Topical application of melatonin around immediate implants

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Abstract

Immediate implant became a treatment of choice in several conditions. However, stability of the implant requires filling the voids with a bone graft or a substitute. The role of Melatonin in bone stimulation was recently considered. Aim of the study: Evaluation of the effect of melatonin granules around immediate implant both clinically and radiographically. Materials and methods: 14 implants were placed in fresh extraction sockets. The patients were divided into 2 equal groups, control and study groups. In the control group gap was filled with Cerasorb bone graft, while in the study group melatonin was added to Cerasorb. Grafts were surrounded by a biocollagen membrane in both groups. Clinical and radiographic assessment was carried out at 1st, 3rd, and 6th post-operative period. Results: No significant difference was recorded between the two groups, while bone density showed significantly higher levels in the melatonin groups. Conclusion: Topical application of Melatonin is recommended in osteotomy sites and around dental implant as a bone stimulator.

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Introduction

Rehabilitation of edentulous jaws either partial or complete using endosseous implants has become an important treatment option with good expected results (1). Following tooth extraction, bone resorption may jeopardize the success of dental implants (2).

The first reports describing the immediate implant placement in a fresh extraction socket were reported by Schulte and Heimke in 1976 (3).

Subsequently, several scientific and clinical researches formulated general criteria for successful immediate implant in fresh extraction sockets, as meticulous sterilization, atraumatic tooth extraction, non-invasive surgery and primary implant stability (4-6).

Among the advantages of immediate implants are reduced bone resorption and treatment time, and proper localization of the implant site (7). In a study conducted by Calvo-Guirado et al (8), progressive increase of values of implant stability quotient (ISQ) occurred after immediate placement of implants, which does not essentially require waiting for complete healing of the socket before implant insertion (9-11).

On the other hand, immediate placement of the implant in the fresh extraction alveolus may result in a vertical gap between the bony walls of the socket and the cervical part of the implant (11). It was reported that if a gap is more than 2mm, bone graft is recommended, while smaller distances could heal spontaneously (9). Controversies regarding the most suitable grafting materials whether autografts, allograft or xenograft were advocated by several authors in order to improve bone synthesis and ensure better survival (7, 11).

However, limitations associated with autografts include limited availability, associated morbidity, the potential transmission of disease and immunological response enhanced the use of alternative biomaterials. (12). Recently, great attention has been directed towards melatonin hormone as a graft material (13).

Melatonin is chemically recognized as *N*-acetyl-5-methoxytryptamine. It is a compound occurring naturally in plants, microbes and animals. The circulating level of the melatonin hormone in animals shows interesting variations, by entertainment of variable biological functions in a daily cycle "*circadian rhythm*". Melatonin called hormone of night is secreted by the pineal gland, and its plasma levels concentration are 50 folds higher in night in comparison to daytime. A variety of peripheral cells play a role in production of melatonin such as epithelial cells, bone marrow cells, and lymphocytes (14). Though melatonin is a hormone, it does not act on a specific organ, it has several functions; stimulation of the synthesis of type I collagen fibers, regulation of the body temperature, sexual development, antioxidant scavenging and detoxifying free radicals thus inhibiting the process of bone resorption through interfering with the function of osteoclasts (15).

Kazuhito et al, suggested in the results of their study in 2007 (16), that melatonin enhanced the production of alkaline phosphatase (ALP), type I collagen, osteopontin, bone sialoprotein which promoted the differentiation and and reduced the maturation of osteoblasts from 12 to 21st day through located receptors on pre-osteoblasts.

Greany in 2008 (15) proved that freeze-dried melatonin was topically applied in osteotomy sites led to enhanced bone formation.

Accordingly, this present study aimed at clinically and radiographically evaluating the effects of the melatonin granules applied around immediately placed dental implants in maxillary anterior teeth.

Aim of the study

Clinical and radiographic effects of the melatonin granules around immediately placed dental implants in maxillary anterior teeth.

