability is a mechanical fixation, which is obtained during the insertion of the implant. Secondary stability is biological stability obtained by bone regeneration and remodeling [9].

There are several procedures to improve osseointegration such as the application of Bone morphogenetic proteins, Melatonin, and Advanced-Platelet-Rich Fibrin (A-PRF). Bone morphogenetic proteins are the growth factors that are naturally found within the bone matrix and they play a role in the regulation of bone volume and bone regeneration. The applications of recombinant human bone morphogenetic proteins onto the implant surface before threading the implant into the osteotomy site may improve osseointegration and implant stability [10].

Melatonin hormone stimulates the synthesis of type I collagen fibers and acts on osteoclasts to reduce the resorption of the osseous matrix. Local administration of melatonin in the osteotomy site increases bone density and improves the osseointegration processes around immediate-loaded implant supported overdentures [11].

A-PRF is the last generation of platelet concentrates. Platelet concentrates are autologous biological products generated from the blood of patients and are rich in platelets and growth factors (GFs). Soft and hard tissue regeneration can be improved by using platelet concentrates alone or as an adjunctive treatment in dentoalveolar and maxillofacial surgeries [12,13].

Bone density can be measured by Hounsfield Unit (HU), which is the calibrated grey value. HU is relatively consistent across different Multi-Detector Computed Tomography (MDCT) scanners, unlike CBCT. In addition, the calibration of HU is an integrated part of quality control in MDCT. Ultra-low dose- CT examination of the jaws may decrease the effective dose to be equal to the full mouth examination utilizing intra-oral films [14,15].

Resonance frequency analysis (RFA) is a noninvasive-diagnostic system, which can measure implant stability through structural and vibration principle analysis. RFA is simpler, more objective, and more reliable than the other noninvasive-diagnostic systems. Based on RFA, Implant stability quotient (ISQ) values are displayed on Osstell apparatus for measuring implant stability [16,17].
This study aimed to determine the effect of Advanced-Platelet-Rich Fibrin on bone density and implant stability in immediately loaded implant-assisted mandibular overdentures clinically and radiographically using Osstell and ultra-dose CTscan at baseline, three, six months, and one year. The null hypothesis of this study was that there was no effect of Advanced Platelet-Rich Fibrin on bone density and implant stability in immediately loaded -implant-assisted mandibular overdenture.

MATERIALS AND METHODS

Ethical considerations

The purposes of the study, the nature of implant surgery, possible risks, complications, the photography of the procedure, and the frequency of exposure to radiation were explained to the patients. Informed consent was obtained according to guidelines on human research adopted by the Research Ethics Committee, Faculty of Dentistry, Tanta University which approved the performance of this study after fulfilling the necessary requirements of the committee with code # RP-2-20-3.

Sample size calculation

The total sample size in this study is ten patients based on the data taken from a previous study which evaluated clinically and radiographically the effect of leukocyte platelets-rich fibrin (L-PRF) on the stability and crestal bone resorption of early loaded implants [18]. The significance level was 0.05, the power sample size was more than 0% for this study and the confidence interval was 95% and the actual power was 96.08%. The sample size was calculated using a computer program G power version 3.

The formula for sample size was:

\[ \text{Sample Size} = \frac{Z^2 \times P \times (1-P)}{c^2} \] (1)

where: \( Z = Z \) value (1.96 for 95% confidence level); \( p = \) percentage picking a choice, expressed as decimal; \( c = \) confidence interval, expressed as decimal.

Patient selection

Ten completely edentulous patients (age Group 50-65 years) were selected from the outpatient clinic of the Department of Prosthodontics, Faculty of Dentistry, Tanta University, to participate in this study. Inclusion criteria were that the patients were free of any systemic diseases that affect bone and soft tissue healing, and had normal maxilla-mandibular relationships with limited inter-arch space where locator attachments were indicated. The mandibular intercanine region had sufficient bone to be appropriate for the planned implants. The patients had the psychological and physical ability to tolerate implant surgery. Exclusion criteria were a history of chemotherapy or radiotherapy, para-functional occlusal habit, bad oral hygiene, and heavy smoking. These factors have adverse effects on osseointegration and this study aims to clarify the effect of A-PRF on bone density and implant stability without risk factors. The selected criteria were reported. Five patients with these selected criteria came to the Department of Prosthodontics every month. Opaque-sealed envelopes were used for simple randomization of the subjects.

