



Evaluation of Autogenous Bone Graft around Dental Implant Alone or Combined with Melatonin gel: Randomized Control Trial

Lobna M. Abdelaziz^{1*}, Hala H. Hazzaa², Naglaa A. Shawki³

Codex : 52/20.07

azhardentj@azhar.edu.eg

http://adjg.journals.ekb.eg

DOI: 10.21608/adjg.2020.12761.1142

Oral Medicine & Surgical Sciences
(Oral Medicine, Oral & Maxillofacial
Surgery, Oral Pathology, Oral Biology)

ABSTRACT

Purpose: The present study was conducted to evaluate the effect of autogenous bone graft on the osseointegration of early loaded dental implant either alone or combined with Melatonin gel. **Material and Methods:** The study was including 10 patients with 20 numbers of sites and age range of 22-52 years. The study groups were designed in two groups, test group treated surgically with dental implant after application of autogenous bone graft mixed with (1.2mg) melatonin gel. Control group treated surgically with dental implant after application of autogenous bone graft alone. **Results:** Clinically, in both groups, there was change in gingival thickness with significant difference within test group. Regarding radiographic marginal bone levels measurements; in both groups the mean marginal bone loss was increased by time, with significant difference between both groups in favor of test group. **Conclusions:** Early loaded dental implants can be successfully used to reduce the healing period. The adjunctive topical use of melatonin seems to have a more valuable outcome in promoting the early osseointegration which reflect the meaningful in clinical and radiographic improvement.

INTRODUCTION

The dental implant is a surgical segment that interfaces with the bone of the jaw or skull to help a dental prosthesis to replace the missed dentition or to help the orthodontic anchorage. In the present days dental

KEYWORDS

Early Loaded Implant,
Bone Graft, Melatonin.

- A paper extracted from Doctor Thesis titled " Evaluation of Autogenous Bone Graft Around Dental Implant Alone or Combined with Melatonin gel: Randomized Control Trial"
- 1. Assistant lecturer of Oral Medicine, Periodontology, Oral Diagnosis and Dental Radiology Department. Faculty of Dental medicine for girls Al-Azhar university Egypt, Cairo, Egypt.
- 2. Professor of Oral Medicine, Periodontology, Oral Diagnosis and dental Radiology. Faculty of Dental Medicine for Girls Al-Azhar University Egypt , Cairo, Egypt.
- 3. Professor and head of Oral Medicine, Periodontology, Oral Diagnosis and Radiology department. Faculty of Dental Medicine for Girls Al-Azhar University Egypt , Cairo, Egypt.

* Corresponding author email: lobnamohammed85@yahoo.com

implant is considered the main procedure to replace the missed teeth through a biologic procedure called osseointegration, where the materials of fixture make close cling to bone. The implant apparatus is first set, with the goal that it is probably going to osseointegrate, and then dental prosthetic applied. A variable period of recuperating time is required for osseointegration before dental prosthesis application⁽¹⁾.

Early loading is characterized by inception of functional capacity between 48 hours and 3 months after fixture placement. As result of enhancement of implant surface by different process, the loading time will be generally abbreviated; as it is there will two months for mandible and four months for maxilla. Unlike the ordinary loading protocol, in which the loading occurs three to six months after fixture placement for osseointegration, the early loading procedure decrease the total time of treatment through reducing healing period. In the first stage of healing, due to reduction in duration of removable prosthesis use or edentulous period, the patient will have easy function and good appearance⁽²⁾.

Bone augmentation is a method which can perform either by utilizing bone blocks or bone particulates or mix of both types. The bone can be gathered from the patients themselves either intra-oral or extra-oral, depending on the amount of available bone and its type (cancellous or cortical). Collecting of autogenous bone is associated with expanded postoperative bleakness and difficulties, which fluctuate contingent upon the donor site⁽³⁾.