Patients Materials and Methods

Fourteen patients were selected from those attending the outpatient clinic of the Oral and Maxillofacial Surgery Department. Patients of both sexes fell under the age range of 25-40 years.
Selection of the patients was based on specific inclusion and exclusion criteria.

Inclusion criteria:
Patient should have good oral hygiene according to O'Leary's index (17), non-restorable maxillary anterior teeth, adequate interocclusal space to accommodate the suprastructure, a space of > 2mm between the fixture mount and the wall of the socket.
Teeth indicated for extractions, should have minimum amount of bone loss, without purulent exudates, with adequate soft tissue health and quantity, as well as bone availability apical to the extraction site to ensure initial stabilization of the implant.

Exclusion criteria included patients suffering from oral habits, local pathology and any systemic disease that could jeopardize surgery.

Materials:

1. Cerasorb bone graft "Cerasorb® M" which consists of calcium and phosphate granules supplied in double sterile packages (sterilization via gamma irradiation) and are for single-use only.
2. Bio Collagen membrane: lyophilized deantigenized animal equine biocollagen resorbable membrane.
3. Melatonin granules 5% (http://www.faqs.org)
4. Implant fixture: Zimmer (Swiss plus system), 2 pieces, non-submerged, biocompatible pure titanium, supplied in one fixture mount/transfer. Its self-tapping design reduces the operation time by faster insertion. It is supplied in sealed gamma sterilized double packing.

Patient grouping:
The patients were divided into two equal groups. They were allocated to their group according to the graft material inserted around the immediately implanted fixture following extraction as follows:

1. Group I "Control": the patients received the implant fixture surrounded by Cerasorb and a bio collagen membrane.
2. Group II "study": the patients received the implant fixture surrounded by Cerasorb bone graft with melatonin and bio collagen membrane.

Methods:
A consent form was signed by the patient after detailed explanation of the procedure.

I) Pre-operative phase:

A pre-operative periapical and panoramic x-ray film were taken for each patient (Fig 1).
Selection of the implant was based on: the length of the original root, the level of the crestal bone, the buccolingual width of the potential implant site in the anterior region. The selected implant should be long enough to be proportionate with the potential prosthesis, wide enough for primary stability, fixed at about 2-3 mm apical to the apex of the socket.

II) Operative phase

The surgical procedure and treatment were performed according to the hospital ethical standards and regulations.

1. All the patients were given infiltration local anesthesia using Articaine hydrochloride 4% (Septocaine ® 1.8 ml. Septodent, USA)
2. Full thickness mucoperiosteal flap was then reflected, and the tooth was extracted atraumatically to preserve as much of the crestal bone as possible (Fig 2)
3. The implant bed at the apical portion of the socket was then prepared by drilling 2-3 mm beyond the apex under copious external irrigation by normal saline as cooling system. (Fig 3)
4. Drilling was initiated using the intermediate drill followed by the successive drills till reaching the final drill which diameter corresponds to that of the selected implant**.**
5. After drilling and socket debridement the implant was held by its cover, applied into the recipient site and screwed in the socket.

For Group I "Study": Cerasorb bone graft was packed around the implant covered by the collagen membrane without melatonin granules. (Fig 10-14)
While for Group II "Control": The melatonin granules and the Cerasorb bone graft were mixed with 1cm patient's blood. The mixture was packed around the immediately placed dental implant, and the collagen membrane was adapted around the socket. (Fig 1-9)

6. Flap was repositioned and sutured using 3-0 non resorbable black silk suture.
7. Provisional crowns were prepared to be 2mm free from occlusion and then placed using temporary cement.

III) Immediate post- Operative phase

Anti-inflammatories and analgesics in the form of Diclofenate Potassium (Cataflam 50 mg tablets, Novartis Pharma AG, Basle, Switzerland) 50mg/8 hours was started immediately after surgery until pain subsided.
Prophylactic antibiotic was given in the form of Amoxicillin (Augmentin Smithkline beecham Pharmaceutical Co., England) 1gm once daily for a week.
Patients were instructed to avoid biting on the provisional crowns and sutures were removed after one week of surgery.