Study design

This study was a split-mouth study; for each patient, two dental implants were inserted in the mandibular inter-foraminal area at the canine region. Each patient served into two Groups, one Group for each side. One side of the mandible received an implant with topical application of A-PRF in the implant osteotomy site (Group I) and the other site received an implant without application of A-PRF (Group II). The trial was triple-blinded as patients did not know which side A-PRF inserted into also observer/radiologist and statistician were blinded.

Surgical and prosthetic procedure

Conventional complete denture was constructed and was delivered for each patient. Duplication of the lower denture was made for the construction of a radiographic stent. Pre-operative CBCT with radiographic stent was obtained for each patient to evaluate the ridge width, height, bone quality, and quantity at canine regions of mandible [19].

The radiographic stent was modified for use as a surgical guide for freehand drilling by removing the lingual flange and leaving the labial flange in the anterior region. Before the
operation, it was kept in 2% glutaraldehyde for 24 hours [20].

Pre-operative medications were prescribed for all patients. Augmentin1g cap (Augmentin cap, GlaxoSmithKline, England) was prescribed every 12 hours before the operation and one week after surgery. Patients were motivated to maintain good oral hygiene and instructed to use 0.12% Chlorohexidine mouthwash before surgery.

The non-limiting surgical guide was inserted to identify the implant site and was then removed. Bard-barker blade no.15 was used to make crestal incisions one cm mesial and distal to the planned implant site. A mucoperiosteal elevator was used to reflect the flap. A bone file was used to flatten the crestal bone and smooth any sharp bone edges.

For each patient, two dental implants (Superline, Dentium Medical Devices Tec. Company, Korea) were inserted in the mandibular canine region. The implants were 3.6 mm in diameter and 12 mm in length.

The protocol [20] for implant osteotomy site preparation:

1- The pilot drill (diameter 2.2 mm) was used to initiate the drilling in vertical direction with moving-up and down. A reduction handpiece and electric motor at speed of 2000 rpm (for D1 and D2) were used with copious amounts of chilled saline external irrigation until reached the length of 9 mm at both osteotomy sites;

2- The paralleling pins were used to detect the parallelism and alignment of the osteotomy sites. Drilling was completed until reached 12 mm depth;

3- The second drill (diameter 2.6 mm) and final shaping drill (diameter 2.85 mm for 3.6 mm fixture) were used for widening the osteotomy. The Countersink of diameter 3.6 was used in highly dense bone D1 and D2 mm for 3.6 mm fixture at about 8 mm length.

Meanwhile, the osteotomy site was prepared; Advanced PRF (A-PRF) was prepared by centrifuge a plain glass tube filled with 10 ml blood from patients’ brachial veins through laboratory mini-centrifuge (Centrifuge model no.800D, Delta Lab Company, China) for 14 minutes with a speed of 1500 rpm. Another glass tube of 10 mL of saline was used in the centrifuge in order to act as a counterbalance [21].

After centrifugation, A-PRF gel was at the top and erythrocytes were at the bottom. (Figure 1a) A-PRF membrane was obtained and was cut into small sections using sterile scissors. The membrane of A-PRF was laid on the orifice of the osteotomy site and was squeezed into the site by threading the implant into the site (Group I) (Figure 1b) However, the implants were installed directly in the osteotomy sites at the right side (Group II). The implants were installed into the osteotomy sites by screwdriver and then by hand ratchet until the implant platform became flushed with the bone (Figure 2).

Prior to immediate loading, implant primary stability was assessed by Osstell Mentor device (Osstell Mentor, Gothenburg, Sweden) (Figure 3). Primary stability is a significant factor for success of the dental implant and crucial with immediately loaded implants. The goal
of primary stability is keeping micromovement within accepted levels between 50 and 150 μm. Primary (mechanical) stability leads to reaching secondary (biological) stability. ISQ values above 65 are considered acceptable for immediate loading if they were not reached shifting to delayed loading were preferred [22,23].