From a biological view, autogenous bone graft the best accessible material, since it is never switch the patient immunogenicity that responsible about graft rejection at the host site. The autogenous graft hold its suitability after transplantation, which permit attraction of MSCs, osteoprogenitor cells, osteogenic cells, and growth factors that prompted new bone formation. Autografts have no related danger of viral transmission; in addition, they

offer auxiliary help to embedded devices and, it eventually, become in corrupted with surrounding bone as one structure through creeping substitution⁽⁴⁾.

Melatonin (N-acetyl-5-methoxy-tryptamine) is an indoleamine synthesized and secreted to circulation by the pineal gland and different organs, as retina, bone marrow, and digestive system tracts in a circadian manner. Extrapineal organs contribute ineffectively, and it starts to secret in response to its circulation concentration. Melatonin impacts in various physiological activities that might be intervened through conjugation of indoleamine to membrane receptors in all tissues cells⁽⁵⁾.

Melatonin appears to work through various ways to decrease oxidative stress. Experimentally melatonin appear to play as direct and in direct scavenger it have ability to switch the antioxidant enzymes, secretion of glutathione it have capacity to expand the productivity of mitochondrial electron transport chain (ETC) along these lines; bringing down electron spillage and diminishing free radical generation⁽⁶⁾.

MATERIAL AND METHODS

Ten patients with 20 numbers of edentulous site and age scope of 22-52 years. They have missed mandibular premolar/molar teeth. They were chosen from those going to the outpatient clinic of Oral Medicine, Periodontology, Diagnosis and Radiology Department, clinic of Dental Medicine, for Girls, Al-Azhar University, Egypt . The trial was accepted by the Research Ethics Committee of Faculty of Dental Medicine, Al-Azhar University for Girls. All subjects were educated about the nature and advantages of their participation in the trial. Very clearing written consent was signed by every patient denoting their convenience about the planned research program and trial design. A point by point medical history in addition to clinical examination was taken from the interest patient to ensure its qualification for the trial design.

All patients must follow the inclusion criteria; Patient with good oral hygiene, absence of any periodontal condition or per apical pathogens, patients having two missing teeth and finally they should have sufficient bone volume in the missing site to be sufficient for implant fixture within 3.5 diameters and 9mm length to allow suitable vertical dimension with opposing tooth.

Exclusion criteria were, Presence of para-function disorder, for example, bruxism, chronic smokers, Patients under radiation treatment, chemotherapy, immunosuppressive medications, corticosteroids and foundational ailments, pregnancy, lactation and patients with systemic condition that affect periodontium or interfere with periodontal treatment.

A randomized split-mouth trial was done on 10 patients with 20 edentulous sites. A computerized tables were utilized to give an irregular and equivalent distribution of patients into two groups; the test group was relegated for the patients underwent dental implant placement (N=10) after use of autogenous bone graft which blended with (1.2mg) melatonin gel.

The control group incorporated those patient enrolled for dental implant (N=10) after utilization of autogenous bone graft bone without mixing with melatonin gel. Before treatment radiographic examination was done including: CBCT for each patient to allow evaluation of fixture position.

Stage I, periodontal treatment was performed for every patient including full mouth debridement in addition to oral hygiene guidelines to maintained healthy oral tissue which will enhance wound healing without complications.

All patients received two pieces dental implant (Nucloss:10018sokakNo:7itoborganizeSanayiBolgeSi35477Tekeli,Menderes/,izmir/turkiye) with inner hexagon connection in one stage. Infiltration anesthesia as 2% lignocaine with 1:80,000 concentration of adrenaline (vasoconstrictor) was utilized. The perioral site was readied utilizing

Betadine crestal cut was performed on edentulous ridge and a full thickness mucoperiosteal flap was reflected buccal and lingual to permit great accessibility.

Low speed engine (2000rpm) was utilized in clock anti clock manner to allow bone removal utilizing trephine bur. Bone block was broken to small pieces utilizing rongeur to enable its application above fixture after its insertion.



Figure (1): Autogenous bone graft

The fixture site was set up by successive penetrating drills according to surgical kit, with decreased low speed (2000 rpm), till the required measurements under enough irrigation system with normal saline along fixture site drilling care must be taken to preserve, the angulation of lost tooth with neighboring without interfere with adjacent tooth arrangement.

