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Stability of dental implants placed in healed bony sites of hyperlipidemic patients: A case series

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Abstract---Background: The effect of elevated levels of serum fats - hyperlipidemia- on the long-term implant stability and bone quality has been heavily examined in animal-model studies. This human-based case series is the first clinical study which aimed at clinical and radiographic evaluation of dental implant stability and the changes in bone density in patients with high lipid profile. Materials and Methods: Twelve female patients, each had a single healed bony site which indicated for implantation together with high serum fasting (Low-density lipoprotein) LDL level (≥ 160 mg/dl) were included in this study. The clinical implant stability values (ISQ) which were measured using the Resonance Frequency Analysis (RFA) method, and CBCT changes were recorded at baseline and six months post-implant insertion. Results: All patients showed implant success after six months. There was a significant increase of implant stability after 6 months from (65.92 ± 6.39 ISQ) to (74.42 ± 6.20 ISQ) ($p < 0.001$). Conclusion: In the light of this very first clinical study on the correlation between dental implant stability and hyperlipidemia, authors didn't find that the stability of delayed dental implants placed in healed bone sites could be affected by high serum LDL levels and thus hyperlipidemia alone is not considered a major risk factor for dental implant stability.

Keywords---Hyperlipidemia, stability, dental implants.

Introduction

The high predictability of dental implants has led to its routine use with a great expectation for success. There are many researches focused on the outcome of delayed dental implants and because of the reported high success rate after placement of a dental implant, there has been an increasing interest in this technique for replacing missing exodontia (*Chen et al., 2004*). Bone is a dynamic tissue that undergoes constant remodeling by different bone cells. In fact, 10% of the human skeleton undergoes remodeling every year (*Feng and McDonald, 2011*). Bone remodeling has proved to be sensitive to environmental changes including metabolic disorders. Among various metabolic pathways, the effect of lipid metabolism on bone and bone cells has significantly advanced in the past decade. The effect of lipid metabolism on bone cells has been recently highlighted. Many researchers have studied the association between bone loss and lipid-altering conditions such as atherosclerosis, obesity and hyperlipidemia and uncover the detrimental effect of lipids accumulation on bone homeostasis (*Kim et al., 2013*).

Peri-implant osteogenesis consists of postsurgical reaction and remodeling of the bone and the initiation and progression of de novo bone formation, which are represented as a reduction in primary stability and development of secondary stability, respectively (*Ogawa et al., 2003; Atsumi et al., 2007*). Dental implant survival is mainly dependent on successful osseointegration following placement. Any alteration of this biological process may adversely affect the success rate. Also, the long-term prognosis is adversely affected by inadequate bone volume at implant sites.

There are several well-known risk factors related to implant failure. Patient-related risk factors such as diabetes mellitus, osteoporosis, and smoking are very common and known to negatively affect implant osseointegration. Recently, some authors suggested that there is a relationship between hypercholesterolemia and adverse dental implant osseointegration (*Keuroghlian et al., 2015; Tirone et al., 2016*). Hyperlipidemia is a state with an abnormal lipid profile, which is characterized by elevated blood concentrations of triglycerides, elevated levels of total cholesterol and LDL, and decreased levels of HDL cholesterol (*Saxlin et al., 2008*). Hyperlipidemia is associated with several diseases such as atherosclerosis and osteoporosis.

The National Health and Nutrition Examination Survey (NHANES III) reported that 63% of osteoporotic patients have hyperlipidemia (**Jacobs et al., 2005**). The main mechanisms of the relationship between hyperlipidemia and bone tissue metabolism are the involved aspects of some metabolic changes, including lower bone mineral density, increase in the number of osteoclasts, and the inhibition of osteoblastic activity. Recently many papers focused on high cholesterol and its impact on bone turn over around dental implants, but all of them are animal studies. Despite the ever-increasing number of published experimental studies on this topic, there is however zero clinical researches on the correlation between hyperlipidemia and dental implants stability.

Subjects and Methods

Study settings:

The present case series study included 12 patients having high serum LDL and healed extraction sockets which were replaced with delayed implants. All of the participants were enrolled by the main investigator from the outpatient clinic of Department of Oral Medicine and Periodontology, Faculty of Dentistry, Cairo University. Screening of patients was continued until the target sample was achieved. Identifying and recruiting potential subjects was achieved through patients' database.

Patients' Selection:

Patients were recruited from the outpatient clinic of Oral Medicine, Oral Diagnosis and Periodontology department, Faculty of Dentistry, Cairo University. The following inclusion criteria were applied: Patients who had missing tooth/teeth with adequate bone width and height, and sufficient inter-arch space (5 mm) for dental implant placement, patient's age was 20 years or older, patients with hyperlipidemia (fasting LDL \geq 160 mg/dl), motivated and hygiene conscious. The patients were excluded on the basis of: uncontrolled diabetes mellitus or other systemic disorders except for hyperlipidemia, Physically or mentally handicapped patients, No or poor patient's compliance, pregnant females, any habits that jeopardize the osseointegration process, such as current smokers, rhinitis or sinusitis, and parafunctional habits that produce overload on implant.