Locator abutments (Positioner abutment, Dentium Medical Devices Tec. Company, Korea) were mounted into the implants. Each flap was repositioned and primary closure was carried by using interrupted 4-0 silk suture (Figure 4).

After surgery, Augmentin 1g every 12 hours and Ibuprofen 400mg every 8 hours were prescribed for one week. During the first 24 hours, patients were instructed to apply cold packs extra orally at the operative site. On the second day, they were instructed to use Chlorhexidine 0.12% mouthwash every 8 hours and rinse with warm saline until the first postoperative week ended. Patients were instructed to eat a soft diet and avoid hard food during the healing period. After one week, the sutures were removed.

Within two weeks post-operatively, the pick-up procedure for the immediate loading mandibular overdenture (Figure 5) was completed as follow: a white block-out spacer was adapted over the corresponding locator abutment. The Locator metal housing with processing insert was positioned over the locator abutment and was marked. The undersurface of the mandibular denture at the abutment sites was sufficiently relieved. Two small holes were made in the lingual surface of the denture to permit the escape of excess acrylic resin material through the pick-up procedure. The denture was tried to ensure complete seating. Locator metal housing was picked up to the undersurface of the lower denture using self-cure acrylic resin, while the patient occluded in centric relation. The block-out spacer was removed. Male nylon inserts replaced the processing inserts. These inserts were provided in different colors ivory, orange, and blue with extra light retention, light retention and medium retention, respectively. The ivory insert was used first then replaced by an orange insert and a blue insert when the retention reduced. The occlusion was checked for any occlusal premature contacts and the overdenture was polished. Patients were instructed to follow strict oral hygiene measures. The patients were recalled every 3 days in the first 3 weeks for denture adjustment and occlusal refinement.

**Implant stability**

Implant stability was measured by Osstell Mentor device during the follow-up period. Locator attachment (Positioner abutment, Dentium Medical
Devices Tec. Company, Korea) was unscrewed by a screwdriver. The smart peg was attached to the implant by finger-tight and stimulated magnetically by a measuring probe. The ISQ values were recorded and the mean values of two perpendicular measurements were obtained. The smart peg was removed then the locator attachment was screwed. Measurements were recorded on the day of surgery, 3, 6 months and 1 year for each implant [24].

**Radiographic assessment**

Radiographic examinations were carried out by CT scanner (Aquilion One, 320 Multi-Detector, Toshiba Medical Systems, Japan) using ultralow dose protocol on the day of surgery, 3, 6 months, and 1 year. Scan parameters were tube voltage of 80 kV, tube current of 50 mAs, pitch of 0.5mm, and Field of view was about (7.5cmx10cm). CT dose index volume was approximately 2.50 mGy [15].

Model Based Iterative Reconstruction (MBIR) with a standard kernel was used to reconstruct images. Using MBIR produces images with less noise allowing even further dose reductions than the traditionally used filtered back projection. Peri implant bone density was measured by Housefield units (HU). Measurements were performed at 0.5 mm away from each surface of each implant to diminish the scattered radiation effect. The bone densities were measured on the sagittal and coronal views (Figure 6). The mean values of readings were used for statistical analysis.

**Statistical analysis**

Data from the study were collected, tabulated and statistically analyzed. Data were fed to the computer and analyzed using IBM-SPSS software package version 20.0. (Armonk, NY: IBM Corp). Quantitative data were described using range, mean and standard deviation. Significance of the obtained results was judged at the 5% level.

The used tests were: ANOVA with repeated measures for normally distributed quantitative variables, to compare between more than two periods, and Post Hoc test (Bonferroni adjusted) for pairwise comparisons. Student t-test was
used to compare between two studied Groups. P < 0.05 was considered to be statistically significant.