The implant fixture was inserted utilizing manual ratchet Torque handle until the full length flushed with bone. Bone chips which harvested from fixture site were applied to above fixture under complete aseptic condition. Then Healing cap immediately applied. In test group 1.2 mg melatonin gel was blended with bone chips before its application above the fixture. The surgical flap was closed utilizing non resorbable suturing material.

After surgical procedure, all patients were educated to apply extra oral ice packs (10-20 minutes) over implant site to avoid hematoma development.

Patients were received augmentin (625 Amoxicillin Trihydrate, 125mg clavulanc corrosive.GSK Glaxo-Smith kline,Egypt) for 7days postoperatively twice/day. Ibuprofen (Brufen kahira pharma& CHEM. IND.CO. Cairo-Egypt), was prescribed as a anti-inflammatory and pain relieving drug, 600mg twice every day for 1 to 3 days after medical procedure. Chlorhexidine mouthwash (Antiseptol Kahira CO. for pharm. what's more, Chem.,IND organization , Cairo, Egypt) was utilizing twice every day for 3 weeks post operatively.

The oral hygiene guidelines were given, and the patients were followed up (by a similar investigator) after suture expulsion till the finish of treatment period.

Stage II: Two months after fixture insertion, the second stage procedure was performed including: The healing cap was supplanted by the abutment; direct impression was made for fixed prosthesis development utilizing heavy and light rubber base material. Metal try in before the final crown (which produced using chorm-cobalt alloy fused with porcelain) cementation. All implants in the present trial were single tooth implant with single crown.

Outcomes measurements:

Clinical and radiographic evaluations were done at zero line and at 6months. Utilizing Planameca machine (promax 3DxM mid. Planameca Finland). For CBCT imaging, the orientation beam was utilized to adjust the jaw bone parallel to the reference surface. The tube voltage was 90kvp, the current was 12mAs and the exposure time was 4-12s a indicated by Field of view (FOV) of pulsed exposure.

The radiographs were taken for liner examination for marginal bone. Exposures were taken by a similar administrator under stander protocol. It was guaranteed that every radiograph demonstrated an undistorted view of implant in addition to 5 mm of bone apical to implant fixture. Zero line CBCT were taken for evaluation of implant site bone width and stature and its relation to vital structure.

Peri-implant soft tissue thickness:

Peri-implant soft margin thickness was measured by using an endodontic file with a pointer, with the aid of a millimeter ruler the thickness was measured at the mid-point between the cervical limit of the free peri-implant margin and the apical limit of the attached peri-implant margin. The patients were clinically evaluated immediately after implant insertion and at 6months the same calibrated researcher did all the measurements.

Linear measurements of bone:

Linear estimations of bone loss around implant were done as follows: On the window of CBCT cross sectional and sagittal cut was chosen in which the edge of the implant was all around outlined. Utilizing the instruments from software represents for linear measurements; a line was drawn from reference point; collar margin of implant to the alveolar crest of ridge at mesial, distal, buccal and palatel sides. These lines represent bone loss around the implant four measurements were done for each implant.

Information were gathered, amended, coded and entered to the Statistical Package for Social Science (IBM SPSS Chicago, IL, USA) version'23. The quantitative information was displayed as mean, standard deviations and extents when their appropriation found parametric. Likewise subjective factors were introduced as number and percentages. The examination between two free gatherings with quantitative information and parametric conveyance were finished by utilizing Independent t-test. The correlation between two matched gatherings with quantitative information and parametric dispersion was finished by utilizing combined t-test. The examination between two increasingly combined gatherings with quantitative information and parametric conveyance was finished by utilizing Repeated ANOVA test. The outcomes were spoken to in tables and graphs. The certainty interim was set to 95%and the safety buffer acknowledged was set to 5%.

RESULTS

The present trial included 10 patients who were somewhat edentulous for at least one year before date of insertion. The age of the patients extended from (22 to 52 years). Concerning treatment resilience, the two treatment modalities were all tolerated by our participants with no complication. Over the period of trial, patients in the two groups showed stable and equivalent oral guidelines. All patients proceeded with their clinical follow up visits. All implants show no clinical peri-implant during the study period.

