Clinical Report

Implant Stability, Bone Graft Loss and Density with Conventional and Mineralized Plasmatic Matrix Bone Graft Preparations - A Randomized Crossover Trial

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Introduction

Dental implants (DI) are a safe and predictable type of treatment provided that a sufficient amount and quality of bone are available. The reduction of alveolar bone volume is an anticipated complication of tooth loss1. Bone augmentation is to be considered for cases of tooth loss with severe bone loss either simultaneously with the placement of the implant or beforehand. This should overcome several complications such as compromising vital structures of the jaw like nerves and blood vessels2,3 and eliminating dead space. Further contours are optimized thereby enhancing bone and soft tissue healing and reducing susceptibility to infections. Unfortunately, oral health in many developing countries has deteriorated and this is manifested by tooth loss at an early age4-6. Subsequently, advanced restorative solutions are needed to compensate for the expected adverse outcomes of bone resorption7. This becomes particularly important for younger populations that may co-exist compromised nutritional status8.

Guided bone regeneration proved over the years to be a reliable technique for alveolar ridge augmentation and restoration of bone loss9. Recently, this technique has been reported to provide an alveolar bone gain of heights exceeding 8.5 mm on average in cases of marked bony defects or atrophy of the residual ridge10. Bone replacement materials (bone grafts) are basically scaffold materials that maintain the space needed for the function of osteogenic cells11,12. Allografts are used frequently, and these can be either mineralized or demineralized freeze-dried human bone with the former known to dissolve in tissue fluids, and release calcium ions into local tissue13.

The bone graft material is usually supplied in the form of granules. These are applied to the surgical site after mixing with saline or whole blood obtained from the patient. A basic disadvantage of granules is that they are difficult to handle and stabilize in the intended location. Barrier membranes are used to handle granules and stabilize them in place until osteogenic cells perform their function. The employment of protein therapy in grafting procedures is helpful and may eliminate the need for the use of membranes13. One such technique of utilizing proteins is the mineralized plasmatic matrix (MPM) which employs the patient's plasma, facilitate the shaping of graft material, and produce a platelet-rich fibrin (PRF) type membrane14. This procedure is particularly useful in

Abstract: This study aimed to compare implant stability, bone loss, and bone density using the mineralized plasmatic matrix (MPM) and conventional bone grafting methods. Patients were recruited in a stratified sample and each received 2 implants one at each side of their upper jaws. MPM was randomly placed in the surgical site around one implant on one side while a conventional graft, was placed on the other side in a cross-over design clinical trial. A total of 84 implants were placed in 42 patients. A total of 42 implants utilized conventional grafts (GM1) and a total of 42 implants utilized mineralized plasmatic matrix (GM2). Mean Perio test measurements for implants in the group (GM1) were lower than that for implants in the group (GM2) (1.21±3.0 versus 3.57±2.9). Mean radiographic density at grafted sites with GM2 was: 665.2±236.5 whereas for GM1 it was: 577.8±201.2. Implant stability with MPM in males was significantly higher than females (P<0.001). Bone graft loss with MPM in males was significantly less than females (P=0.001). There were no differences between older and younger patients regarding implant stability, bone loss, and bone density (P>0.05). It is concluded that utilizing MPM in implants may be associated with better implant treatment outcomes of implant stability, bone graft loss, and density when compared to conventional bone grafts. Gender but not age differences may be noticed when comparing implant stability and bone graft loss in implants utilizing MPM.

Key words: Bone graft, Bone loss, Bone density, Dental implantation, Mineralized plasmatic matrix, Periotest
the role of MPM in improving treatment outcomes of dental implants has been explored by a few case reports\textsuperscript{13,14}. Other related studies were histological in nature, and those investigated bone formation rate when using MPM\textsuperscript{13}. While these studies reported the efficiency of MPM in bone formation and hence its role in increasing implant stability, it is important to validate these results by clinical trials that evaluate the clinical treatment outcomes including implant stability, bone graft loss, and density.

Up to the authors’ knowledge, no clinical trials were conducted to investigate the efficiency of MPM in enhancing the stability of DI. Therefore, this study aimed to assess implant stability, as well as bone graft loss and density among patients receiving dental implants that utilize either MPM or conventional bone granules.