**RESULTS**

The results showed that implant stability changed over time in both Groups. There was a statistically significant difference between baseline, 3, 6 months and 1 Year where P < 0.001 for both Groups. The mean and standard deviation values of implant stability decreased at three months of follow-up period and then increased at six months and 1 year in both Groups (Table I).

Using the student t-test to compare between two Groups regarding implant stability revealed that there was no statistically significant difference between Group I and Group II at all follow-up periods. At baseline $p_0 = 0.584$, at three months $p_0 = 0.677$, at six months $p_0 = 0.600$, at 1 year $p_0 = 0.496$ (Table I).

The results showed that peri-implant bone density changed over time in both Groups. The mean and standard deviation values of peri-implant bone density in both Groups decreased at three months of follow-up period and then increased at six months and 1 year. There was a statistically significant difference...
between baseline, 3, 6 months and 1 Year where P<0.001 for both Groups (Table II).

Using the student t-test to compare between two Groups regarding peri-implant bone density revealed that there was no statistically significant difference between Group I and Group II at all follow-up period. At baseline p₀=0.947, at three months p₀=0.911, at six months p₀=0.908, at 1 year p=0.818 (Table II).

**DISCUSSIONS**

This study was a split-mouth design because it permits reducing variability and bias through self-controls increasing the statistical efficiency. It allows the greatest opportunity for comparability and reduces the sample size [25]. However, it was found that due to the mechanical connection of the two implants of different intervention Groups by superstructures, loads on one implant would be transferred to the other; which may result in carry-across effects. Carry-across effects on results cannot be tested or assessed [26].

Two implants have been considered as the minimum request for mandibular implant overdenture treatment with a high success rate and a cost-effective treatment for edentulous individuals [27]. Immediate loading protocol was followed in this study because it improves the quality of life and patient satisfaction by decreasing the rehabilitation time [28,29]. However regarding two-implant mandibular overdenture with various loading protocols and locator attachments, the implant survival rates for locator with immediate loading were less than that with delayed loading [30].

Advanced Platelet-Rich Fibrin was applied in this study because it is an autologous bioactive material that can accelerate soft and bone tissue healing in implant surgery. Components of A-PRF are fibrin, Leukocytes, and platelets. Growth factors are released from activated platelets in A-PRF and promote cell proliferation, collagen synthesis, and osteoid production. Enhanced implant osseointegration could make early and immediate loading more predictable [31,32].

For this study, implant stability was measured in ISQ value by the Osstell apparatus. Osstell ISQ measurements are quantitative, highly reliable, and reproducible measurements for implant stability so were used to assess the osseointegration, immediate load possibility, and follow-up [33]. ISQ values in this study were above 65 at the insertion of implants (implant primary stability), which supports the use of immediate loading [34].

CBCT has many applications for different aspects of implantology either pre-surgical or postsurgical such as assessing anatomical structures, bone volume, shape, quality, static surgical guide fabrication, dynamic guided surgery, the evaluation of graft healing, and assessing complications related to neurovascular trauma [35,36].

This study focused on monitoring the changes in bone density and their relation to immediate loading after the application of A-PRF in osteotomy sites. Understanding these changes...
is necessary to achieve improvements in implant survival rate [37].

This study did not depend on CBCT for the evaluation of bone density throughout follow-up periods for many reasons such as; the lack of standardized grey value, limitations of reconstruction algorithms currently applied, and asymmetrical patient position. In addition, CBCT lack Hounsfield scoring (standardized grey level calibration). Hounsfield units have been designed for medical CT but are not applicable for CBCT. Compared with Hounsfield units for medical CT, grey values for CBCT device has been found to be unreliable and only can be used as a qualitative method to determine the change of the bone around dental implants with significant variations [38].

The radiographic images in this study during follow-up were derived from ultra-low-dose Multi-Slice Computed Tomography scans, because Multi-Slice Computed Tomography (MSCT) is the gold standard for measuring bone density based on Hounsfield values. In addition, the mean absorbed dose using an ultra-low-dose- MSCT of 2.5 mGy is equivalent to a full mouth survey with intra-oral films [39]. Density estimation errors due to differences in angulation of scanning by MSCT are less than CBCT. Misalignment during scanning is affected by different types of sources. MSCT scan uses a fan beam source, but CBCT uses a cone beam source [40].

