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Implant treatment in patients with osteoporosis

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Abstract

Osteoporosis is very common, particularly in post-menopausal women and is characterized by a decrease in bone mass and strength. Osteoporosis also affects the jawbone and it is considered a potential contraindication to placement of dental implants. The present paper reviews the literature regarding the effect of osteoporosis on osseointegration of implants. Experimental models have shown that osteoporosis affects the process of osseointegration, which can be reversed by treatment. However, studies in subjects with osteoporosis have shown no differences in survival of the implants compared to healthy individuals. Therefore, osteoporosis cannot be considered a contraindication for implant placement. Oral bisphosphonates are the most commonly used pharmacological agents in the treatment of osteoporosis. Although there have been cases of osteonecrosis of the jaw in patients treated with bisphosphonates, they are very rare and it is more usually associated with intravenous bisphosphonates in patients with neoplasms or other serious diseases. Nevertheless, patients treated with bisphosphonates must be informed in writing about the possibility of this complication and must give informed consent. Ceasing to use bisphosphonates before implant placement does not seem to be necessary.

Key words: *Osteoporosis, biphosphonates, osseointegration, implant.*

Introduction

Osteoporosis is a systemic skeletal disease characterized by reduced bone strength that predisposes to an increased risk of fractures (1). It is a very common disease which affects an estimated 300 million people worldwide. It is prevalent in females and its incidence increases with age. In Spain it is estimated that osteoporosis affects 2 million women, with prevalence above 50% in women older than 70 years. It is characterized by a deterioration of bone microarchitecture with reduced bone mass and strength and increased fragility. The resistance reflects the amount of bone density and bone quality. Bone density is determined by the maximum value of bone mass (measured in grams per cm2) and the magnitude of their loss. The bone quality is made up of different factors that influence bone fragility (microarchitecture, bone turnover, or the microfractures and degree of mineralization).

The diagnosis of osteoporosis was established based on the classical values of bone mineral density (BMD) achieved in the bone densitometry, so that osteoporosis was considered when the T-score of less than -2.5 SD (the T number of standard deviations that a subject deviates from the average BMD of a population group of healthy young women). Currently the BMD is only considered a risk factor that must be assessed in the context of age, sex, smoking, body weight, family history and / or personal fracture, etc... The most frequent risk factors for osteoporosis are present in Table 1. Thus, the decision to treat or not the patient will be based not only on the result of the density but also on risk factors (1). On the one hand, we use the term primary osteoporosis for those situations in which the decrease in bone mass, can be explained by involutional changes of aging, as well as the hormonal changes of menopause. On the other hand, we use the concept of secondary osteoporosis for the one caused or emphasized by other diseases or medications (2).

There are different treatments for osteoporosis, all aimed at reducing the risk of fractures. Thus, estrogen treatment in post-menopausal women, selective modulators of estrogen receptors (especially raloxifene), calcitonin, a recombinant form of parathormone (teriparatide), strontium ralenate, and especially bisphosphonates, are drugs widely used in clinical practice (3).

The use of dental implants in patients with osteoporosis, whether being treated for it or not, is a controversial topic to be discussed in depth in this article.

Table 1. Most important risk factors for osteoporosis and bone fractures. Modified by: Hortal R, Martín R, Fernández N (6).

1. High risk factors
- Age over 65 - Estrogen deficiency: early physiological or surgical menopause (<45 years), primary or secondary amenorrhea of more than one year. - Prior osteoporotic fracture - Treatment with corticosteroids (5 mg / day for 3 months or more of prednisone or equivalent) - Endocrine diseases: Hyperthyroidism, Hyperparathyroidism, Male hypogonadism - Osteoporotic fracture in first-degree relative - Low birth weight (<40 kg or BMI <19 kg/m2)
2. Moderate risk factors
- Physiological menopause - Low calcium intake (<500-850 mg / day for prolonged periods) - Smoking (> 20 cigarettes / day) - Alcoholism -Osteopenic diseases: gastrointestinal (malabsorption, bowel resection, inflammatory bowel disease, gastrectomy), chronic liver disease, transplantation, rheumatoid arthritis, chronic renal failure, chronic obstructive pulmonary disease, diabetes mellitus. -Drugs: lithium, anticomicial level (diphenylhidantoine, phenobarbital, etc), L-thyroxine, heparin, immunosuppressants (cyclosporine), hormonal blockade (aromatase inhibitors and gonadotrophins), chemotherapeutic drugs.
RISK FACTORS FOR FRACTURES
BMD compatible with osteopenia and osteoporosis
Age over 65
Prior osteoporotic fracture
Osteoporotic fracture in first-degree relative
Low weight
Increased risk of falls: muscle weakness, impaired gait, balance or mobility, visual or cognitive deficits, history of falls, etc.