Table (1) shows the change in gingival thickness within two groups in the whole study period. Through

test group, the mean of gingival thickness was (2.10 ± 0.38) at base line and (2.50 ± 0.41) at 6 months. There was a statistically significant increase from base line to 6 months, (p-value = 0.005). Within control group, the mean of gingival thickness was (2.55 ± 0.42) at base line and (2.15 ± 0.53) at 6 months. There was no statistically significant difference from the base line to 6 months, (p-value = 0.06).

Table (2) shows the changes in mean marginal bone loss. Concerning bone dimension at 6 months, there was a noticeable significant increase in mean of marginal bone loss. Control group shown higher reduction values (1.66 ± 0.28 mm) in comparison with test group (0.67 ± 0.14 mm).

Table (1): The mean and SD values and results of comparison in GT within two groups.

GGingival thickness		Control group	Test group	Test value	P-value	Sig.
		No. = 10	No. = 10			
Base line (mm)	Mean±SD	2.55 ± 0.42	2.10 ± 0.38	2.518	0.021	S
	Range	2 – 3	1.5 – 3			
6months(mm)	Mean±SD	2.15 ± 0.53	2.50 ± 0.41	-1.655	0.115	NS
	Range	1 – 3	2 – 3			
Paired t-test	t	2.097	3.748			
	p-value	0.065	0.005			

*Significant difference (p value < 0.05).

Table (2): The mean, standard deviation (SD) for the comparison of marginal bone level in the two groups

Marginal bone loss		Control G	Test G	Test value	P-value	Sig.
		No. = 10	No. = 10			
Mesial	Mean±SD	1.85 ± 0.47	0.66 ± 0.28	6.849	0.000	HS
	Range	0.85 – 2.8	0.2 – 0.98			
Distal	Mean±SD	1.55 ± 0.42	0.75 ± 0.34	4.640	0.000	HS
	Range	1 – 2.04	0.06 – 0.98			
Buccal	Mean±SD	1.70 ± 0.53	0.60 ± 0.27	5.883	0.000	HS
	Range	1 – 2.5	0.02 – 0.92			
Lingual	Mean±SD	1.52 ± 0.31	0.67 ± 0.29	6.405	0.000	HS
	Range	1.04 – 1.92	0.14 – 0.92			
Average	Mean±SD	1.66 ± 0.28	0.67 ± 0.14	9.912	0.000	HS
	Range	1.35 – 2.19	0.48 – 0.91			

> 0.05 NS: Non-significant; < 0.05 S: Significant; < 0.01 HS: Highly significant

DISCUSSION

Regarding gingival thickness, there was statistical difference within test group from base line to 6months that was agreed by the finding of El-Gammal et al, who reported that melatonin could keep and pick up the integrity of gingival tissues through increasing collagen, decorin, and IL10 expression and decreasing the matrix metalloproteinase-1/ tissue inhibitor of metalloproteinases-1 ratio, and improve wound healing without scars, adding its antioxidant properties ⁽⁷⁾.

In the present study, contrasting the control group and the test group, the less measure of marginal bone loss was appeared in the test group at the four sides (mesial, distal, buccal and lingual). This change was huge toward the end of trial, ($p=0.0001$). This outcome could be upheld by the discoveries of studies which expressed that melatonin acts by inhibiting the action of osteoclasts. This is an immediate activity going on for an extremely brief time, as there is no bone rebuilding yet but just the presence of inter-thread bone and all peri-implant bone region. Therefore, melatonin keeps on following up on a piece of the bone that has endured vigorous placement of the implant, requiring remodeling by osseous matrix production which expects 5 to 8 weeks ⁽⁸⁾.

Another study revealed that, after a two-week treatment period, melatonin significantly improved the outer limits of bone that was in direct contact with the treated implants; furthermore, they reported that there was increase in osteoblast proliferation by melatonin in the peri-implant zone. Intermittently, they reported that the expected dose of melatonin required to increase osseointegration of dental implant and diminish the marginal bone resorption is 1.2 mg of melatonin powder for each implant that was in contour with the selected dose in this current study ⁽⁹⁾.