Treatment Protocol:

A thorough history and medical evaluation were done before the initiation of treatment. Cone- beam computed tomography (CBCT) was done to perform accurate measurements in three dimensions and to evaluate the dimensions of the healed bony sites accurately. All the patients underwent pre- surgery screening and initial periodontal therapy. All procedures were performed by the same operator under adequate aseptic conditions and local anesthesia (Septocaine*) using a local infiltration technique for maxillary teeth and inferior nerve block technique for mandibular teeth.

Crestal incision at the pre-determined edentulous area was performed using 15c blade, followed by intrasulcular incisions around the adjacent teeth and then the flap was reflected using suitable size mucoperiosteal elevator. Sequential drilling was performed and all osteotomies had been prepared using a drilling speed of (1200 rpm) according to manufacturer instructions under copious irrigation with normal saline. Proper implant[†] length and diameter based on CBCT measurements was then inserted. Primary implant stability was measured immediately after implant seating using Penguin Resonance Frequency Analysis

* Septocaine, Articaine with epinephrine 1:100000, Septodont, Canada.

† SOLVO UK™, London/ United Kingdom.

(RFA) Monitor[‡] with its corresponding stud called the MulTipeg[§] which made of titanium with a sealed magnet in its top. The MulTipegs are calibrated against a reference to ensure consistent ISQ values. The mean of three successive implant stability quotient (ISQ) values with 5 minutes interval between one reading and the other one was recorded, then the cover-screw was tightened in place using the hex supplied in the surgical kit by the manufacturer.

Simple interrupted suture using 4-0 resorbable suture^{**} to reposition the flap in place. Immediate post-operative CBCT scans were done on the same day or maximum within 3 days post-surgery, to check for proper implant position in the bony housing, and for comparison of peri-implant crestal bone dimensional changes and bone density later on at the end of the follow up period. Postoperatively, systemic antibiotic (Amoxil^{††} 500 gm capsules) was prescribed three times daily for 5 days together with Non-steroidal anti-inflammatory (NSAIDS) (Ibuprofen^{‡‡} 600mg tablets) twice daily for 3 days. Patients were instructed to avoid any hard brushing and rinse with antiseptic mouth rinse (0.12% Chlorhexidine) three times per day starting from 24 hours post-operatively for two weeks (Zucchilli *et al.*, 2018). Tooth brushing -using a soft tooth brush- was resumed after sutures removal at the treated sites one week to 10 days post-operatively.

Patients were recalled for sutures removal, and collection of pain and swelling records 10 days post-operatively. After a healing period of six months, the 2nd CBCT scan was done for each participant in order to assess the quality of osseointegration, implants were exposed surgically, healing abutments were placed and suturing was done. One week later, impressions were taken using Polyvinylsiloxane material and the final crowns were fabricated and cemented.

Statistical analysis

Ordinal data were presented as frequency and percentage values. Numerical data were presented as mean and standard deviation values (SD). Normality was assessed using Shapiro-Wilk test. Parametric data were compared using repeated measures ANOVA followed by Bonferroni post hoc test. While non-parametric data were compared using Freidman's test followed by Dunn's post hoc test. The significance level was set at $P \leq 0.05$ within all tests. Statistical analysis was performed with IBM[®] SPSS[®] Statistics Version 26 for Windows.

Results

All patients showed implant success after six months. There was a significant increase of implant stability after 6 months from (65.92 ± 6.39 ISQ) to (74.42±6.20 ISQ) ($p < 0.001$).

[‡] Integration Diagnostics AB, Goteborg, Sweden.

[§] Integration Diagnostics AB, Goteborg, Sweden.

^{**} Assut sutures of Switzerland.

^{††} Amoxicillin Trihydrate 500 mg, GalaxoSmithKline, UK.

^{‡‡} Ibuprofen 600 mg, Abbott, Egypt.

[®] IBM Corporation, NY, USA.

[®]SPSS, Inc., an IBM Company.

Discussion:

In 2015, *Keuroghlian et al.*, concluded that HFD-inducing hyperlipidemia has been remarkably correlated with impaired implant osseointegration and implant loss due to retarded bone formation around the implant in the mouse ~~femur~~femur, and they recommended human clinical correlation. Based on this recommendation, together with the data obtained by the E-search about the correlation of hyperlipidemia and dental implant stability, the authors selected the case series model to be the type of the presented study as to the best of the authors knowledge, this case series is the first prospective human-based clinical study discussing this topic. Hence, the aim of the present study was to clinically evaluate the stability of dental implants placed in healed bony sites in hyperlipidemic patients and associated bony changes.

Regarding the inclusion criteria of the participants only non-smoker, medically fit female patients with hyperlipidemia were included in the study to standardize the healing capabilities of all the participants as suggested by *Moy et al.*, in 2005. In a systematic review published by *Keenan et al.*, in 2016, smoking was proved to increase marginal bone loss around the dental implants, as well as the risk of postoperative infections and the failure rates.

