

Immediate Implant Surrounded by Mixture of Plasma Rich Fibrin, Xenograft With Melatonin Granules Vs. Immediate Implant Surrounded By Plasma Rich Fibrin And Xenograft At Premolar Region: A Randomized Controlled Clinical Trial

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Introduction: dental implants can help patient to restore function and appearance, so all studies were done to improve bone density by using different grafts like xenograft or melatonin, however melatonin needs more studies with dental implants in human. **Objectives:** The aim of this double-blinded randomized clinical trial was to evaluate the effect of mixing melatonin combined with xenograft and PRF versus xenograft and PRF alone when used around immediate implants inserted in the upper premolar region on the radiographic bone density, marginal bone loss as well as postoperative pain. **Methods:** The present study included 16 patients (7 males and 9 females, aged 20 to 45 years) suffering from at least one non-restorable tooth in the premolar zone that needed to be extracted. **Results:** Regarding radiographic bone density, from baseline to 3 month there was a statistically significant reduction in bone density in both groups. From 3 to 6-month, control group showed a statistically significant reduction in bone density while study group showed a non-statistically significant increase in bone density. Regarding marginal bone loss, both groups showed a statistically significant increase in bone loss throughout the study period with no statistically significant difference between them. **Conclusion:** Both treatment modalities (xenograft + PRF or xenograft + PRF mixed with melatonin) failed to minimize marginal bone loss at 6-month post-immediate implant placement.

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Introduction

Implant has been one of dental options which was used to restore function and appearance of teeth after its extraction. Implants could be placed delayed or immediately after extraction of teeth. (Simsek et al., 2003). Nowadays, there are increasing demands from patients for shortening the period of osseointegration of the implants which takes a relatively long time (3-6 months) to regain masticatory function and aesthetic appearance of their replaced teeth. Therefore, Immediate implant became the treatment of choice for both dentist and patient (Chen et al., 2006).

Immediate Implant placement in the extraction socket may lead to a gap between the bony walls of the socket and the implant (Coelho et al., 2010). Moreover, placing implants immediately after extracting teeth can lead to crestal bone loss. The crestal bone resorption which is formed after immediate implant placement can cause bad appearance to the patient and decrease success of the implant (Simsek et al., 2003). The amount of this bone loss at the crest of the ridge could not be predicted with immediate implant placement (Araújo et al., 2005). Bone grafts and different types of membranes have been used with immediate implant placement to fill the gap formed after extraction of tooth beside decreasing the rate of bone loss and bone remodeling (Araújo et al. 2005; Chen and Busser, 2009).

Different types of bone graft have been used with dental implant such as xenograft, autogenous graft, alloplast and allograft. Xenograft has been one of the most common types of grafts used in implant dentistry due to its availability and osteoconductive property (Esposito et al., 2011). Xenograft was used successfully in conjunction with immediate implant placement to fill the gap between implant and socket. However, some studies showed that mixing xenograft with melatonin particles could give better results in preserving the bone after its remodeling procedure (Esposito et al., 2011).

Several studies proved that bone

regenerative procedures might be stimulated by the addition of specific growth factors. Plasma rich fibrin (PRF) was found to be rich in these growth factors that could help in the healing process and could act as a membrane (Naik et al., 2013). However, there aren't enough studies that used a mixture of melatonin

with bone grafts to provide a clear image about its role in preserving bone around immediate implants (Cardinale et al., 2003).

MATERIAL AND METHODS

The present study included 16 patients (7 males and 9 females, aged 20 to 45 years) suffering from at least one non-restorable tooth in the premolar zone that needed to be extracted. All procedures were done under completely aseptic conditions, where the patients were asked to rinse with chlorhexidine 2 mouth wash (0.12%) for 1 minute (Van Strydonck et al., 2012). Patients were anaesthetized at the surgical site by Articaine (Septocaine with epinephrine 1:100000, Sebtodont Canda) hydrochloride 4% with 1:100000 Epinephrine, which was administrated by buccal and palatal infiltration (Malamed et al., 2000). Periome was used to cut the periodontal ligaments of the remaining root of upper first or second premolars. Then upper premolar forceps were used to remove the remaining root atraumatically by rotation only to avoid any fracture of the surrounding bone. Preparation for osteotomy site was performed by sequential drilling as provided in the implant surgical kit 5 (NeoSurgical kit). Stopper was used to avoid exceeding the length that was chosen. Drilling of the implant in bone was performed using sharp drills and low speed "1500-2000rpm" high torque and externally irrigated hand piece 6 of NSK surgical motor (Fig. 2). Careful cooling with copious sterile saline was performed as well (Booms. 2014).

