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Major clinical approaches to osseointegrated implants: a concise systematic review

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Abstract

Introduction: Reconstructive surgery is an important component of the specialty of oral and maxillofacial surgery. The maxillofacial skeleton is subject to various types of defects secondary to trauma, craniofacial/congenital deformities, and tumor ablation. The complex anatomy and function of the maxillomandibular complex impact the choice of reconstruction for maxillofacial defects. **Objective:** It was to carry out a concise systematic review to present the main considerations of osseointegrated implants. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from September to November 2022 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 127 articles were found, and 57 articles were evaluated and 30 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 10 studies with a high risk of bias and 28 studies that did not meet GRADE. Most studies showed homogeneity in their results, with I2 =95.8% >50%. It was concluded that orofacial defects affect both the form and function of the most prominent and complex part of the body, the face. Several options, such as vascularized flaps, non-vascularized autogenous grafts, or allogeneic materials, are available to reconstruct maxillofacial defects. The complex anatomy and function of the maxillomandibular complex impact the choice of reconstruction for maxillofacial defects. The real effect of bisphosphonates on osseointegration and survival of dental implants is still not well established.

Keywords: Osseointegration. Dental implant. Bisphosphonate. Complications.

Introduction

In the context of osseointegration and dental implants, reconstructive surgery is an important component of the specialty of oral and maxillofacial surgery. The maxillofacial skeleton is subject to various types of defects secondary to trauma, craniofacial/congenital deformities, and tumor ablation. Given the nature of tumors, ablative surgery results in complex bone and soft tissue continuity defects. Orofacial defects affect both the form and function of the most prominent and complex part of the body, the face [1].

Several options, such as vascularized flaps, non-vascularized autogenous grafts, or allogeneic materials, are available to reconstruct maxillofacial defects. They are used based on the size, location, extent of tissues involved, cause of the defect, and host environment. Due to the superior results and versatility of the vascularized graft, for critical-size bone continuity defects of the maxilla or mandible, vascularized grafts are the preferred option [1]. Vascularized bone can be obtained from several sites, such as the iliac crest, scapula, or fibula, among others. The complex anatomy and function of the maxillomandibular complex impact the choice of reconstruction for maxillofacial defects [2-4].

In this sense, one of the major causes of osteopenia in women over 60 years of age is estrogen deficiency [5]. This deficiency associated with aging

causes an osteoporotic picture. A hormone replacement is necessary for an adequate treatment of the symptoms of menopause and to prevent possible osteoporosis [6,7]. Some drugs help in the treatment of postmenopausal osteoporosis, they are calcitonin, bisphosphonates (BP), and the selective modulators of estrogen receptors [8]. Thus, BP has been the best drug associated with significant improvement in the quality of life of patients with bone diseases such as Paget's disease, bone metastases, osteogenesis imperfecta, hypercalcemia, and even severe osteoporosis.

These drugs are used worldwide in cancer patients and are given intravenously as zoledronic acid (Zometa®). They can also be administered orally, such as alendronate (Fosamax®) and risedronate (Actonel®) for the treatment of postmenopausal osteoporosis. In 2003, a side effect associated with the use of BP with oral manifestation called Osteonecrosis Associated with BP was described for the first time [8].

In this context, osteoporosis is a prevalent global bone disease in human aging. BPs are commonly used as therapy because they influence the calcium metabolism of hard and soft tissues. Mucosal and dermal ulceration with exposure of the underlying bone results from incomplete epithelial recovery due to reduced desmosome formation due to a lack of available calcium. However, pathological situations, such as BP-related jaw osteonecrosis, have been described. This hypothesis states other situations that require intact functional desmosomes such as skin healing over chronic pressure points leading to pressure ulcers and hemidesmosomes such as epithelial seals in contact with titanium surfaces will have a higher prevalence of collapse among patients treated with BP. This can be proven by the decreased modulation of calcium ions due to BP and its effect on intercellular communicating junction formation [5].