IV) Prosthetic phase: Final porcelain crowns were constructed after 6 months healing period fabricated on a master cast obtained by silicone based impression material poured in stone.

V) Post-operative evaluation phase

A) Clinical Parameters

It was performed according to the periodontal based clinical parameters using implacare implant instruments to avoid scarring and/or damage of the implant surface:

1) The presence of pain, swelling or infection: The patients were observed to detect the presence or absence of any possible complications such as: Pain, tenderness, peri-implant infection, suppuration and edema. Their presence was a sign of peri-implant complication and possible accelerated bone loss.
2) Probing Depth according to Glavind and Loe (18)**:** it refers to the distance from the gingival margin to the bottom of the pocket. Mesial and distal pockets were measured from the buccal aspect close to the contact points, while labial and lingual pockets were measures at the midline of the implant, with light probing force (0.2-0.3N)
3) Papillary bleeding index (PBI) (19): Bleeding was provoked by sweeping the sulcus by probing under light pressure from the base of the papilla to its tip along the mesial and distal aspects of the implant and waiting for 20 sec.
   Scoring was in 4 grades: Grade1: a single bleeding point; Grade 2: A fine line of blood; Grade 3: Bleeding at the interdental triangle; Grade 4: Profuse bleeding.
   PBI is calculated by dividing the bleeding number (is the sum of the recorded scores), by the total number of the papillae examined.
4) Mobility according to Mckinney and Koth (20): Clinical implant mobility scale is; Scale 0: Absence of mobility in any direction; Scale 1: Slight detectable horizontal mobility; Scale 2: Moderate visible horizontal mobility up to 0.5 mm; Scale 3: Severe horizontal mobility greater than 0.5 mm; Scale 4: visible Moderate to severe horizontal mobility and any visible vertical movement.

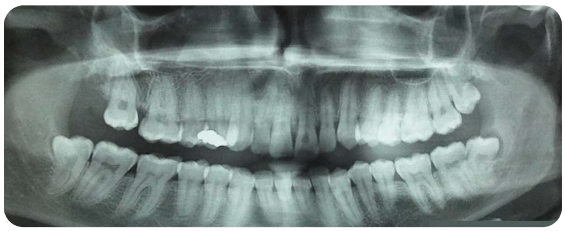


Fig1: Pre-operative panoramic x-ray film

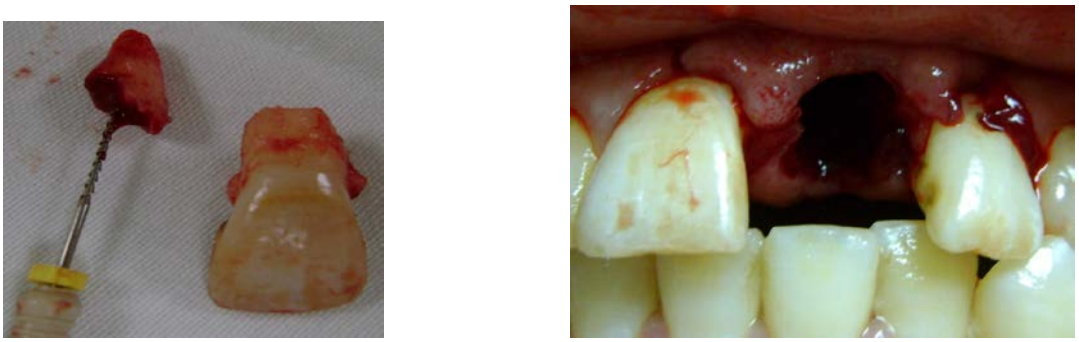


Fig 2: Extraction of fractured left maxillary central incisor.

