

EFFECT OF HYPERBARIC OXYGEN THERAPY ON OSSEOINTEGRATION OF DENTAL IMPLANT RETAIN MANDIBULAR OVERDENTURES WITH BISPHOSPHONATE TREATED PATIENTS

Nasser H. Shaheen* and Essam I. Elkhatat**

ABSTRACT

Aim of the study: This study aimed to evaluate the effect of hyperbaric oxygen therapy on success rate of implants used to retain mandibular overdentures and possibility of osteonecrosis of the jaw in Bisphosphonate treated osteoporotic patients.

Materials and methods: Eight systemic free patients were selected as control group (CG) and eight osteoporotic patients treating with Bisphosphonate drugs orally more than two years were selected as study group (SG). For both groups, patients received mandibular implant retained overdentures with locator anchors following two stage surgical protocol. Patients of study group were received Hyperbaric oxygen thereby (HBO) after the first stage surgery, while those of control group were not received (HBO). Peri-implant marginal bone height and density were evaluated at six months (T6), twelve months (T12) after insertion using Cone Beam Computed Tomography (CBCT).

Results: No failure of dental implants were recorded with 100% cumulative survival rates for both groups. Both groups showed increase in bone density and decrease in marginal bone height through a period of one year follow-up. However, the group that received HBO therapy showed less marginal bone loss and more increase in bone density than the control group.

Conclusion: Hyperbaric oxygen therapy is valuable and effective treatment for osteoporotic treated Bisphosphonate patients receiving implant retained mandibular overdentures as it eliminate the possibility of Bisphosphonate associated osteonecrosis of the jaw (BONJ), reduces bone loss and increase bone density around dental implant resulting in normal survival rate.

KEYWORDS: Hyperbaric oxygen, Bisphosphonate, implant, overdenture.

* Associate Professor, Department of Removable Prosthodontics, College of Oral and Dental Surgery, Misr University for Science and Technology, Egypt. Associate Professor, Prosthetic Dental Sciences Department, Al-Farabi Collage, Saudi Arabia.

** Assistant Professor, Preventive Dental Sciences Department, Al-Farabi Collage, Saudi Arabia.

INTRODUCTION

Normally, the skeleton carries out several functions as support, mobility, and protection for vital organs and acting as reservoir for calcium and phosphate. The skeleton remain in a dynamic equilibrium between osteoblastic and osteoclastic activity for bone remodeling procedure. This bone remodeling procedure occurs in a regular manor, resulting in minimal change in the amount of bone. At the end of twenties, individual reaches maximum bone mass then the balance between bone formation and resorption changes with relative increases in bone resorption leading to bone loss most of bone loss after the age of 65 is cortical bone loss; however, bone loss after menopause is mainly trabecular bone loss.

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration, with a consequent increase in bone fragility and susceptibility to fracture, particularly of the vertebral body, distal forearm and proximal femur in postmenopausal women^[1]. Reduced bone strength results from a loss of bone tissue, a consequence of imbalances between bone formation and resorption, as well as a subsequent deterioration in skeletal microarchitecture^[2]. Osteoporosis is classified into primary and secondary osteoporosis based on the precipitating factors. Recently, many authors supporting the idea that, there is a growing acknowledgement for the involvement of the immune system in the pathogenesis of osteoporosis precipitating the emergence of the field of osteoimmunology^[3]. Bisphosphonate group of drugs are pyrophosphate analogues. They have a high affinity to bone and are taken up by osteoclasts during natural bone resorption. Bisphosphonates work by acting on osteoclast function to reduce bone resorption. They are important in treating many conditions such as osteoporosis, Paget's disease, hypercalcaemia, osteogenesis imperfecta, skeletal defects associated with metastatic cancer,

primary hyperparathyroidism and malignancy. Despite the bisphosphonates have an excellent safety record, there have been case reports of Bisphosphonate associated osteonecrosis of the jaw (BONJ) particularly after surgical procedures,) that might be caused by long-term use. Thus, completely edentulous patients who are receiving oral Bisphosphonate for the treatment of osteoporosis are not allowed to have implants^[4-9].