Materials and Methods

Study identification

Ethical approval was obtained by the Research Ethics Committee at Jouf University (#39-4-1441) following principles of the Helsinki Declaration (9th version, 2013). The methodology was reviewed by an independent statistician. The study was carried out during the period from October 2015 to January 2019.

Patients

A stratified sample of patients was selected from the waiting list of Implant clinics at the College of Dentistry, Jouf University. Inclusion criteria for the patients were as follows:

1. Healthy or well-controlled diabetic and hypertensive patients.
2. No intake of aspirin or anticoagulants at least two weeks before surgery.
3. No local conditions that can affect the success of treatment such as infections
4. Non-smokers and non-alcohol drinkers.
5. Bilaterally badly broken first or second molar teeth that are indicated for extraction.
6. Willingness to enroll in the study.

Patients with periodontitis were excluded. The nature of the study was explained to patients and a signed consent form was obtained.

Study protocol

History and clinical examination were performed thoroughly for all patients. In particular, drug history was taken at the time of surgery to investigate the efficiency of MPM in enhancing the stability of DI.

Bone graft materials in either preparation were applied to the extraction defect, on top and around implants up to the level of CEJ of adjacent teeth. CEJ of the adjacent natural tooth was always used as the reference point to measurements of the original level of bone graft materials. Stabilization of the membrane and the underlying graft material was accomplished by using both horizontal mattress sutures and multiple interrupted 3.0 sutures. The implant at the side of the jaw (right or left) at which either preparation was applied was randomly selected. The other side received always the other preparation. Patients received verbal and written post-operative instructions and non-steroidal anti-inflammatory medications. Patients were called back after 4 months for the connection of abutments following a cone-beam computed tomography (CBCT) scan to assess both implants before the second surgical procedure to uncover the DI.

Measurement criteria

Implant stability: this was measured using a Periotest device (Medzintechnik Gulden e K, Modautal, Germany). Measurements were carried out 4-5 months after implantation following abutment connection. Bone graft height loss: This was calculated in millimeters from the CEJ of the adjacent tooth to the most coronal level exhibited by the bone graft on that side as demonstrated by the CBCT. Bone density of the graft material: This was measured from the same postoperative CBCT 4 months after implantation. Bone densities were calculated also from CBCT images at crestal one-third area of bone graft, implants stability was measured using the periotest. All measurements were performed by the first author.

Statistical analysis

Statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) version 20.
for Social Sciences v.21, 2012, IBM Corp). Descriptive statistics were carried out to obtain means, standard deviations, and ranges of values. Data of: age, bone height, implant stability (periostest measurements), bone density (grayscale data) were all analyzed using parametric tests to compare differences between groups’ means. Measurements of bone height, implant stability, and bone density were tested for reliability after one week and Kappa was measured to be approximately 85% which was judged to be an acceptable value.

Results

A total of 47 patients were initially included in this study, however, at the extraction stage, five patients were excluded either due to loss of buccal plate of bone during extraction or because there was a need for a sinus lift. There were 24 (57.1%) males and 18 (42.9%) were females. The age range for participants was 33-62 years (mean= 50.5±9.2 years). The ages of males (50.5±8.7 years) were close to females (50.6±9.9 years) with no significant difference between them (P=0.994).

Mean values of Periostest measurements, mesial bone loss, distal bone loss, average bone loss, and density of bone for GM1 (n=42) and GM2 implants (n=42) are presented in Table 1. Data in Table 1 shows that Periostest, bone loss (at mesial, distal, and average values) and bone density values were better for the sides with GM2 compared with sides with GM1 as indicated by the mean values of the corresponding measurements. However, the only statistically significant difference was noticed in mean values of Periostest measurements (P<0.001) where implants in GM2 had better values than implants in GM1. Significance of

| Measurements                                      | GM1 Mean ±SD | GM2 Mean ±SD | P value |
|--------------------------------------------------|--------------|--------------|---------|
| Periostest for implant                           | 40 -1.20±3.07 | -3.75±2.95   | <0.001  |
| Bone loss mesial to implant                      | 40 0.46±0.31 | 0.39±0.35    | 0.285   |
| Bone loss distal to implant                      | 40 0.67±0.33 | 0.62±1.39    | 0.835   |
| Average bone loss                                | 40 0.57±0.27 | 0.53±0.69    | 0.766   |
| Radiographic Density of bone                     | 42 577.8±201.2 | 665.2±236.5 | 0.07    |

