**EVALUATION OF THE EFFECT OF CALCITONIN ON OSSEOINTEGRATION OF DENTAL IMPLANT**

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**ABSTRACT**

The aim of the present study was to evaluate the effect of Calcitonin on bone mineral density around dental implant. Fourteen implants were placed in 6 partially edentulous patients. Extreme ages, smokers and medically compromised patients were excluded from the study. Swiss plus delayed loading implant system was used. The surgical protocol was applied for each patient under complete aseptic conditions, using successive drills and proper coolant to avoid heat generation, periapical views were taken after every step with the use of paralling pins to ensure proper parallelism. Salmon Calcitonin, resembling Calcitonin hormone which is normally secreted by thyroid gland for bone formation in the human body was injected in each patient post operatively in order to increase bone mineral density around implants placed and to enhance osseointegration. Radiographic evaluation was done using Dual Energy X ray Absorptiometry (DEXA) in addition to Computed Tomography (C.T) preoperative and 16 weeks postoperatively to measure bone mineral density at the proposed site for implant placement. Preoperative and postoperative values were compared. The result of the study concluded a significant increase of bone mineral density was observed in all patients postoperatively.

**KEYWORDS:** Dental implant, osseointegration, calcitonin, DEXA

**INTRODUCTION**

Osseointegration is the basic aim of placing implants in edentulous areas. It results in permanent attachment of Titanium to human bone. In order to achieve proper osseointegration certain criteria are mandatory such as proper diagnosis, treatment plan and follow up. It is so important to select the suitable cases for implant placement. Medically compromised patient, extreme ages are not preferred. Smoking should be prohibited as it interferes with healing. (1, 2)

In recent years, several modifications of specific surface properties such as structure, chemistry, surface
charge, and wettability have been investigated to improve osseointegration of titanium implants. Numerous materials with osteoconductive or osteo-inductive capacity have been used to improve new bone formation. These materials are available in unlimited quantities in the hope of eliminating or limiting the need for harvesting iliac crest bone grafts. In the last 10 years, osteoinductive materials, such as bone morphogenetic proteins (BMP), have received much attention, mostly as a result of their capacity to improve proliferation of osteo-transforming cells derived from undifferentiated cells. Also Calcium hydroxyl appatite, biphosphonates, plasma proteins, growth factors as platelet derived growth factors, platelet rich plasma and bone cement were also utilized.

Calcitonin is a major hormone secreted by thyroid gland responsible for bone formation and decrease of blood calcium level. It has been proved that the synthetic Salmon Calcitonin enhance bone growth in depth as well as in width that is why it has been used as a treatment for bone diseases and fractures. Salmon Calcitonin is a mixture of amino acids plus a modifying agent. It was reported that the calcitonin affect bone healing around titanium implants and there is growth in endosteal bone in width and height. (7, 8)

Calcitonin is approved for the treatment of osteoporosis and other diseases involving accelerated bone turnover. It is an endogenous inhibitor of bone resorption. Several studies have shown its effects on bone mineral density in postmenopausal female. When salmon calcitonin was given to postmenopausal women, new vertebral fractures were decreased. This has been interpreted as a quality effect of antiresorptive agents beyond the effect on bone mineral density. (9-10) Januario A. and associates (7) have observed the effect of calcitonin on bone healing around titanium implants in an experimental study. The adult rabbits received titanium implants one in each femur. Bone analysis was done after 6,8,12 & 18 weeks. Growth in endosteal bone was observed in width and height after 12 & 18 weeks.

Dual energy x ray Absorptiometry (DEXA) measures bone mineral density (amount of minerals) to assess the bone quality in a volumetric value (pre and post operatively) around implants. It is a non invasive, non painful safe and quick tool in the form of low dose of radiation. It is a two dimensional image, which lacks details and cannot differentiate between cortical and cancellous bone. C.T. scan is another method to measure bone mineral density around implants and in proper placement of the implant, as well as measuring precisely bone width and height of alveolar ridge. It can detect approximation of vital structures, identify any pathological lesions or any bone abnormality. It can differentiate between cortical and cancellous bone as it is done in slices. The main disadvantages of C.T. scan that it exposes the patient to a high radiation dose besides being of a high cost. (11-13)

Changes in bone density are likely to contribute to implant fixation failure. Bone densitometry provides useful information with regard to bone architecture around implants, and various techniques have been employed to measure the degree of bone density change around implants with varying degrees of accuracy. These techniques include radiographic Absorptiometry, dual energy X-ray absorptiometry (DEXA), and quantitative computed tomography (qCT). (11,14,15).