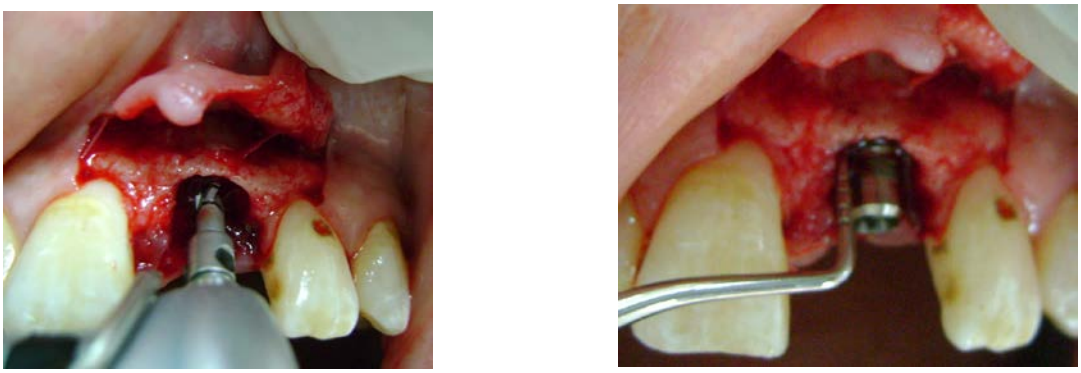
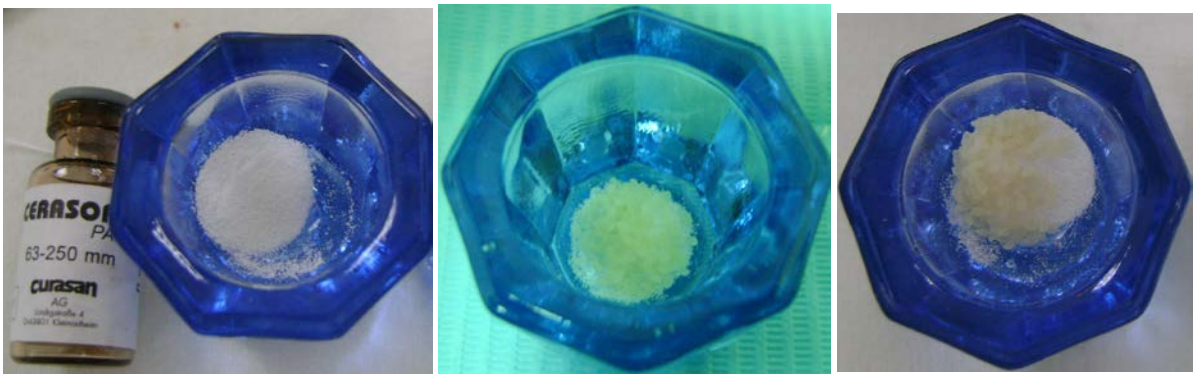


Fig 3: Implant drilling and insertion.

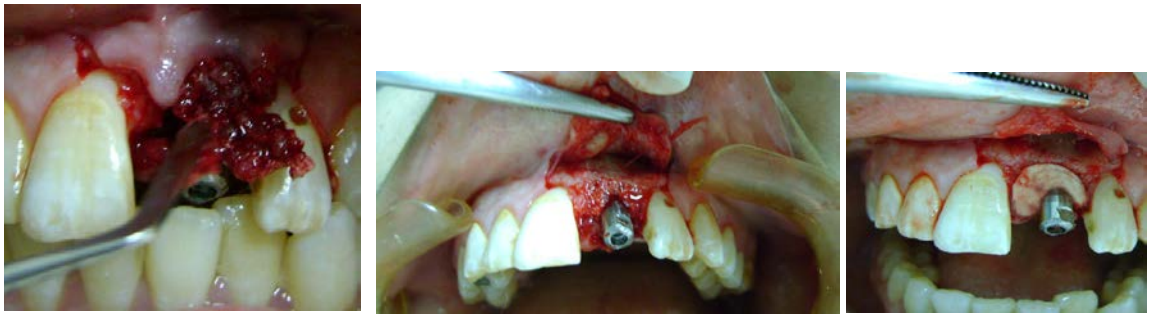


A B C

Fig 4: A: Cerasorb, B: Melatonin granules, C: Mixture of Cerasorb and Melatonin.

A B C

Fig 5: Mixture of Cerasorb and Melatonin mixed with blood (A: blood sample, B & C: Mixture).