Effects of osteoporosis on osseointegration of implants

Osseointegration, which is measured by the percentage of contact between the surface of the implant and the bone, can be affected not only by the characteristics of the implant and surgical procedure, but also by patient-dependent variables that can affect the quantity and quality of bone. To achieve the osseointegration of implants is necessary to secure their adequate primary stability. Thus, osteoporosis, characterized by bone loss, alteration of the microstructure and the reduction in the regenerative capacity of bone, has been considered a possible contraindication or a risk factor for dental implant placement.

It has been established the hypothesis that osteoporosis affects the jaws in the same manner as other bones of the skeleton, and also that altered bone metabolism may reduce the scarring around the implants.

The revised literature shows that the osteoporosis induced in experimental animal models, before, after or simultaneously with the placement of implants, alters the process of osseointegration, especially in trabecular bone, and produces a significant reduction in the bone-implant contact.

Duarte et al. evaluated the influence of estrogen deficiency in bone around implants placed in ovariectomized rats. They analyzed the bone-implant contact and also the area and the density of bone around the implants, distinguishing the cortical region of the spongy region. The authors found significant differences between the study group and the control group, with lower values in the spongy region of the group with induced osteoporosis(4).

Giro et al. analyzed the influence of estrogen deficiency and its treatment with alendronate and estrogen on bone density around osseointegrated implants in rats. The radiographic analysis of bone density showed that estrogen deprivation has a negative effect only on the trabecular bone, and that treatment with estrogen and alendronate are effective in preventing bone loss around osseointegrated implants. In this sense, there are other studies that investigate the effects of replacement therapy with estrogen on bone healing around implants in animals with osteoporosis. There were positive results which lead to consider this treatment to improve the long-term success of implants in postmenopausal patients (5).

There are histological studies in humans conducted on osseointegrated implants which are removed to patients with osteoporosis by a prosthetic failure. They show healthy bone in close contact with the implant surface and the percentages of bone-implant contact confirm that osseointegration was produced (6,7).

Shibili et al. performed a comparative histological analysis between implants with load removed in patients with and without osteoporosis. The percentages of bone-implant contact did not show differences between both groups. The histomorphometric results were not different either between groups once the osseointegration was established. These data suggest that osteoporosis cannot be considered a contraindication to placement of implants in patients with osteoporosis (8).

Implants in subjects with osteoporosis

The success of osseointegration depends largely on the health status of the patient. Although the prevalence of osteoporosis increases with age and after menopause, the literature reviewed does not show the relationship of the implant failure rate with age and sex. The tactile valuation of bone quality during the preparation of the implant area, and the already achieved primary stability, bring more information that densitometric measurements of peripheral bones about the probability of failure (9).

The reduction of bone density and of mineral content of peripheral bones has been associated with high resorption and atrophy of edentulous jaws, but no relationship was found with greater loss of implants (10). In a study to evaluate osseointegration in postmenopausal women aged between 48 and 70, 19 of them with a densitometric diagnosis of osteoporosis and 20 whose diagnosis was normal, 82 mandibular implants were placed (39 in the osteoporosis group and 43 in the control group) and osseointegration was analysed after 9 months. Results determined by panoramic x-rays showed no significant differences between the group of osteoporosis and the control group. Also histological analysis of jaw biopsies showed no differences in bone formation and bone resorption between the two groups. The failure rate of 1.2% (only one implant lost) is compatible with the literature and cannot be attributed to osteoporosis (11). In another retrospective study with a follow up to 3 years and 4 months for 70 implants placed in patients diagnosed with osteoporosis at lumbar level of the spine and hip, there was a success rate of 97% for the maxilla and 97.3% for jaw (12). The results of the reviewed studies show that it is feasible to place implants in subjects with osteoporosis, with success rates similar to those obtained in healthy subjects, even in cases in which there was poor quality of bone during or placement.

Bisphosphonates and dental implants. Application in the treatment of osteoporosis

Bisphosphonates (BP) are a group of drugs used to treat various bone diseases such as osteoporosis, multiple myeloma, metastatic bone tumor (primarily breast and prostate cancer), Paget's disease and malignant hypercalcemia.

Its clinical utility is based in its ability to directly inhibit bone resorption. The BP are deposited in the bone, inhibit the resorptive activity of osteoclasts and induce their apoptosis, prevent its formation from hematopoietic precursors and stimulate the production by osteoblasts of a factor inhibiting osteoclasts. Some BP as pamidronate and zoledronic acid also present antiangiogenic effect that makes them important agents in cancer therapy (13). Compounds of BP have high affinity for bone tissue, especially in areas that are remodeling. They accumulate for long periods of time in the mineral matrix of bone. Depending on the duration of treatment and BP specific requirements, those compounds of BP can remain for years. In the process of bone resorption the BP are released and can be incorporated into the new formed bone.