**PATIENTS AND METHODS**

This study comprised fourteen implants distributed among six partially edentulous patients free from any systemic disease, non smokers, with age ranging from 24 – 48 year. Diagnosis of the cases was based on Personal, medical and dental history, clinical exami-
nation as well as radiographic assessment. Oral health care were done for each patient one week before implant placement. Two stages surgery of delayed loading dental implants (Swiss Plus Zimmer Implants, Dental Anchorage Germany) have been utilized. Dual Energy X ray Absorptiometry (DEXA) Fig. (1) was done for each patient preoperatively to measure bone mineral density at the proposed implant site, as well as post operatively at different intervals one, five and sixteen weeks. The bone mineral density around the implants was measured and compared with the preoperative values. Computed Tomography C.T. scan was performed for each patient preoperatively and at the end of the study. Patients were injected with Salmon Calcitonin (Micalcin 100 I.U., Novartis Switzerland) 5 I.U/kg I.M. each ampoule contains 100 I.U. three times a week post operatively for the period of twelve weeks. The size of implant (Length & diameter) was determined according to the panoramic view, C.T. scan and ridge mapping. All patients were given same preoperative drugs including anxiolytic as Bromazepam (Calmepam, Glaxo Smithklien USA.) and anti inflammatory Dexamethasone (Dexamethazone, Sigma Egypt) to decrease post operative inflammation and edema.

Surgical procedures

Local analgesia (Mepicaine, Alexandria Company Egypt) was injected. Para-crestal incision and flap was reflected to achieve complete coverage of dental implant. Primary bone indentation was done using a surgical round bur, after precise measurement with a surgical ruler for exact locating of drilling point. Bone drilling with primary bone drill accompanied by copious saline irrigation according to predetermined length of implant Fig. (2). Paralleling pin was introduced to adjust the parallelism of the drilling Fig. (3). Final bone drill accompanied also by copious saline irrigation, implant inserted and periapical film was taken. The healing screw was placed Fig. (4) and the flap was replaced and sutured by the use of black silk size 000. Postoperative instructions were given to the patients and prescription of drug was performed including Antibiotic Rovamycin (Rovac, Delta Pharma Egypt) for five days, analgesic Ketoprufen 50 mg (Ketofan, Al Ameryah Company Egypt) for post operative pain and mouth wash Betadine( Betadine, Al Ahram Company Egypt). Sutures were removed after 7 days of surgery.

Fig. (1)  DEXA showing increase in bone mineral density as depicted from reading in image starting from below upward.

Fig. (2) Flap reflected and primary bone drilling
Postoperative radiographic assessment and statistical methods

Dual Energy X ray Absorptiometry (DEXA) was done after one, five and sixteen weeks post operatively and bone mineral density was measured. Digital computed tomography C.T. was done at the end of the study after sixteen weeks and radiodensity value was compared to preoperative value. Data were presented as means, standard deviation (SD) and standard error (SE) values. The coefficient of variation (CV) was calculated to allow the comparison between the two methods (C.T. scan and DEXA) without the need of equaling the units. Paired t-test was used to study the changes by time with each method. Pearson’s correlation coefficient was used to determine significant correlation between the two methods.

The significance level was set at \( P \leq 0.05 \). Statistical analysis was performed with SPSS 16.0® (Statistical Package for Scientific Studies) for Windows.

**RESULTS**

The postoperative course was uneventful. All cases included in the study showed complete healing. No postoperative complications were seen from the injected salmon Calcitonin. A significant increase was observed in bone mineral density around dental implants when postoperative values compared with postoperative values.