A high serum fasting LDL level of (≥ 160 mg/dl) was a prerequisite for the screened individuals to participate in this study based on the most recent guidelines of cholesterol management by the third report of *Adult Treatment Panel III (ATP III)* which have been issued in *May 2001* by the national cholesterol education program (NCEP) which defined this high level of serum LDL to be atherogenic. Serum LDL level was selected to be the major determinant of hyperlipidemia rather than total cholesterol (TC) level in accordance with *Tirone et al.*, 2016 who reported that, serum LDL level is the actual factor which worsen the bone metabolism rather than TC level.

Diabetes mellitus and hyperlipidemia was proved to co-exist in many patients presented as a disease state known as 'metabolic syndrome' (*Ford et al.*, 2008). Accordingly, glycosylated hemoglobin test (HbA1c) was requested from all participants to exclude diabetes mellitus as a confounding factor which would have definitely affected the validity of the obtained results. Patients who have HbA1c percentage of more than 6% were excluded from this study. Regarding the gender of the included participants, all of them were females, although this wasn't planned from the start of the study to widen the pool of the patients, luckily, this ended up to be a plus for our study, as according to *Fuh et al.*, 2010, there is a gender variation in bone densities which should be taken into consideration when talking about the success rate of dental implants; such variations may be referred to the differences in hormonal profiles between males and females, together with the inherent higher bone mass in males. Therefore, omitting this variation, added some reliability to the results of this study.

Concerning the surgical procedures, all implants were inserted in accordance with the manufacturer's recommendations. *Salles et al.* 2015 reported that the process of drilling to perform the surgical bed (osteotomy) for the installation of endosseous implants produces noticeable local inflammatory reaction which

eventually adversely affect osseointegration, and this can be controlled and/or reduced by the use of adequate irrigation techniques, consequently, drilling was performed under copious amount of normal saline irrigation. Additionally, *Grandi et al., 2015*, recommended minimally traumatic surgical procedure during implant insertion for maximum preservation of the healing potential of bone as well as to reduce crestal bone loss as possible for successful osseointegration; hence, all included participants were subjected to a delicate and atraumatic surgery using sequential drilling osteotomy preparation.

Graham et al., 2021 stated that the formation of a hard implant/bone interface is for years believed to be extremely vital for the short -and long- term function of an implant, therefore, achieving implant stability is a central necessity for successful osseointegration. The major cause of implant loss can be referred mainly to the biomechanically induced failures (*Mesa et al., 2008*). Primary implant stability (mechanical stability) is accomplished when the implant is placed in the bone in such a position that it is “well-seated”, and this comes from mechanical engagement of the implant to the surrounding bone, which is influenced by local bone quality and quantity, the surgical technique itself, and the implant design. Once the implant became adapted to the host bone, secondary stability (Biological stability) is best described by ‘osseointegration’ achieved. (*Sennerby and Roos, 1998; Swami et al., 2016*).

There are various methods to measure implant stability as suggested in literature. Among these methods, the Periotest^{§§} and the Resonance Frequency Analysis (RFA) devices, have proved to be the most reliable, easy to handle and commonly used ones (*Mohapatra et al., 2016*). However, the Periotest although efficient, it has some usage limitations as it can’t detect a ‘borderline’ stability cases (i.e. failing implants), neither can it measure implant stability at the early phases of osseointegration as the percussing force on the implant may deteriorate its stability (*Chang et al., 2010*). Accordingly, many researchers. *kim et al., 2009, Dubey et al., 2013 and Gupta et al., 2021* all recommended the use of RFA devices as an accurate measuring tool for implant stability before the final abutment is connected. Hence, the authors of this study utilized the RFA device as the tool used to measure implant stability.

Sachdeva and co-workers in 2016 reported that the range of ISQ values within which an implant is considered stable is between 75 and 82 ISQ. In our study as regards to the ISQ values indicating the implant stability, the mean of the ISQ values at the baseline was (65.92), while the mean of ISQ values after 6 months was (74.42), that’s to say there was a significant increase of implants’ stability after 6 months from (65.92 ± 6.39) to (74.42±6.20) (p<0.001).

Conclusions

In the light of this very first clinical study on the correlation between dental implant stability and hyperlipidemia, authors didn’t find that the stability of the delayed dental implants placed in healed bony sites could be affected by high

^{§§} Siemens AG, Bensheim, Germany.

serum LDL levels and thus hyperlipidemia alone is not considered a major risk factor for dental implant stability considering the current study limitations.

Recommendations

More clinical studies with comparators, larger sample size and longer follow up periods are required to reach a consensus regarding the effect of hyperlipidemia on dental implant stability and osseointegration.

Limitations

- The follow up period is relatively short, only 6 months, to evaluate complications and longevity of the inserted implants.
- Screened male patients were unfortunately diabetic, so the participants in this study were all females, the thing which made the conclusion less generic.
- The patient's LDL serum levels were all above 160 mg/dl -atherogenic level- according to ATP III guidelines, but definitely there were variations among the participants regarding their LDL serum levels ranging from 170 to 360 mg/dl.

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