Edentulism is considered as a debilitating handicap condition duo to difficulties in denture retention and stability^[10]. Particularly in case of mandibular denture as reduced supporting area, motion of the tongue and continuous alveolar ridge resorption. In fact, the most reliable management which provide both retention and stability of the prosthesis for edentulous mandible is inserting of two implants in the canine region, either splinted or not^[10]. Several types of anchors can be used to retain the overdentures to the implants, such as locators, balls, bar attachments and magnets^[11]. Locator attachments are flexible anchor, self-aligning, have different degrees of retention values, have some built-in angulation compensation, can be used successfully with limited inter-arch distance. In addition, repair and replacement are simple and easy.

Hyperbaric oxygen (HBO) therapy improve the success of osseointegration, as it improves bone maturation^[12,13]. HBO protocol is the inhalation of 100% pure oxygen inside a hyperbaric chamber that is pressurized to greater than 1 atmosphere absolute (ATA) till 3 ATA. The duration of HBO session is ranged from 90 to 120^[14]. HBO therapy results in increases dissolved oxygen in the blood and results in high partial pressure of oxygen (PaO₂) in body tissues. The increase of oxygen tension in regenerating tissue mimic the growth of new blood vessels, promotes collagen and adenosine-triphosphate (ATP) synthesis, increasing osteoblastic and osteoclastic activity^[15,16] causes cellular differentiation to osseous tissue^[17], so improving osteogenesis, bone

remodeling and healing ^[18,19], which result in more bone formation ^[20].

HBO therapy affect several conditions as osteoporosis, improved bone formation in patients treated with Bisphosphonate, gas gangrene, necrotizing soft-tissue infections, acute ischemia's, exceptional blood loss anemia, refractory osteomyelitis, compromised skin grafts, thermal burns and intracranial abscesses and involved in diabetes ^[21,22]. It is interestingly, to know that HBO also affect management of many restorative materials, according to Hossam et. al. in 2007, 2009 ^[23,24]

From understanding the mechanism and physiology of Hyperbaric oxygen therapy, it could be used as a treatment protocol for Bisphosphonate induced patients requiring implants. The purpose of this study is to evaluate the effect of HBO therapy on osseointegration of implants supporting mandibular overdenture in bisphosphonate treated osteoporotic patients.

MATERIALS AND METHODS

Patients' selection

Sixteen edentulous individuals (eight of them diagnosed osteoporosis and received oral Bisphosphonate drugs more than two years) and the other eight individuals diseased free with mean age of 54.9 years.

Patients were included in the study, provided that they fulfilled the following criteria:

- Free from any other systemic diseases.
- At least four months of healing following tooth extraction prior to implant placement.
- Sufficient bone volume to receive implants with a diameter of 3.75 mm and a minimum length of 11 mm. This was verified by Cone Beam Computed Tomography to allow for assessment of the alveolar ridge resorption in both vertical, horizontal and buccolingual dimensions.
- Sufficient attached gingiva (keratinized tissues)

Exclusion criteria include: bone grafted or irradiated arches, neurologic or immunologic diseases, microvascular or macrovascular complications, liver dysfunction, anticoagulant therapy and smoking habits. In addition, all patients with contraindications to hyperbaric oxygen therapy such as untreated pneumothorax, upper respiratory infections, high fevers, and emphysema with CO₂ retention, history of thoracic surgery, claustrophobia and convulsions were excluded. The eight systemic free patients were considered as control group while, the eight osteoporotic patients under Bisphosphonate treatment for two years were considered as study group. The study was conducted according to Rules of Helsinki Declaration, and the Faculty's Clinical Research Ethics Committee at Misr University for Science and Technology (MUST) approved the study protocol. Patients were informed about the study protocol and objectives before they signed an informed consent.

Surgical procedures

Bilateral endosteal implants (Tiologic® Implants, Dentaurem, Ispringen, Germany) were inserted at the location of the former cuspids of the mandible following the standardized two-stage submerged surgical protocol suggested by Branemark, which include implant submerging and undisturbed healing of three months. Implants were inserted using a surgical guide for every patient to ensure proper angulations and positioning. The diameter of the final osteotomy done with respect to the surgeon's evaluation of the bone quality to allow for excellent primary implant stability.