**Changes of bone mineral density measured by DEXA**

The means, standard deviation and \( p \)-value results of paired t-test for studying changes by time in bone density measured by DEXA as follow: pre operative mean equals 1.21, the Standard Deviation equals 0.5. The post operative one week mean equals 1.43 and the Standard Deviation equals 0.6. The post operative 5 weeks mean equals 1.52 and the Standard Deviation equals 0.6. The post operative sixteen weeks mean equals 1.7 and the Standard deviation equals 0.4.

Table (1) Fig. (5). There was no statistically significant change in mean bone density after one week and after 5 weeks and the only statistically significant increase in bone density was seen after 16 weeks with \( p \)-value equal 0.04.

**Fig. (3) Paralleling pins**

**Fig. (4) Implants inserted covered with healing screw**

**Fig. (5) Changes by time in bone density measured by DEXA**
EvAluAtion of thE EffEct of cAlcitonin

Changes bone mineral density measured by C.T

The means, standard deviation (SD) values and results of paired t-test for studying changes by time in bone density measured by C.T. are as follow:
The preoperative values, the mean equals 468, the Standard Deviation equals 106.5, the sixteen weeks postoperative values, the mean equals 736.2, the Standard Deviation equals 286.2, with P-value equals 0.031 which is statistically significant being less than 0.05 that means there was a statistically significant increase in mean bone density after 16 weeks. Table (2). Fig. (6, 7)

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean</th>
<th>SD</th>
<th>Comparison</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative</td>
<td>1.21</td>
<td>0.5</td>
<td>Postop – 1 week</td>
<td>0.092</td>
</tr>
<tr>
<td>1 week</td>
<td>1.43</td>
<td>0.6</td>
<td>Postop – 5 weeks</td>
<td>0.113</td>
</tr>
<tr>
<td>5 weeks</td>
<td>1.52</td>
<td>0.6</td>
<td>Postop – 16 weeks</td>
<td>0.041*</td>
</tr>
<tr>
<td>16 weeks</td>
<td>1.7</td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: Significant at P ≤ 0.05

Fig. (6) Changes by time in bone density measured by C.T.

TABLE (1) Paired t-test for the changes by time in bone density measured by DEXA

<table>
<thead>
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Fig. (7) Showing pre & postoperative C.T.

TABLE (2) Paired t-test for changes by time in bone density measured by C.T.

<table>
<thead>
<tr>
<th>Pre-operative</th>
<th>16 weeks</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>468</td>
<td>106.5</td>
<td>736.2</td>
</tr>
</tbody>
</table>

*: Significant at P ≤ 0.05
Correlation between the two methods (DEXA and C.T.)

The correlation coefficient of preoperative value equals 0.048 and the P-value equal 0.334. The correlation coefficient postoperatively sixteen weeks equals 0.279 and the P-value equals 0.539. There was no statistically significant correlation between C.T. and DEXA measurements pre-operatively and after 16 weeks post operatively as the P-value was greater than 0.05 Table (3).

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>16 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation coefficient (r)</td>
<td>0.481</td>
<td>0.279</td>
</tr>
<tr>
<td>P-value</td>
<td>0.334</td>
<td>0.593</td>
</tr>
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### DISCUSSION

The present study utilized the idea of benefits of Calcitonin hormone in bone formation in an attempt to enhance bone mineral density around dental implant. Calcitonin has the advantages of increasing bone mineral density in depth as well as in width. Dental implants have been used over the past decades as the best replacement option for missing teeth. Review of literature regarding factors that enhance of bone mineral density showed calcitonin did not used in a human trial in dental implant. This drug has lower side effect this idea encouraged this study to use Salmon Calcitonin in order to enhance bone formation around implants in human being using minimum therapeutic dose of the drug.

In the present study there were several criteria for patient selection in order to achieve success. The patients are systemically free, not medically compromised, and non smokers as smoking retards healing as well as having good oral hygiene. Extreme ages were avoided, as patients below 18 years are likely to have undeveloped bone and patients over 60 years will be suffering from bone resorption and impaired healing according to Sugarman P.B. and associates. Plasma sprayed Titanium implants has been utilized in the present study being the best implant enhancing osseointegration, according to Yang Y. et al.