A B C

Fig 6: Mixture of Cerasorb and Melatonin applied around the implant site A&B: mixture applied, C: Biocollagen membrane applied).

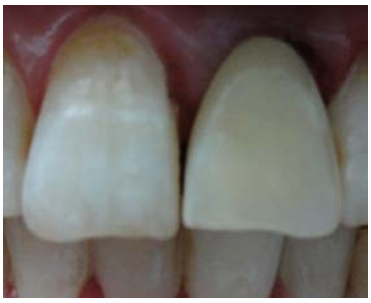


Fig 7: Provisional crown.

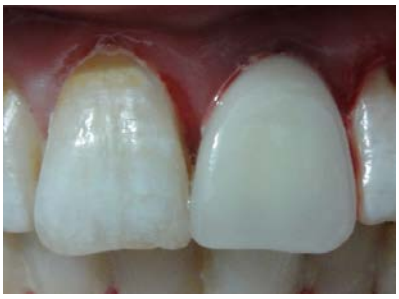


Fig 8: Final crown.

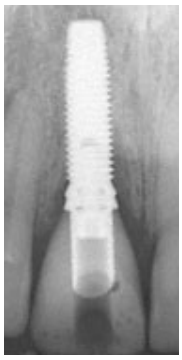


Fig 9:post-operative x-ray.

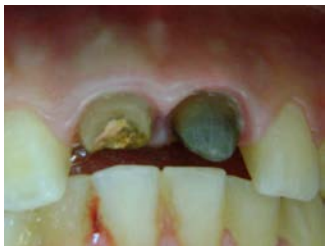
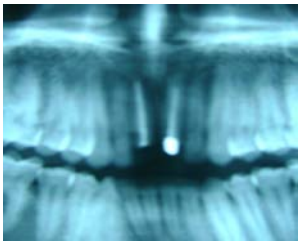
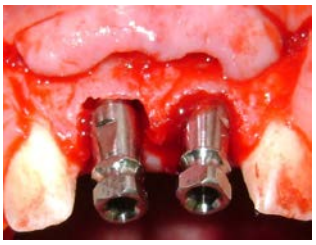




Fig 10: Case of group I. Fig 11: Panoramic x-ray. Fig 12: Inserted Implants.

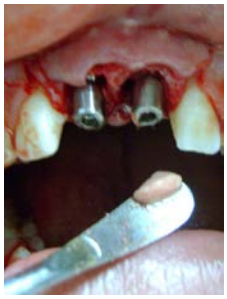
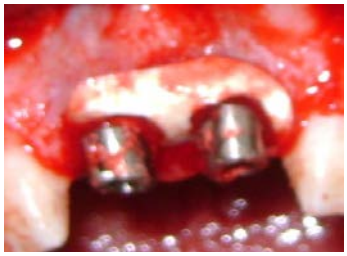



Fig 13: Cerasorb applied. Fig 14: Biocollagen membrane applied.

B-Radiographic Parameters:

Marginal bone height:

Bone density:
Computer-assisted densitometric image analysis using Linux software was used to evaluate bone density mesial and distal to each implant through measurements taken using rectangular selection tool to specify the area, where two standardized controlled square areas (33 x 33 pixels) were defined mesial and distal at the implant bone interface. The status bar gives the location of the selection and its dimensions in pixels. The tool of region of interest (ROI) was used to add the selected area to the list and saved. The measure tool was used to measure the selected area expressed in numbers from 0 (darkest) to 255 (lightest or brightest) representing the brightness level of a stored individual pixel.(Fig 15)
The mean standard deviation, minimum and maximum readings were automatically displayed by the system

Statistical analysis: Comparison of different follow-up period in each group separately was performed using Wilcoxon Signed test, while Mann-Whitney test was used for comparing between study and control groups. Statisticalsignificance was at p value < 0.05.

Results

A) Clinical evaluation revealed that the immediate follow-up period went uneventful with no pain, swelling or suppuration.