Hyperbaric Oxygen Therapy (HBO)

Patients of control group received no Hyperbaric Oxygen therapy. While, those of study group were managed following a protocol of five sessions of HBO therapy (once/day) ^[25,26] for five consecutive days at the multi place HBO chamber Fig. (1). Hyperbaric therapy were completed under the supervision of hyperbaric medical specialist at



Fig. (1): Multi place HBO chamber

Egyptian Air Force Aero-Medical Institute, Cairo, Egypt. The Hyperbaric therapy session started by compression pressurization where the room pressure was raised from 1 ATA to 2.4 ATA for 15 minutes, followed by oxygen breathing for one hour at 2.4 ATA and finally decompression pressurization for 15 minutes from 2.4 ATA to 1 ATA so each session lasts 90 minutes^[27].

Prosthetic procedures

Patients of both groups received new maxillary and mandibular complete dentures following conventional technique. Two weeks following implant insertion, the patient's existing mandibular dentures were relieved over implant sites and refitted to the mucosa. Three months post-surgically, implants were exposed, and healing abutments were placed. The Locator attachment (Tiologic® Implants, Dentaaurum, Ispringen, Germany) used to retain the mandibular dentures for both groups comprises a self-aligning double retention cylinder with retention surfaces on the inner and outer areas (Fig 2,3). A metal body is incorporated in the base of the denture and nylon elements in the negative form of the abutment connect the prostheses with the implant. Pink nylon male inserts were fitted to the locator matrix in this present study. The fitting surface of the new mandibular dentures

directly above the implants was relieved to provide space for the attachments. For both groups, the outer matrix with the pink inserts were picked up intraorally to the fitting surface of mandibular dentures with cold-cure acrylic resin while patients close in centric occlusion. The new dentures were delivered to the patients with emphasize on oral hygiene instructions, regular recall visits for proper adjustments and replacement of nylon inserts if any worn or fracture occurred.



Fig. (2): Locator abutments and overlying locator matrices attached to the implants intra-orally



Fig. (3): Locator retained mandibular overdentures

Radiographic assessment

Patients were recalled at time of insertion, six and twelve after denture insertion for follow-up. At these intervals, patients were returned for assessment of implants, prosthesis' function and standardized

evaluation of their oral health. Cone Beam Computed Tomography (CBCT) was used to evaluate peri-implant bone height and bone density. The acquired and reconstructed three-dimensional volume images were exported and saved as DICOM-files (Digital Imaging and Communications in Medicine) on a compact discs and viewed on personal computer. For image analysis, software (OnDemand3D CD Viewer) was used for assessment of peri-implant bone height and density.

Assessment of peri-implant bone height

Mesial and distal marginal bone height were calculated from the reconstructed corrected sagittal views by drawing a line parallel to the implant serration extending from the marginal bone to the apical end of the implant. By the same way, buccal and lingual marginal bone height was measured by using cross-sectional views. Average readings of the four sides at each interval were calculated and tabulated for statistical analysis Fig. (4).

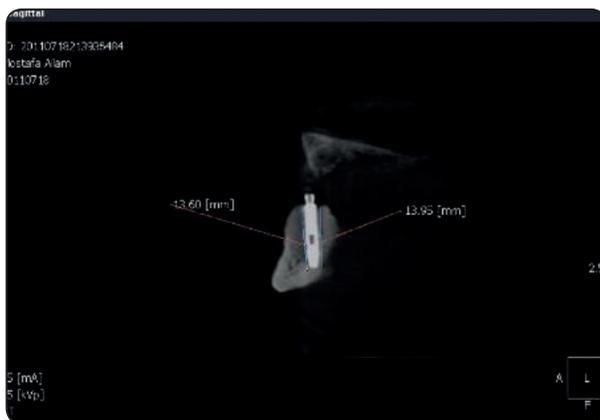


Fig. (4):peri-implant bone height measurements using CBCT

Assessment of peri-implant bone density

The density measurements were performed by calculating the Hounsfield units (HU) 1mm away from the surface of each implant at all buccal and lingual sides (cross sectional views) and mesial and distal sides (corrected sagittal views). Average readings of the four sides were calculated to indicate