The current study, a survey was done as regard the therapeutic dose of Salmon Calcitonin for treatment of different bone diseases in human. Since there were no previous studies showing the use of Salmon Calcitonin in healthy patients previously, so it was decided to choose the minimal therapeutic dose which could be safe for patients as prophylactic and effective at the same time. Each patient received three intramuscular injections per week, each ampoule contains 100 I.U. according to body weight and that is supposed to be the minimum therapeutic dose as indicated for osteoporotic patients.

In the present study it is preferred to inject the patients with Salmon Calcitonin via intramuscular route rather than using nasal spray. Salmon calcitonin is available as intranasal it is not as well absorbed as injectable calcitonin. The oral route is ineffective due to its decreased absorption. Although intranasal calcitonin is widely used and has wide patients acceptance, seems to be more convenient and easier administration, however it has got other side effects as it is not as well absorbed as injectable calcitonin, also causing rhinitis, nasal congestion, nasal dryness, sneezing and inflammation in nasal mucosa. That is why in the present study it is preferred to inject the patients with Salmon Calcitonin via intramuscular route. The Salmon Calcitonin has been used in the present study via intramuscular I.M. route, as it is better absorbed rather than other routes to assure that the predetermined dose will reach the circulation, also
to guarantee direct supervision on patients avoiding the human factor. And finally to overcome local side effects of other routes as decreased absorption and allergies. The concept of using intramuscular I.M. route was supported by M. A. Porgel (17) and associates.

Osseointegration normally takes from three months in mandible and six months in maxilla to occur, accordingly the time allowed for post operative radiographic evaluation has been estimated in this study to be as average sixteen weeks to assure osseointegration in either jaw. Dual Energy X ray Absorptiometry (DEXA) has been utilized in this study for its benefits. As it has low radiation dose, availability, capability to evaluate multiple sites, low cost, reproducibility and ease of use have made DEXA the most widely used technique for measuring bone mineral density.

The current study utilized Dual Energy X ray Absorptiometry (DEXA) to measure bone mineral density preoperatively and compare it to postoperative values around dental implant. It denoted an increase in the bone mineral density around implants. These finding were supported by results of Gulsahi (18) and associates and Martini F. (19) and coworkers who used DEXA to measure bone mineral density around implants in previous studies. Such data was beneficial in the implant field. According to previous studies made, it is possible to use Dual Energy X ray Absorptiometry DEXA to evaluate bone density around dental implants and according to their findings DEXA has succeeded in detecting bone changes around implants. Use of DEXA to measure bone mineral density around implants after injection of Salmon Calcitonin in the present study according to review of literature was the first attempt in the field of implantology.

In the present study Dual Energy X ray Absorptiometry (DEXA) was used in addition to C.T. scan to measure bone mineral density preoperatively and compare it with postoperative values around the dental implant. The values of the bone mineral density measured by DEXA and C.T. sixteen weeks post operatively have increased noticeably in all patients around dental implants after being injected with the predetermined dose of Salmon Calcitonin for twelve weeks, so the values obtained by DEXA is confirmed by the finding of C.T.

Findings at the end of the present study showed that bone mineral density was increased in all patients as compared to preoperative values as measured by DEXA and verified by C.T. this denotes that the suggested used dose of Salmon Calcitonin seems to be suitable in normal subjects to enhance bone mineral density around dental implants. The findings obtained from readings of DEXA and C.T. preoperatively and sixteen weeks postoperatively showed significant increase in Bone mineral density denoted that DEXA can be used separately for assessment of bone mineral density around implants and gaining the benefits of low radiation dose.

CONCLUSION

Salmon Calcitonin is recommended for increasing bone mineral density around dental implants. Dual Energy X ray Absorptiometry DEXA is an accurate safe method to measure bone mineral density around implants with a minimum radiation exposure dose than computed Tomography C.T. density around implants.

REFERENCES