Also, as yet another example of literary support, one paper reported a type of localized osteonecrosis that can occur in patients who had successfully osseointegrated implants for many years and then started anti-resorptive therapy. Eleven female patients who successfully implanted but were placed on anti-resorptive therapy (BPs or denosumab) several years later and developed osteonecrosis around the implants were identified. In each case, osteonecrosis occurred only around the implants and not around the patient's remaining teeth. Implants from eight patients were removed with bone sequestration firmly attached to the implant. This is different from the normal pattern of implant failure. Implant failure can occur when patients with successfully integrated implants are subsequently placed on anti-resorption therapy, and osteonecrosis takes on a particular form where a sequestration forms that remain adherent to the implant. Why the remaining adjacent teeth are not affected is unclear [6].

Therefore, the present study carried out a concise systematic review to present the main considerations of osseointegrated implants.

Methods

Study Design

The rules of the Systematic Review-PRISMA Platform (Transparent reporting of systematic reviews and meta-analysis-HTTP://www.prisma-statement.org/) were followed.

Data sources and research strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): "*Osseointegration. Dental implant. Bisphosphonate. Complications*". The research was carried out from September to November 2022 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar. Also, a combination of the keywords with the booleans "OR", "AND", and the operator "NOT" were used to target the scientific articles of interest.

Study Quality and Bias Risk

The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

Results and Discussion

A total of 127 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not address the theme of this article. In total, 57 articles were fully evaluated and 30 were included and evaluated in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 10 studies with a high risk of bias and 28 studies that did not meet GRADE. Most studies showed homogeneity in their results, with I2 =95.8% >50% (**Figure 1**).

Figure 2 presents the results of the risk of bias in the studies using the Funnel Plot, through the calculation of the Effect Size (Cohen's Test). The sample size was determined indirectly by the inverse of the standard error. The number of clinical studies evaluated was n=30. The graph showed symmetric behavior, not suggesting a significant risk of bias in studies with small sample sizes, which are shown at the bottom of the graph.

Figure 1. Flow Chart of Study Eligibility (Systematic Review).

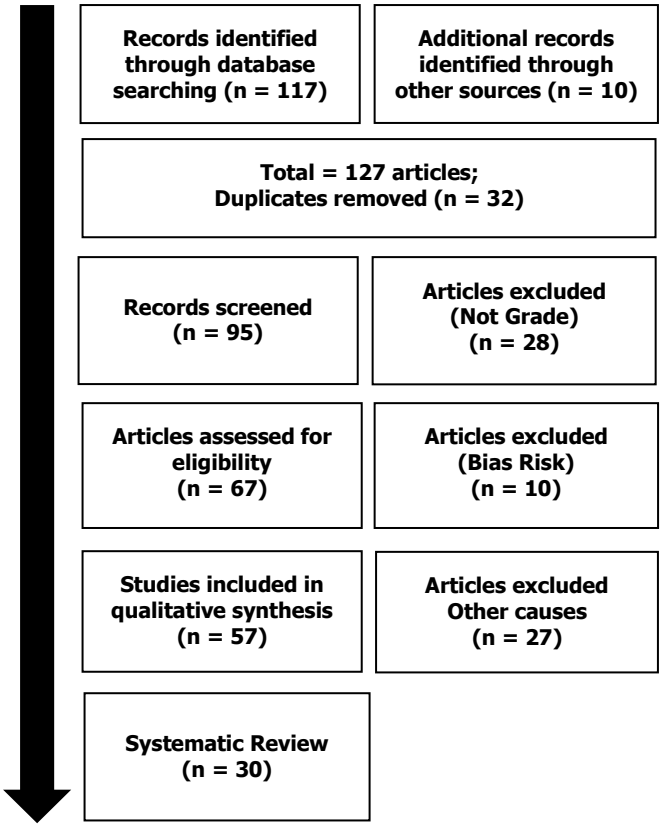
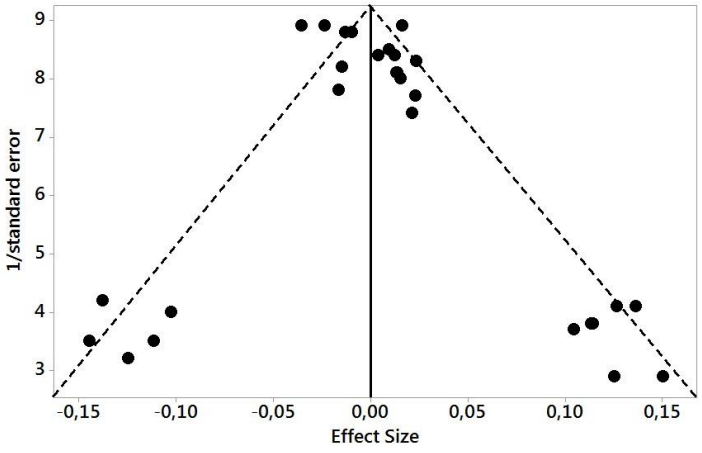


Figure 2. The symmetric funnel plot does not suggest a risk of bias between the small sample size studies that are shown at the bottom of the graph (N=30 studies).