Thoma et al found that melatonin has a positive effect in the new bone development around implant

through the differentiation of new preosteoblasts, which are transported from bone marrow to the alveolar bed. Moreover, melatonin advanced expression of genes for bone sialoprotein, alkaline phosphatase, and osteocalcin after a time of 5 to 9 days ⁽¹⁰⁾.

In a study detailed the marginal bone loss in 15 years follow up of osseointegrated dental implants in the edentulous mandible demonstrated more prominent bone loss through the first year of prosthesis stacking, averaging 1.2 mm with a scope of 0– 3 mm. This finding shows that utilization of autogenous bone graft with dental implant decreased the marginal bone resorption ⁽¹¹⁾.

CONCLUSION

In the light of finding of present study, the two groups demonstrated positive clinical and radiographic changes with test group which got dental implant with autogenous bone graft with 1.2mg melatonin than control group who got dental implant and autogenous graft only.

REFERENCES

1. Papaspyridakos P, Mokti M, Chen CJ, Benic GI, Gallucci GO, Chronopoulos V. "Implant and Prosthodontic Survival Rates with Implant Fixed Complete Dental Prostheses in the Edentulous Mandible after at Least 5 Years: A Systematic Review. *Clin Implant Dent Relat Res.* 2014; 16:705-17.
2. Beldar A, Bhongade ML, Byakod G, Buregoni C. Early loading of single-piece implant for partially edentulous posterior arch: a prospective one-year case report. *Case Rep Dent.* 2013; 2013: 854062.
3. Pistilli R, Felice P, Piattelli M, Nisii A, Barausse C, Esposito M. Blocks of autogenous bone versus xenografts for the rehabilitation of atrophic jaws with dental implants: Preliminary data from a pilot randomised controlled trial. *Eur J Oral Implantol.* 2014; 7:153–71.
4. Greenwald AS, Boden SD, Goldberg VM, Yusuf K, Laurencin CT, Rosier RN. Bone-graft substitutes: facts, fictions, and applications. *J Bone Joint Surg.* 2001; 83: 98–103.

5. Permuy M, López-Peña M, González-Cantalapiedra A, MuñozIntv F. Melatonin: A Review of Its Potential Functions and Effects on Dental Diseases. *Int J Mol Sci.* 2017; 18: 865.
6. Reiter RJ, Tan DX, Mayo JC, Sainz RM, Leon J, Czarnecki Z. Melatonin as an antioxidant: biochemical mechanisms and pathophysiological implications in humans. *Acta Biochmi Pol.* 2003; 50:1129–46.
7. El-Gammal MY, Salem AS, Anees MM, Tawfik MA. Clinical and Radiographic Evaluation of Immediate Loaded Dental Implants With Local Application of Melatonin: A Preliminary Randomized Controlled Clinical Trial. *J of Oral Implantol.* 2016; 42: 119-25.
8. Karasek M, Stawerska R, Hilczer M, Zylinska K, Lewinski A. Melatonin circadian rhythm in women with idiopathic hyperprolactinemia. *Neuro endocrinol Lett.* 2004; 25: 411-14.
9. Cutando A, Gomez-Moreno G, Aran, C, Munoz F, Lopez-Pena M, Stephenson J, et al. Melatonin stimulates osteointegration of dental implants. *J. Pineal Res.* 2008; 45: 174–79.
10. Chappuis V, Cavusoglu Y, Buser D, Arx T V. Lateral Ridge Augmentation Using Autogenous Block Grafts and Guided Bone Regeneration: A 10-Year Prospective Case Series Study. *Clin Implant Dent and Rel Res.* 2017;19: 85-96.
11. Thoma D, Maggetti I, WallerT , HämmerleC H F Jung R E. Clinical and patient-reported outcomes of implants placed in autogenous bone grafts and implants placed in native bone: A case–control study with a follow-up of 5–16 years. *Clin Oral Impl Res.* 2019; 30:1–8.