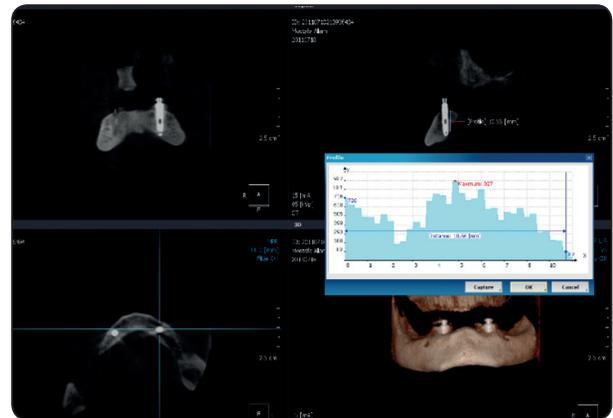


Fig. (5): Measurement of bone density

the density of the bone engaged with the threads of each implant. Results at each interval were tabulated for statistical analysis Fig.(5).

Statistical analysis

The statistical analysis of data was performed using Excel program and SPSS program (Statistical Package for Social Science) version 22.0. One-Sample Kolmogorov-Smirnov Test was used to diagnose normality of data distribution of all variables. The data was parametric and normally distributed and were presented using mean \pm standard deviation. Between-groups comparisons for marginal bone height and bone density were performed using student t-test. Repeated measure ANOVA followed by LSD was used to detect significant differences between observation times. Kaplan-Meier analysis was used for evaluation of implant survival rates and Log rank test was used to compare survival between groups. P-values <0.05 were considered to be significant.

RESULTS

Patients of both groups completed the follow-up examination visits and showed success of the implants resulted in 100% survival rate following Kaplan-Meier analysis for survival rates (Fig. 6).

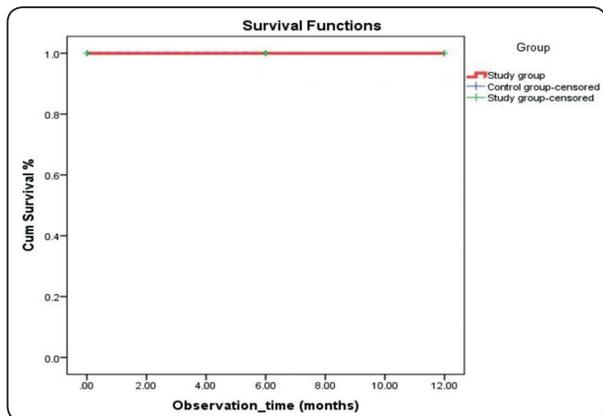


Fig. 6: Kaplan-Meier survival analysis for both groups.

Peri-implant bone height:

Table (1) shows significant difference in peri-implant bone loss for both groups during the follow-up periods. There was a significant difference in peri-implant bone loss between groups at (T6) and (T12). Study group recorded lower significant differences in peri-implant bone loss than control group at T6 and T12 (p=0.00 and 0.001 respectively). For both control and study groups, there was a significant difference in peri-implant bone loss between the follow-up periods (p=0.03 and 0.05 respectively).

TABLE (1) Comparison between the deference of peri-implant bone height in mm for both groups at T6, and T12.

	Control group X±SD	Study group X±SD	Independent samples t-test (p value)
6 months after insertion (T6)	0.82±0.21	0.65±0.19	0.00*
12 months after insertion (T12)	0.96±0.23	0.87±0.16	0.001*
Paired sample t-test (p value)	0.03*	0.05*	

X; mean. SD; standard deviation. * Significant difference at 0.05

Peri-implant bone density

Table 2 shows the bone density (in HU) for both groups at T0, T6 and T12. There was a significant difference in bone density between both groups during all follow-up periods. Study group was significantly higher than control group regarding the peri-implant bone density at different follow-up periods (p=0.10, 0.00 and 0.01 respectively). For both control and study groups, there was a significant difference in bone density between the follow-up periods (p=0.02 and 0.00 respectively).

TABLE (2) Comparison of bone density (in HU) for both groups at T(0), T(6) and T(12).