Major Clinical Findings

The World Health Organization (WHO) defined osteoporosis as a level of bone mineral density greater than 2.5 standard deviations below the average of normal young women [9-17]. After 60 years of age, a third of the population has this disorder, it occurs twice more in women than in men and its diagnosis is made with greater prevalence from the third decade of life [18,24].

Among the systemic alterations, osteoporosis is one of the dysfunctions commonly found by implant dentists [21]. Osteoporosis acts by modifying the metabolism of the bone tissues, disorganizing the trabecular architecture of the cortical and alveolar bone, which are responsible for tooth support. It is estimated that 1.3 million of all fractures and 133,000 hip fractures occur each year as a result of osteoporosis [24].

Osteoporosis can be classified as type I and type II. Type I (postmenopausal) occurs when there is the loss of trabecular bone mass, resulting in fractures of the vertebrae and wrists, which may be more evident in the mandible and the alveolar bone, is associated with the aging and plasma decrease of estrogen in the menopause, affecting mainly women; And Type II (senile), occurs when there is the loss of trabecular bone mass that can affect both cortical and spongy bone, resulting in hip fractures, which can affect both sexes and in ages over 70 years [12-17].

There is a higher prevalence of the development of osteoporosis in women, and there are some risk factors that may explain this difference, such as early menopause, artificial menopause, nulliparous, and estrogen replacement [25-28]. For men, reduced testicular function (male hypogonadism) can be cited as a risk factor. Several other risk factors may predispose to both sexes: heredity, tobacco, alcohol, caffeine, obesity, absence of physical activity, ethnicity, changes in calcium levels, malnutrition, decreased levels of vitamin D, elevated Levels of parathyroid hormone, and other hormones, all these factors may manifest in both men and women with osteoporosis [17,21].

The recommended intake of calcium is 800 mg day-1, in women who have already gone through menopause, 1.5 g may be required to maintain a positive calcium balance [29,30]. For patients with established osteoporosis, there are drugs that, in general, act directly in the process of bone remodeling, seeking to reduce bone resorption, among them, is BP, which are drugs of proven efficacy that act in the prevention and treatment of several Bone diseases [30].

In this context, dental implants are defined as supports or structures of titanium metal, which through surgeries are fixed in the maxillary bone replacing the dental roots, thus allowing the artificial teeth to fit the metal. Dentistry uses several rehabilitation techniques for masticatory functions, and osseointegrated implants are considered safe, provided they are implanted in areas of good quantity and bone quality [16]. However, some systemic conditions may interfere with implant stability, such as osteoporosis. Implantology has shown increasing success rates when it presents a harmonious bone/implant relationship.

The discovery of osseointegration occurred through studies of microcirculation in the bone marrow performed on the rabbit fibula, developed by Per-Ingvar Branemark. He verified in Branemark's studies that a

titanium implant when inserted into the medullary space, under certain conditions, and remaining immobile without mechanical trauma during the period of bone repair, end up full of compact bone without the interference of other tissues [17-19].

In this context, osteoporosis is a factor that retards the regeneration of maxillary bone in patients who have undergone implant surgery, prolonging the normal recovery time of maxillary bone which can vary from three to six months [29]. Therefore, it is necessary that people affected by this disease who will receive dental implants need a longer time for bone repair [29]. Due to the increase in life expectancy, rehabilitation with implants in people over 60 years old is the most common age group in which there is a higher probability of metabolic pathologies [30].