A statistically significant decrease was recorded in implant stability from baseline to 3 months for both Groups. Implant stability quotient (ISQ) values were to some extent low, but within the acceptable range. The explanation for that decreasing may be related to the transformation from primary stability to secondary stability in this phase; initial bone remodeling is characterized by increasing osteoclastic activity that led to decrease the bone-implant anchorage [41]. In addition, the immediate loading of non-splinted implants might increase micro-movements and marginal bone loss affecting implant stability. These results were in agreement with other studies of immediate loading for lower overdentures [42,43].

When comparing the two groups, there was no statistically significant difference between both Groups at each follow-up period. These results were in agreement with another study, which reported the long-term effect of PRF on implant stability [44]. This can be related to A-PRF which has an effect on osseous regeneration during the early stage of the healing process. A-PRF released the greatest amount of platelet-derived growth factor AB and transforming growth factor beta 1 on days 7 and 14, respectively. On 14 days, A-PRF demonstrated the highest alkaline phosphatase activity and A-PRF treated osseous cells demonstrated the peak of mineralization [45,46].

The results of this study were in disagreement with other studies, which reported that PRF may improve implant stability and the PRF Group had higher ISQ values in comparison to non-coated implants. This improvement can be explained as they tracked the effect of PRF on the implant stability during the early phase of osseointegration at 1, 4, and 6 weeks with a lack of long-term follow-up [47,48]. Kalash S et al. [49] reported that A-PRF may cause improvement in implant stability at 3 months and 6 months of follow-up. This can be attributed to the use of xenograft in combination with A-PRF around dental implants in their study.

On comparison between both Groups at all follow-up periods, no statistically significant difference regarding bone density was reported. These results were in harmony with the study of Alhaj et al. [50] who examined the efficiency of using an advanced platelet-rich fibrin–autogenous bone graft mixture around immediately placed dental implants in the mandibular molar region. They reported no difference regarding bone density when using this mixture around immediately placed implants. The explanation may be that the growth factors are released rapidly leading to the short-term effect of PRF on osseointegration [25]. In addition, the dense clotting of platelets and fibrin on titanium surface was 1000 times weaker with platelet concentrates than with whole blood [51].

On the other hand, El Shafei et al. [52] investigated the effect of using PRF alone and PRF loaded with simvastatin (a pharmacological drug) on bone changes around implant. They reported that PRF loaded with simvastatin enhances bone healing, particularly in patients with compromised bone quantity or quality. Another experimental study by To et al. [53] investigated A-PRF clots in sockets of beagle dogs after tooth extraction examined osteopontin and osteocalcin activities during bone formation in the socket by using...
immunofluorescence staining, and evaluated the bone formation ratio by histological analysis. The study results showed that the application of A-PRF may enhance and accelerate new bone formation by increasing osteoblastic activity.

Tracking the effect of A-PRF during the early phase of osseointegration (short-term follow-up) and small sample size are limitations of our study. Further studies using different forms of platelet-rich fibrin could be recommended.

CONCLUSIONS

Advanced Platelet-Rich Fibrin has no effect on implant stability and bone density in immediately loaded-implant-assisted mandibular overdenture. Application of Advanced Platelet-Rich in implant osteotomy site does not improve the implant stability in immediately loaded-implant assisted mandibular overdenture cases.

Author’s Contributions

ESAA: Conceptualization, Resources, Data Curation, Methodology, Writing – Original Draft Preparation. FEAE: Conceptualization, Supervision, Methodology, Writing – Review & Editing. HMAR: Conceptualization, Methodology, Supervision, Writing – Review & Editing. MTMH: Conceptualization, Methodology, Supervision, Writing – Review & Editing.

Conflict of Interest

None.

Funding

None.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subject’s oversight committee’s guidelines and policies of the ethical committee; Faculty of Dentistry, Tanta University. The approval code # RP-2-20-3

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Date submitted: 2023 Aug 08
Accepted submission: 2023 Oct 16