

Clinical and Radiographic Assessment of Dental Implants Modified by Bisphosphonates versus Hyaluronic Acid: Randomized Controlled Trial

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Abstract:

The main cause of lower rate dental implant success in maxilla than mandible is the bone quality. So this study assessed the effect of hyaluronic acid and bisphosphonates immediately coated implant surfaces on the hard tissue parameters.

Introduction:

Implant surface wettability is an important factor that influence the osseointegration of dental implants (*Sartoretto, 2015*). Biologic interactions after implant placement occurs between tissues and implant surface. Wettability in terms of surface hydrophilicity enhances those biologic interactions, hence, improving and accelerating the osseointegration (*Guastaldi et. al, 2013; Sartoretto, 2015*). Several implant surface modifications have been developed to improve the surface wettability as material coating implant surfaces (*Wang et. al, 2017*).

Bisphosphonates are pyrophosphate analogues that having a high affinity to bone (*Akram et. al, 2017*). They are locally delivered with dental implants to improve implant osseointegration, enhance the bone formation (*Kellesarian et. al, 2017; Shah et. al, 2017*) and increase the bone implant contact (*Aggarwal et. al, 2016*). They are also used in the treatment of periodontal diseases as they inhibit the osteoclastic activity and enhance the differentiation of osteoblasts (*Akram et. al, 2017; Kanoriya*

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et. al, 2016).

Hyaluronic acid is a natural constituent in different body tissues as the periodontium. It is used in different medical fields due to its multiple functions. It has anti-inflammatory, anti-microbial, antioedematous, angiogenic and osteogenic effects. It plays a role in tissue healing (*Bertl et. al, 2015*). It enhances bone formation by many mechanisms as the enhancement of osteogenic effect of bone morphogenic protein-2 (BMP-2), inhibition of BMP antagonists and enhancing osteoblastic differentiation (*Kawano, 2011*). It was used in periodontal treatment combined with surgical and non-surgical treatment (*Bertl et. al, 2015*). It also was used as a carrier for different materials with dental implants improving the osseointegration (*Korn et. al, 2014; Lee et. al, 2014; Pan et. al, 2015; Wang et. al, 2015*).

In our knowledge, no previous studies used zoledronic acid (type of bisphosphonates) or hyaluronic acid as immediate surface modification of implant surface in human, so this study assessed the effect of zoledronic acid versus hyaluronic acid modifications of dental implant surface.

Subjects and Methods:

Seventeen patients were recruited from the outpatient clinic of Faculty of Dentistry Ain Shams University for this interventional randomized double-blinded study according to the following inclusion criteria: patients with partially premolar-molar edentulous ridge needing implant placement, the edentulous ridge having good bone volume both vertical and horizontal adequate for implant placement, medically free patients according to modified Cornell's medical index, patients with good oral hygiene measures. The exclusion criteria included local infections that may compromise implant site healing, periodontitis affected adjacent teeth, pregnant or lactating females, smokers, alcoholic patients, drug abusers, handicapped and prisoners. The included patients were informed about the procedure

in details and signed the informed consent.

Seventeen implants were placed after the sites has been randomly divided into 3 groups. Each patient share one or two implants. Randomization was performed using computer-based randomization. Group 1 received bisphosphonates modified titanium dental implants, group 2 received hyaluronic acid modified titanium dental implants and group 3 received titanium dental implants without any modifications. It was considered the control group.

Following a full mouth initial therapy including full mouth scaling and root planing using hand and ultrasonic scalers and cruets, all patients received local anesthesia (articaine hydrochloride 4%, 1/100000 epinephrine). Paracrestal incision using pardparker 15C was performed without vertical incision to expose bone of the edentulous area and one tooth on each side. Full mucoperiosteal flap was elevated using mucoperiosteal elevators. Immediately modified titanium implants were placed up to the crestal bone level using the manufacturer instruction manual. Flap Suturing with non-resorbable 4-0 polypropylene sutures was performed.