To obtain osseointegration of the implant, which is the direct and structural unit of the bone tissue to the titanium and function, it is necessary to respect several principles, among them, those related to the surgical technique, respecting tissue physiology [28]. Thus, it is necessary to control the traumatogenic factors during surgery such as intensity, frequency, and duration of the milling (osteotomies), which can generate excessive trauma to the bone tissue, impairing the bone repair potential of the injured area. Facing situations where the traumatic stimulus exceeds its physiological limit, the implant may be involved by fibrous connective tissues, leading to the formation of a bone or fibrous per implant interface, without osseointegration.

For the success of osseointegrated implants, other factors must also be considered, not only related to the professional (surgical technique), but also the industry and the patient himself. In addition to performing the appropriate surgical technique, it is up to the professional to select the patient, evaluating it as a whole, from his complaint, including his expectation regarding the treatment, mainly comprising his pre-operative systemic and local conditions [29,30]. At the moment of preparation of the receptor bone bed for the subsequent installation of the osseointegrated implant, bone necrosis occurs, which will be replaced by new bone tissue. When there is osteoporosis, the process of bone remodeling can be compromised, preventing or delaying osseointegration [30].

Several authors Ourique et al. [21] have already reported on the importance of knowledge of systemic alterations so that necessary measures are taken to minimize or prevent eventual damages caused by osteoporosis in the anatomical, physiological and functional integrity of the alveolar bone. All care is necessary for the success of this process since the immediate benefit of the rehabilitative treatment with implants is observed in the improvement of the capacity to crush the food, and in the physical and psychological well-being of the patient.

Ishii et al. [16] state that although osteoporosis is a significant factor that can interfere with bone volume and density, it cannot be considered an absolute contraindication for implant installation. It is essential that during the anamnesis, all patients are questioned about their state of health, reporting the use of medications and the type of medical treatment they are undertaking so that a safe and effective treatment plan is drawn up for each case.

In this sense, BP is a widely used drug group for various bone disorders and has been approved by the U.S. Food and Drug Administration for the treatment of osteoporosis, metastatic bone cancer, and Paget's disease [28]. They were first used for industrial purposes in the 19th century to prevent corrosion in the textile, fertilizer, and oil industries. In 1968, the first paper describing the use of BP in medicine was published, however, in 2002 serious side effects of these medications were reported following dental surgery procedures. This includes osteonecrosis, avascular necrosis, osteomyelitis, osteochimionecrosis, and maxillary BissPhossy [28].

Thus, at the moment there are two main types of BP those containing nitrogen (oral: alendronate and risedronate, intravenous: pamidronate and zoledronate) and those that do not contain (etidronate, clodronate, and tiludronate). BP act by suppressing and reducing bone resorption by osteoclasts, directly preventing the recruitment and function of osteoclasts, and indirectly stimulating osteoblasts to produce inhibitors of osteoclast formation [29].

Besides, BP are drugs derived from inorganic pyrophosphate, which are present in the body and physiologically regulate calcification and bone resorption. Pyrophosphate also provides greater resistance to chemical and enzymatic hydrolysis [19]. Camargo, Minosso, and Lopes, (2007) [10] report that treatment should always combine an anti-resorptive agent with a non-pharmacological measure such as physical exercise and consumption of calcium and vitamin D by diet. Antireabsorption agents are described by Ishii (2009) [16] as estrogen replacement therapy, selective estrogen receptor modulators, BP, and calcitonin, and also describe bone formation stimulating agents such as a parathyroid hormone.

Also, alendronate, for osteoporotic patients, can be administered orally at 10.0 mg/day or 70.0 mg/weekly, and cannot be exceeded because it causes gastrointestinal changes such as erosive esophagitis. It is necessary to use this medicine in fasting, for being little absorbed in the intestine, and to wait 40 to 60 minutes to feed. It is a drug that deposits about 40-60%

rapidly into the bone and the rest is released through the urine. The plasma half-life of BP is very short, ranging from thirty minutes to two hours, so after these medications are absorbed by the bone tissue, they may persist for more than 10 years in skeletal tissues [21].