	Control group X±SD	Study group X±SD	Independent samples t-test (p value)
At time of insertion (T0)	911.63±82.19	1036.21±33.08	0.01*
6 months after insertion (T6)	1032.61±69.57	1068.33±32.30	0.00*
12 months after insertion (T12)	1093.83±91.17	1110.00±18.08	0.01*
Repeated measures ANOVA (p value)	0.02*	0.00*	

X; mean. SD; standard deviation.

* significant difference at .05

DISCUSSION

Very few studies have been conducted to analyze the effects of HBO therapy on success rate of osteoporotic patients received Bisphosphonate drugs [28,29].

The beneficial role of HBO in the treatment of various human pathologies either alone or in combination with other therapies have reported in few studies [28,29].

The achieved 100% survival rate observed in this study were expected due to the selection criteria and increased cellularity, vascularity and enhanced soft tissue and bone healing and regeneration after hyperbaric oxygen therapy [30,31]. Five consecutive HBO sessions used in this study was reported in a study aimed to aid in the postoperative stability of orthognathic surgical corrections in patients with severe dentofacial deformities [32] and in a study conducted to evaluate the effect of hyperbaric oxygen on osseointegration around dental implant in uncontrolled diabetic patients [33]. The mean peri-implant bone loss in study group (osteoporotic patients under Bisphosphonate therapy who receiving HBO therapy) was $(0.87 \pm 0.16 \text{ mm})$ which remain within the normal range of values reported in literatures (1.2 mm in the first year) [33, 34].

However, the mean peri-implant bone loss in control group (systemic free patients) was $(0.96 \pm 0.23 \text{ mm})$ which is less than this value. In the results of this study the peri-implant bone loss during the follow-up periods was significantly less in the study group which received HBO therapy. This might be attributed to the physiologic effects of HBO on the study group which includes improved oxygenation, vasoconstriction, increased antimicrobial activity, bactericidal and bacteriostatic effect and modulation of inflammation. Blood and tissue oxygen tensions were documented to remain elevated for over an hour following a single HBO treatment in an experimental rat wound model [35]. The increase in oxygen tension promotes collagen and adenosine-triphosphate (ATP) synthesis, capillary in growth, osteoblastic and osteoclastic activity and has a triggering role in bone remodeling [36].

There is a correlation between the high level of oxygen tension and elevated osteoblastic and osteoclastic activity [36]. The increase in oxygen tension causes cellular differentiation to osseous tissue, whereas decreased oxygen tension results in cartilage formation. The results of peri-implant

bone height in this study agree with the study of Nilsson et al. who proved that HBO treatment causes a significant increase in bone formation [36]. It also agrees with the studies of Sawai et al. [37], who showed that there is an acceleration in bone healing and an increase in the amount of new bone formation with HBO therapy. The authors found that bone density in both groups are significantly increased after the surgery and during the first year of loading with high levels in the HBO group. The increased bone density with advance of time in both groups may reflect a positive response to the applied forces within the physiologic limit and adaptive capacity. Proper distribution of the load falling on the implants might have enhanced the structural orientation of bone trabeculae and hence increased the bone density around the implants [38]. The increased bone density in study group may be due to osteoporosis treatment by Bisphosphonate drugs which characterized by high bone mass and, with a consequent increase in bone hardness causes enhancement of bone-to-implant contact (BIC) and bone thickness. Also, as a result of hyperbaric therapy, Similarly, Johnson, et al. in 1999 [12] and Granstorm et al. in 2006 reported that Hyperbaric oxygen (HBO) therapy improve the success of osseointegration, as it improves bone maturation [13]. Similarly, several studies reported improving osteogenesis, bone remodeling and healing, which result in more bone formation [34,35,36]. In addition, the increased bone density after HBO in osteoporotic patients is in line with Elsyad, et. al. in 2012 who studied new surgical template with a handpiece positioner for use during flapless placement of four dental implants to retain a mandibular overdenture and reported that, there is more bone formation [37].

Our results revealed that, there is positive effect of HBO treatment agree with the study of Shaheen and El-Talawy in 2016 who concluded that, hyperbaric oxygen therapy is valuable and effective treatment as it associated with increased implant survival rate and bone density [31].

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