1) The results proved that there was a mild increase in the mean probing depth in both groups as measured throughout the follow-up period which decreased at 6 months, however, these changes proved to be statistically non-significant in each group and between both groups.
2) Probing depth: in the control and statistical significant difference was observed between the 1st (1.52 ± 0.09) and 6th follow-up periods where the mean values were and 1.63 ± 0.10) respectively. In the study group there was statistical significant difference between the 1st (1.58 ± 0.09) and 6th follow-up periods where the mean values were and 1.6 ± 0.09). However, no significant difference was observed between both groups (Fig 15).
3) The results revealed a reduction in PBI scores in both groups. The overall implications suggest that the clinical improvement of PBI might be attributed to the continuous reinforcement of home oral hygiene measures and the professional dental care program during the whole follow-up period. There was a significant decrease in the PBI in the control group if compared with first (1.27 ± 0.11), 3rd (0.85 ± 0.16) and 6th months (0.67± 0.07), while in the study group significant decrease was observed between the first month (1.29 ± 0.15) and the 3rd month (0.93 ± 0.15), and between the first and 6th month ((0.79 ± 0.16), while no significant difference was recorded between the 3rd and 6th months. Moreover, No significant difference was observed between both groups at (p>0.05). (Fig 16)
4) Mobility: The absence of mobility throughout the study was confirmed by both clinical and radiographic evaluation, which revealed no critical peri-implant radiolucency which is a positive sign of successful osseointegration (Fig 9).

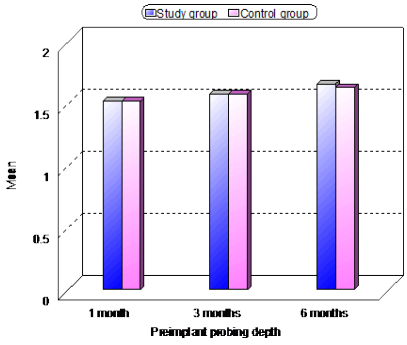


Fig 15: Peri-implant probing depth.

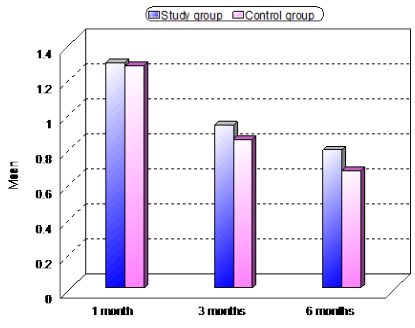


Fig 16: PBI.

B) Radiographical evaluation

Bone density showed significant difference between the 2 groups specially at the initial follow-up period where it was (93.31± 0.9) in the 1st month of the study group and while it was (90.85±1.66) in the same period of the study group

Discussion

Within the limitations of the present research, the use of melatonin as a graft material around immediately placed dental implant in conjunction with bone graft showed relative success. Selection of the cases was based on having a gap of > than 2 mm around the implant. This was attributed to the fact stated by Esposito et al (9) that bone graft recommendations are limited to defects exceeding 2 mm. Regarding implant mobility all implants showed no detected mobility throughout the evaluation period indicating progressive osseointegration, since it is considered an important criterion of implant success as advocated by Porter and Von Fraunhofer (21). This was further confirmed in the radiographic evaluation held during the study. The mean probing depth and bleeding index showed no statistical significant difference between both groups in any period this could be attributed on the good adaptation of the sulcular epithelium which conforms to Hansson et al (22) findings.

In accordance with Joly et al (23) assessment of bone density was radiographically evaluated which is a non-invasive and fast technique. Increased bone density associated with Melatonin implantation around implant fixtures can be attributed to Kasuhito et al (16) advocations that melatonin showed increase in the activity of alkaline phosphatase (ALP) when applied in osteotomy sites and enhanced mRNA expression of the early phase type I collagen and shortened time of mature osteoblast differentiation. Bone grafting and melatonin are thus considered as bone stimulators through enhancing osteoblastic differentiation, proliferation and potential early matrix production and mineral deposition.

Conclusion

Melatonin can be successfully used in combination with bone substitutes in promoting osteogenesis and early osseointegration of immediate implant placed in extraction sockets.

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