Furthermore, a review study with Meta-Analysis included clinical human studies, randomized or not. A total of 18 publications were included in the review. Regarding implant failure, the meta-analysis found a risk ratio of 1.73 (95% confidence interval [CI] 1.21-2.48, p = 0.003) for BP patients when compared to patients who did not take the medicine. The probability of an implant failure in patients receiving BP was estimated at 1.5% (0.015, 95% CI 0.006-0.023, standard error [SE] 0.004, p<0.001). BP cannot be suggested to affect marginal bone loss from dental implants due to a limited number of studies reporting this result. Due to a lack of sufficient information, the meta-analysis for the outcome of "postoperative infection" was not performed. The results of the present study cannot suggest that dental implant insertion in patients taking BP affects implant failure rates due to a limited number of published studies, all characterized by a low level of specificity, and most of them dealing with a limited number of cases without an adequate control group. Therefore, the real effect of BP on osseointegration and survival of dental implants is not yet well established [7].

Conclusion

It was concluded that orofacial defects affect both the form and function of the most prominent and complex part of the body, the face. Several options, such as vascularized flaps, non-vascularized autogenous grafts, or allogeneic materials, are available to reconstruct maxillofacial defects. The complex anatomy and function of the maxillomandibular complex impact the choice of reconstruction for maxillofacial defects. The real effect of bisphosphonates on osseointegration and survival of dental implants is still not well established.

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Not applicable.

Informed consent

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

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References

1. Gangwani P, Almana M, Barmak B, Kolokythas A. What Is the Success of Implants Placed in Fibula Flap? A Systematic Review and Meta-Analysis. J Oral Maxillofac Res. 2022 Mar 31;13(1):e3. doi: 10.5037/jomr.2022.13103.
2. Sendul SY, Yildiz AM, Yildiz AA, Akbas E. Osseointegrated Implants for OrbitoFacial Prostheses: Common Complications and Solutions. J Craniofac Surg. 2021 JulAug 01;32(5):1770-1774. doi: 10.1097/SCS.0000000000007360.
3. Tonini KR, Hadad H, Egas LS, Sol I, de Carvalho PSP, Ponzoni D. Successful Osseointegrated Implants in Hypertensive Patients: Retrospective Clinical Study. Int J Oral Maxillofac Implants. 2022 May-Jun;37(3):501-507. doi: 10.11607/jomi.9425.
4. Srivastava A. Considerations and techniques for removal of osseointegrated implants. J Prosthet Dent. 2022 Nov;128(5):843-844. doi: 10.1016/j.prosdent.2022.10.002.
5. Touyz LZG, Afrashtehfar KI. Implications of bisphosphonate calcium ion depletion interfering with desmosome epithelial seal in osseointegrated implants and pressure ulcers. Med Hypotheses. 2017 Sep;107:22-25. doi: 10.1016/j.mehy.2017.07.013. Epub 2017 Jul 18.
6. Pogrel MA, Ruggiero SL. Previously successful dental implants can fail when patients commence anti-resorptive therapy-a case series. Int J Oral Maxillofac Surg. 2018 Feb;47(2):220-222. doi: 10.1016/j.ijom.2017.07.012. Epub 2017 Aug 10.
7. Chrcanovic BR, Albrektsson T, Wennerberg A. Bisphosphonates and dental implants: A meta-analysis. Quintessence Int. 2016 Apr;47(4):329-42. doi: 10.3290/j.qi.a35523.
8. Basso FG, Pansani TN, Soares DG, Cardoso LM, Hebling J, de Souza Costa CA. Influence of

bisphosphonates on the adherence and metabolism of epithelial cells and gingival fibroblasts to titanium surfaces. Clin Oral Investig. 2018 Mar;22(2):893-900. doi: 10.1007/s00784-017-2167-2. Epub 2017 Jul 8.