The bone site preparation was initiated using the external irrigated pilot drill with diameter 1.5 mm and penetrated to the

predetermined length (Booms. 2014). Externally irrigated intermediate drill was used to initiate enlargement of the implant site and penetration to the predetermined length of the implant. The intermediate drill used was 2 mm or 2.5 mm in diameter for the 2.9 mm and 3.4 mm implants respectively (Lorenz. 2011). Final shaping was performed using the final drill with diameter 2.5 mm or 3 mm for the 2.9 mm and 3.4 mm implants respectively. The final drill penetration was to two-thirds of the predetermined socket length; this technique is called countersinking and was used to enhance initial implant stability (Lorenz .2011).

The drilling motion was performed in upward and downward direction to prevent oversizing the implant site and to allow the irrigation solution to reach the depth of the size (Lorenz. 2011). Before implant placement,

a parallel pin was used to check the implant parallelism (Glantz et al., 1993). Then the implant was inserted by motor implant fixture ratchet which was done with fixed torque 30 and speed 20 in order to standardize the force of insertion (Lorenz. 2011). In both groups, Neo biotech IS-II active Fixtures (Korea) dental implants⁷ have been used. They have tapered body, powerful apex with a macro thread design in the upper part. The surface of IS-II active has a combination of macropores and micropores formed by HA (Hydroxy Apatite) sandblasting with a particle size less than 50 μ m and acid etching. Different diameters and lengths were used according to each case bone volume in the study. Then finally the implant fixture was covered by the cover screw to prevent the growth of soft tissue into the implant during the healing period (Lau et al., 1999). The 16 patients were divided into two groups: Control group: 8 patients had immediate implant placement at upper premolar region surrounded by bone xenograft and PRF. Study group: 8 patients had immediate implant placement at upper premolar region surrounded by melatonin mixed with bovine xenograft and PRF. Platelet rich fibrin (PRF) was prepared by drawing 20 ml of blood from the antecubital patient vein using Winged infusion set (Fig. 4). Then it was transferred into two

glass coated test-tubes without anticoagulant. The blood sample was immediately centrifuged in an electric centrifuge⁸ at 2500 rpm for 10-12 min (Choukroun 2010).

Outcomes:

Primary outcome: Radiographic bone density measured by direct digital radiography at 3 and 6 months post implant insertion.

Secondary outcomes: Postoperative pain: Pain score reported by the patient directly through Visual Analogue Scale score (between 0 and 10. 0: no pain, 1: minimal pain, 5: moderate pain, 10: severe pain) (Fig.11) (Price et al., 1983). VAS will be recorded daily for 1 week (Wyrebek, Gorski and Gorska, 2018) as pain reach its maximum level at the initial healing phase. Radiographic marginal bone loss measured by direct digital radiography at 3 and 6 months post implant insertion.

Radiographic evaluation: Digital periapical radiographs with paralleling technique were taken immediately after the implant placement and at the follow-up periods at 3 and 6 months. For taking the digital periapical radiographs, Digora optime DXR-50 001 (Soredex-Finland) digital

intraoral imaging system with Size 2 Photostimulable phosphor plate (PSP) (Fig. 12) and a customized acrylic bite block and Rinn XCP film holder were used (Fig.13). Images were displayed on the computer monitor and analysed using Digora for Windows (DFW) 2.7 software program (Soredex-Finland).

Statistical analysis

Data will be analyzed using IBM SPSS advanced statistics (Statistical Package for Social Sciences), version 21 (SPSS Inc. Chicago, IL). The data was explored for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test showing normally distributed data. Numerical data was described as mean and standard deviation. Categorical data was described as median and interquartile range. Bone density and marginal bone loss data showed parametric distribution, Comparisons between the 2 groups were done using the independent

t-test at each time point; for percent change comparisons were done by Mann Whitney test. Comparison over time was done by paired t-test in each group for marginal bone loss and was done by Repeated measure ANOVA followed by Bonferroni post hoc test in bone density. All p-values are two-sided. P-values ≤ 0.05 were considered significant.

Results

Postoperative pain: The results of pain score for both the control and study groups are compared throughout the study period, In the control group, median of pain score value at baseline was 3 and one week after implant placement, it reached 0. There was a statistically significant reduction in pain score with p-value = 0.016. The same was observed for the study group as at baseline, median of pain score value was 3 and reached 0 one week after implant placement. There was a statistically significant reduction in pain score with p-value = 0.015.

1. Bone Density:

A. Changes by time in bone density within each group:

For the control group: At baseline; the mean bone density was 97.0 ± 18.4 . At 3 months, it changed to 71.8 ± 20.4 and finally reached 62.6 ± 16.6 at 6 months. Pairwise comparisons revealed that there was a

statistically significant reduction in bone density from baseline to 3 month and from 3 month to 6 month while For the study group: At baseline; the mean bone density was 92.3 ± 23.4 . At 3 months, it changed to 75.5 ± 21.9 and finally reached 79.5 ± 26.3 at 6 months. Pairwise comparisons revealed that there was a statistically significant reduction in bone density from baseline to 3 month and a non-significant increase in density from 3 month to 6 month.

B. Comparisons between the 2 groups:

The changes in the bone density of the immediate implants for both the control and

study groups are compared throughout the study period and presented in table (3) and figure (45).