Table 2. Differences between patients when they were divided into 2 groups according to age: <51 and ≥51 years of age.

| Measurements                                      | <51 years Mean±SD | ≥51 years Mean±SD | P value |
|--------------------------------------------------|--------------------|--------------------|---------|
| Periostest for implant (GM1)                      | -0.28±3.0          | -1.92±2.90         | 0.084   |
| Bone loss mesial to implant (GM1)                 | 0.38±0.20          | 0.52±0.37          | 0.163   |
| Bone loss distal to implant (GM1)                 | 0.56±0.30          | 0.73±0.35          | 0.108   |
| Average bone loss (GM1)                           | 0.47±0.21          | 0.62±0.29          | 0.065   |
| Periostest for implant (GM2)                      | -3.30±3.5          | -4.09±2.50         | 0.408   |
| Bone loss mesial to implant (GM2)                 | 0.38±0.30          | 0.39±0.39          | 0.897   |
| Bone loss distal to implant (GM2)                 | 1.04±2.08          | 0.32±0.27          | 0.113   |
| Average bone loss (GM2)                           | 0.73±0.98          | 0.38±0.30          | 0.113   |
| Bone density (GM1)                                | 564.9±189.3        | 587.5±213.1        | 0.724   |
| Bone density (GM2)                                | 644.9±256.8        | 680.4±224.6        | 0.637   |
differences was calculated using paired t-test, however, this eliminated data for both implant pairs when one of them was for a failed implant (i.e. missing). When independent samples t-test was used to make use of data for the other successful side that did not fail, significance was not changed with corresponding \( P \) values being: \(<0.001, 0.298, 0.893, 0.814, 0.072\) for the same variables respectively (Table 1). The statistical analysis software excluded data for each patient when one of the implants was a failed implant as this constituted unpaired data. The effect of age and gender on Periotest values, bone loss, and bone density is illustrated in Table 2. Table 2 shows that Periotest values, bone loss values, and bone density values were generally better for males than females. However, these differences were only significant for Periotest values for implants with MPM (\( P = 0.001 \)) and bone loss values with MPM (\( P = 0.001, 0.032, \) and \( 0.001 \) for bone loss differences on mesial, distal, and average values respectively). Results varied among the two age groups. Periotest values with bone grafting method 1 or MPM were better for the older age group, average bone loss values with the bone graft were better for younger age group, average bone loss values with MPM were better for older age group, bone density was better for the older age group with a bone graft or MPM. However, none of these differences was significant. There were no significant differences in Periotest values, bone loss, or bone density between younger (35-45 years) and older (46-62 years) female groups.

**Discussion**

This study evaluated implant stability, bone loss, and bone density around dental implants when utilizing one of the two methods of bone grafting. Implants that utilized MPM were associated with better values for Periotest, bone loss, and bone density, than those utilizing bone granules only. However, the statistically significant differences were evident in Periotest only, but not bone density or bone loss.

One of the factors that influence implant stability is the quality and quantity of bone, and it plays a critical role for successful osseointegration, in fact, this measurement is considered one of the methods that can be used to assess osseointegration of dental implants which is a prerequisite for the function of dental implants. Periotest quantifies the mobility of an implant by measuring the reaction of the peri-implant tissues to defined impact load. It uses an electro-magnetically driven and electronically controlled tapping rod in a handpiece. Periotest is a widely accepted implant stability measurement method. Further, Periotest measurements appear to be highly reproducible and capable of detecting minor changes in the bone-implant complex within a specific range of rigidity.

Clinically integrated implants were shown to demonstrate a range of -8 to +9 Periotest values (PTVs) that approximates the Miller Mobility Index used for natural teeth. In this study, both bone grafting methods were associated with a negative mean of PTVs, which indicates that both methods are associated with improved implant stability. However, there was a statistically significant difference with MPM indicating it was performing better.