9. Gelazius R, Poskevicius L, Sakavicius D, Grimuta V, Juodzbalys G. Dental Implant Placement in Patients on Bisphosphonate Therapy: a Systematic Review. J Oral Maxillofac Res. 2018 Sep 30;9(3):e2. doi: 10.5037/jomr.2018.9302. eCollection 2018 Jul-Sep.
10. Camargo EP, Minosso M, Lopes LC. Caracterização do Uso de Alendronato de Sódio no Tratamento de Osteoporose por Clínicos da Rede Privada de Duas Cidades do Interior de São Paulo. Rev. Ciênc. Farm. Básica Apl., v.28, n.1, p.77-83, 2007.
11. Carvalho PSP. et al. Principais Aspectos da Cirurgia Bucomaxilofacial no Paciente sob Terapia com Bifosfonatos. RFO UPF [online]. 2010, vol.15, n.2, pp. 183-189. ISSN 1413-4012.
12. Duarte PM, Nociti Júnior FH. Impacto da Deficiência de Estrógeno e suas Terapias sobre o Tecido Ósseo ao Redor de Implantes de Titânio e na Periodontite Induzida em Ratas Ovariectomizadas. Tese (Doutorado) – Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba. Piracicaba, 2004. XVII, 131p.
13. Embracher Filho, A. Projeto Colosso: Desenvolvimento de um sistema de implante osseointegrável. Da teoria a prática. Tese (Doutorado) - Faculdade de Odontologia de Araçatuba, UNESP, 2003.
14. Ferreira Júnior CD, Casado PL, Barboza ESP. Osteonecrose Associada aos Bisfosfonatos na Odontologia. R. Periodontia. v.1, n.4, dez., 2007.
15. Gegler A. et al. Bifosfonatos e Osteonecrose Maxilar: Revisão da Literatura e Relato de Dois Casos. Rev. Brasileira de Cancerologia 2006; 52(1):25-31.
16. Ishii, J. H. Osteoporose e os Implantes Dentários. São Paulo, 2009. 24 p.
17. Luize DS. et al. A Influência da Osteoporose na Implantodontia. Arquivos em Odontologia, Belo Horizonte, v.41, n.2, p.105-192, abr./jun. 2005.
18. Martins MAT et al. Osteonecrose dos Maxilares Associada ao Uso de Bifosfonatos: Importante Complicação do Tratamento Oncológico. Rev. Bras. Hematol Hemoter 2009; 31(1):41-46.
19. Migliorati CA et al. O Tratamento de Pacientes com Osteonecrose Associada aos Bifosfonatos. Uma tomada de posição da Academia Americana de Medicina Oral. J American Dental Association 2006; 136(12).
20. Misch CE. Implantes Dentais Contemporâneos. Rio de Janeiro: Elsevier. 2008, 3nd.
21. Ourique SAM, Ito AY, Suarez OF. Osteoporose em Implantodontia: O Estado Atual da Questão. Rev. Bras. Implantodontia e Prótese sobre Implantes, 2005: 12(47/48): 23745.
22. Goiato MC, Santos DM, Rondon BCS, Moreno A, Baptista GT, Verri FR et al. Care Required When Using Bisphosphonates in Dental Surgical Practice. J. craniofac. surg. 2010; 21(6):1966-70.
23. Chadha GK, Ahmadieh A, Kumar S, Sedghizaded PP. Osseointegration of dental osteonecrosis of the jaw in patients treated with bisphosphonates therapy: a systematic review. J. oral implantol. 2013;39(4):510-20.
24. Mellado-Valero A, Ferrer-García JC, CalvoCatalá J, Labaig- Rueda C. Implant treatment in patients with osteoporosis. Med. oral patol. oral cir. bucal. 2010; 15:52-7.
25. López-Cedrún JL, Sanromán JF, García A, Peñarrocha M, Feijoo JF, Limeres J, Diz P. Oral bisphosphonate-related osteonecrosis of the jaws in dental implant patients: a case series. Br. j. oral maxillofac. surg. 2012;51(8):874-9.
26. Kwon T-G, Lee C-O, Park J-W, Choi S-Y, Rijal G, Shin H-I. Osteonecrosis associated with dental implants in patients undergoing bisphosphonate treatment. Clin. oral implants res. 2012; 00:1- 9.
27. Yip JK, Borrell LN, Cho SC, Francisco H, Tarnow DP. Association between oral bisphosphonate use and dental implant failure among middleaged women. J. clin. periodontol. 2012;39:408- 14.
28. Memon S, Weltman RL, Katancik JA. Oral Bisphosphonates: Early Endosseous Dental Implant Success and Crestal Bone Changes. A Retrospective Study. Int. j. oral maxillofac. implants. 2012;279(5):1216-22.
29. Abtahi J, Tengvall P, Aspenberg P. A bisphosphonate-coating improves the fixation of metal implants in human bone. A randomized trial of dental implants. Bone. 2012;50(5):1148- 51.
30. Jacobsen C, Metzler P, Rossle M, Obwegeser J, Zemann W, Gratz KW. Osteopathology induced by bisphosphonates and dental implants: clinical observations. Clin. oral investig. 2013;17:167-75.