All patients received antibiotics (Augmentin 1gm t.d.s. and Flagyl 500mg t.d.s.), analgesic and anti-inflammatory (Cataflam 50 mg t.d.s.) and anti-edematous (Alphintern t.d.s.). Postoperative instructions were given to the patients including tooth brushing and flossing of the entire dentition except for the operation area for 2 weeks. Using chlorhexidine mouthwash 0.12 twice daily for 2 weeks. To resume brushing after 2 weeks following surgery.

The clinical assessment included gingival index and implant stability using osstell at 0, one, 3 and 6 months. In radiographic assessment, Cone Beam Computed Tomography was used immediately after implant placement and six months later. Appropriate statistical analysis tests were applied on the recorded, coded and tabulated data.

Results:

Regarding gingival index, in the same group, there was a statistically significant difference between 0 and 6m, the highest mean score was found in 1m, while the least mean score was found in 3m and 6m. There was no statistically significant difference between the 3 groups.

Regarding osstell readings, in group 1, There was a statistically significant difference between 0m and 3m. The highest mean score was found in 3m, while in group 2 and 3, there was a statistically significant difference between 0m and 6m groups. The highest mean score was found at 6m. There was no statistically significant difference between the 3 groups.

Regarding bone density, there was a statistically significant difference between 0m and 6m in all groups. The highest mean score was found at 6m. There was no statistically significant difference between the 3 groups.

Discussion:

The use of dental implants to replace missing teeth has become the most successful procedure along two decades. (Ekfeldt et al., 2001). Clinical studies suggest that dental implants inserted into the mandible have higher survival rates than those for the maxilla, especially for the posterior area (Tinsley et al., 1999; Jemt and Lekholm, 1995). The main cause is the bone quality (Turkyilmaz et al., 2007). This study was performed in order to investigate the possible effects of implant surface coating with 2 of the known materials that having effects on enhancing bone formation.

Hyaluronan is a natural constituent of connective tissue and bone marrow extracellular matrix. It has an essential role in regeneration and repair of soft and hard tissue due to its osteogenic induction capability, biocompatibility and non-toxic (Hasan and Nada, 2017).

Bisphosphonates are pyrophosphate analogues having high affinity for the bone

hydroxyapatite. They are considered active drugs in treatment of disease affecting bone metabolism, such as osteoporosis, multiple myeloma and bone metastasis of prostate or lung and breast cancer (Madrid and Sanz, 2009). So it is important to evaluate the relation between these materials and implant osseointegration and their effects on enhancing bone density in the maxillary region with low bone quality.

In this study implant stability was assessed using Osstell due to its non-invasiveness and reproducibility (Mariano et al., 2013). CBCT is highly accurate in linear measurements and demonstrated correlation with bone density (Suttapreyasri et al., 2018). Soft and hard tissue evaluations carried out in the present study using gingival index, implant stability and bone density as the most commonly reliable parameters used.

The present study showed statistically non-significant difference between the 3 groups regarding gingival inflammation. So it demonstrated the patients were eligible for including in the study and the non-irritant and biocompatible effects of hyaluronic acid and bisphosphonates on the soft tissue.

The present study reported a non-significant effect of hyaluronic acid implant coating on bone density levels. This finding contradict that of the study by Hasan and Nada (2017) who reported that topical application of hyaluronic acid have an osteoconductive effect that accelerates osseointegration. This unexpected findings could be related to type of HA and its consistency.

Bisphosphonate implant surface coating resulted in a more inferior outcomes compared to the control group regarding hard tissue parameters in spite of the reported osteoinductive effects. Holzinger et al. (2014) reported development of osteonecrosis with dental implants in patients with oral or intravenous bisphosphonates therapy, while Javed and Almas (2010), showed minimal incidence of implant failure in patients with oral and intravenous bisphosphonates, and concluded that dental implants in patients

undergoing bisphosphonates therapy can osseointegrate and remain functionally stable.

Conclusion:

Within the limitations of the current study we can conclude that, no significant improvement added by hyaluronic acid or bisphosphonates implant surface modifications. So re-evaluation of biocompatible materials coating dental implants until a precise protocol is determined.

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