MPM is considered the latest platelet concentrate to be produced since PRP was first described in the late 1990s. Several years after the production of PRP, another preparation, PRF, was described. PRP is the first form of autologous platelet concentrate to replace commercial fibrin glue. A major disadvantage of PRP though is the risk of coagulopathies due to the use of bovine thrombin that is needed during the preparation stage. The second-generation platelet concentrate, PRF, eliminated this risk since it does not need anticoagulants for its preparation. It has several advantages over traditionally prepared PRP including ease of preparation and lack of biochemical handling of blood which makes this preparation strictly autologous. Its use with bone grafts contributes to several physiological outcomes such as hemostasis, wound healing, bone growth and maturation, graft handling, and stabilization. MPM contains platelets and fibrin concentrate in a liquid state which can become bound to bone particles. It also expresses biologically active compounds enhancing the tissue repair mechanisms of chemotaxis, cell proliferation, angiogenesis, osteogenesis, and remodeling. MPM can be viewed as a modification of the PRP protocols in implant dentistry. However, with MPM there is a mineral component which can be autologous bone or bone graft material.

The advantage of the MPM is the integration of bone graft particles inside the fibrin network that is not present in old autologous growth factors membranes in PRF or PRP. The bone grafting materials are prepared and mixed with the autologous growth factors to produce the MPM or what is called Sticky bone. This offers the MPM the positional stability by stabilizing the bone particles, preserving its shape with subsequent “in situ” immobilization of the component of ridge preservation materials.

Under scanning electron microscope MPM demonstrates a dense network of fibrin engulfing the mineral component. The resulting mass can be readily shaped to the shape of the defect or the intended shape of the augmentation without interference or the need to modify the surgical procedure itself. MPM provides clinicians with the benefits of hard scaffold material and tissue engineering techniques, represented in the PRF which is a source of fibrin network, i.e., the extracellular matrix necessary for migration of specific cells in the tissue regeneration or repair. Mineralized plasmatic matrix is also a low-cost source of growth factors and the material can be easily prepared. This means that the technique provides the advantages of bone blocks and titanium mesh at only a fraction of the cost or effort.

Although autogenous bone (either extraoral or intraoral) is considered the “gold standard” of bone grafts, it is associated with many drawbacks attributed to donor site morbidity. Donor site morbidity includes complications such as immediate postoperative pain and edema, infections, neurosensory deficits, and hematomas.

It was also clear in this study that males had significantly better values than females in implants utilizing MPM for Periotest and bone loss measurements. It was proposed that postmenopausal women that don’t take hormone replacement therapy have a poorer quality of bone than men. However, there were no gender differences in mean age in our study sample, with a mean age for both males and females being 50.5 years. Another explanation may be related to gender differences in the composition of MPM. We could not find any studies that discuss the difference in composition of MPM between genders, however, previous research pointed out the possibility of differences in similar preparations like PRP. Whereas some studies showed that there were no gender differences in growth factor content in PRP, men were shown to have higher cytokine and growth factor levels in PRP in some studies. Other studies found that females had higher growth factors’ levels and they linked this to sex steroids such as the increased levels of TGFβ-1 associated with estrogen. It was also shown previously that females were 1.54 times more likely to lack primary implant stability than males, so this can be manifested later in measurements such as Periotest and radiographic findings of bone loss.

Bone loss around dental implants can be attributed to many factors such as implant shape and geometry, nature of graft material, and grafting technique. Of particular importance is the hormonal factors that strongly determine the rate of bone resorption. Vitamin D deficiency...
was found to be prevalent among women, particularly young ones, in Saudi Arabia\textsuperscript{19}, and mandibular osteoporosis prior to implant placement is thought to be a risk for minor accentuation of bone loss\textsuperscript{20,27}. It should be emphasized that type of implant and surgical procedure were standardized for all patients. Further, all patients included in this study did not have osteoporosis, which excludes this disease as a contributing factor in bone loss. However, it was noticed that males had a higher bone density than females which could explain the lower bone loss values among males.

Non-significant differences in treatment outcomes were noticed between both age groups. This could be explained by the relatively high mean of 50 years in our study sample. It is thought that people older than 25 years of age will have reduced levels of growth factors\textsuperscript{27}. All participants were older than 30 years, which could mean that the participants in this study have comparable factors when bone healing potential is addressed.

In conclusion, implants utilizing MPM have better treatment outcomes with implant stability, bone density, and bone loss than those utilizing bone granules only. There seem to be comparable treatment outcomes for patients older than 30 years of age, however, males may show better implant stability and less bone loss than females.

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Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

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