At baseline: The mean bone density for the control group was 97.0 ± 18.4 and 92.3 ± 23.4 for the study group. There was no statistically significant difference between both groups with a p value = 0.665.

At 3 months: The mean bone density for the control group was 71.8 ± 20.4 and 75.5 ± 21.9 for the study group. There was no statistically significant difference between both groups with a p value = 0.773. At 6 months: The mean bone density for the control group was 62.6 ± 16.6 and 79.5 ± 26.3 for the study group. Study group showed a non-significant increase with a p-value = 0.147.

2. Marginal Bone Loss:

A. Changes within each group and comparison between them:

The mean and SD values for marginal bone loss in the two groups throughout the study period are compared.

At 3 months: The mean \pm SD values for marginal bone loss in control and study group were 1.37 ± 0.29 and 1.36 ± 0.29 respectively. There was no statistically significant difference in marginal bone loss between both groups with p-value = 0.977. At 6 months: The mean \pm SD values for marginal bone loss in the control group was 1.68 ± 0.30 and 1.58 ± 0.41 for the study group. There was no statistically significant difference in marginal bone loss between both groups with p-value = 0.594.

B. Comparisons between groups in percent change:

The median and range for percent change in the marginal bone loss from 3 month to 6 month for both the control and study groups is compared.

The median percentage of marginal bone loss for the control group was 25.1% that ranged from 2.5 to 53.3 and median percentage of bone density for the study group was 16.0%

that ranged from 5.2 to 29.5 for the study group. There was no statistically significant difference in percent change of marginal bone loss between both groups from 3-6 months with p-value =0.382.

DISCUSSION

the aim of this double-blinded randomized clinical trial was to evaluate the effect of mixing melatonin combined with xenograft and PRF versus xenograft and PRF alone when used around immediate implants inserted in the upper premolar region on the radiographic bone density, marginal bone loss as well as postoperative pain. The study population included a total of 16 patients (7 males and 9 females, with mean age 32 ± 6) with at least one non-restorable tooth in the premolar zone that needed to be extracted. The 16 potential implant sites were assigned randomly into two equal groups (control and study group), the control group received immediate implants with xenograft and PRF while the study group received immediate implants together with xenograft, melatonin and PRF.both groups showed statistically significant reduction in postoperative pain one week after implant placement.

These results are in line with those of Arora et al., (2016), who compared immediate implants with PRF (test group) versus immediate implants without PRF (control group) regarding soft tissue healing and minimum postoperative morbidity. They observed that the patients in test group are favored with rapid soft tissue regeneration, improve with early wound closure, which helps in achieving an esthetic outcome and better patient acceptance. The same was observed by El Bahnasy Sleem et al. (2018) who investigated the effect of PRF in combination with dental implant and found PRF was able to significantly reduce postoperative pain.

Regarding radiographic bone density:

At 3 month as well as at 6 month, control group showed a statistically significant

reduction in bone density, whereas study group showed a

statistically significant reduction in bone density at 3 month and a non-statistically increase in bone density at 6 month.

The obvious increase in bone density in the study group could be attributed to the potential role of melatonin in ontogenesis. This goes in line with Cutando et al., (2008) who evaluated the topical application of melatonin on osteointegration of dental implants in the oral cavity on Beagle dogs and their histomorphometric results revealed that melatonin significantly increased all parameters of osteointegration and enhanced new bone formation.

The results of Guardia et al., (2011) emphasizes the effect of melatonin as they found the topical application of melatonin Beagle dogs improves osteointegration of dental implants at 5 and 8 weeks after implant insertion with a significant greater percentage of inter-thread bone and new bone formation.

Regarding marginal bone loss:

Both groups showed a statistically significant increase in marginal bone loss at 3 and 6 month with no significant difference between them. However, median percent marginal bone loss was lower in the study group (16%) compared to control group (25.1%) although the difference was not statistically significant which shows the role of melatonin in alveolar bone preservation.

Longitudinal studies with initial X-rays obtained at implant placement reveal most bone loss to occur in the first 6 months before insertion of the definitive restoration (Hermann et al., 2000; Hartman and Cochran, 2004; Lee et al., 2007 ; Cochran et al., 2009).

Several studies investigated the dimension of the bone in grafted types of immediate implantation and reported a mean reduction of the bone height to be 0.5-1 mm at 4-6 months after surgery (Botticelli et al., 2004; Chen et al., 2005).

CONCLUSIONS

Within the limitations of the present study, the following can be concluded:

The use of xenograft combined with PRF for augmentation around immediate implants was successful in postoperative pain reduction 1

week after immediate implant placement. Combination of xenograft and PRF wasn't able to enhance bone density around immediate implants. Adjunctive use of melatonin mixed with xenograft together with PRF led to statistically non-significant increase in bone density 6 months after immediate implant placement. Both treatment modalities (xenograft + PRF or xenograft + PRF mixed with melatonin) failed to minimize marginal bone loss at 6-month post-immediate implant placement.

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