In the treatment of osteoporosis, the oral BP (in most cases) or intravenous pharmacological agents are the choice, because as result to their mechanism of action, they are effective in increasing bone mineral density and reduce the risk of fractures (14).

In the last 5 years a new complication has been described associated with treatment with BP: osteonecrosis of the jaw (ONJ), which consists of the appearance of foci of bone necrosis with exposure of maxillary or jaw bone and which has a slow healing process (or not heal) in 6-8 weeks. The causal relationship between BP and ONJ is still in research, but there is a clear correlation with the systemic administration of aminobisphosphonates (15). In a review published in 2006 about 368 cases of ONJ, 4.1% was found in patients who received BP for the treatment of osteoporosis, and 91.6% in patients treated for multiple myeloma and breast or prostate cancer. 60% of cases occurred after dentoalveolar intervention and in other cases the cause was not identified (16). Reviewing the literature from 2003 to 2005, ONJ is mostly associated with BP administered by injection, and also with greater activity (pamidronate and zoledronic acid), which were used in over 80% of cases for the treatment of multiple myeloma and breast cancer. It has also been reported for the orally administered BP, including alendronate, but they are of low frequency. A recent revision in 2007 also reported a low risk of ONJ in patients receiving oral therapy with BP (1/10.000-1/100.000) (17). The main factors associated with the development of ONJ are enumerated in table 2. As it is stated in the literature, more than 90% of the cases occur in patients receiving intravenous BP (pamidronate and zoledronic acid) for treatment of multiple myeloma and metastatic breast cancer or prostate cancer, while cases in patients receiving the BP orally for the treatment of osteoporosis are rare. The risk increases with treatment time due to the long half-life of these drugs, and within the oral cavity, jaw is the primary location of the foci of osteonecrosis.

The fact that osteonecrosis associated with the treatment takes place in the oral cavity and especially in the jaw could be explained by the constant microtrauma caused by the forces of chewing, which make the bone be constantly remodeling and BP reach there concentrations higher than in other parts of the body. The necessity of repairing and remodeling of bone increases when conducting any dentoalveolar intervention. Depending on the dose, route and time of drug administration such capabilities may be seriously undermined. If we also add the antiangiogenic effect of some BP, and the constant presence of microorganisms in the mouth that cause cavities and periodontal disease, the risk of infection of the affected area increases considerably. Then, pain appears and dehiscence of the alveolar mucose progresses, and with all this bone exposure too.

In a revision of 468 implants placed in 115 patients treated with oral BP, there was no evidence of ONJ and only 2 implants failed. Thus the success rate is comparable to that of patients not treated with BP. Implant placement and osseointegration during the first 3 years of treatment with oral BP, without the presence of other diseases or medications, can be conducted in a safe manner (18). Another retrospective study of the placement of implants in 61 patients treated with oral BP during an average period of 3.3 years, shows no cases of ONJ during follow-up (12-24 months) and the success rate is 100% according to Albrektsson criteria (19).

Special recommendations for implant placement in patients with osteoporosis treated with oral bisphosphonates

Although patients treated with oral BP do not require any special protocol, as opposed to intravenous (20), it is desirable to adopt a series of preventive measures, which aim to restore a proper state of oral health before the start of therapy with BP. Inform the patient of the convenience of periodic revision and instruction in oral hygiene procedures to ensure adequate dental and periodontal health. As for the orthodontic implications little is known, but according to the antiresorptive effect of bone that BP have, the movement of teeth can be reduced or prevented after initiating treatment.

Before any type of surgery the start of treatment with BP will be delayed as far as possible until the wound is completely healed.

Table 2. Risk factors for development of ONJ. BP: bisphosphonate; ONJ: osteonecrosis of the jaw.

RISK FACTORS FOR DEVELOPMENT OF ONJ	
Systemic factors	- Type BP - Dosage and administration time - Concomitant medications: immunosuppressives, steroids, antiangiogenic, and so on. - Systemic diseases: diabetes, immunodeficiencies, etc...
Local factors	- Dental extractions - Oral Surgery - Trauma of the mucose by rubbing - Periodontal disease - Poor dental hygiene

In the case the patient with osteoporosis has already commenced oral treatment with BP:
- The first 3 months are not of any risk for any dental intervention.
- The non-invasive treatments (fillings, endodontics, carvings, root debridement...) can be conducted without specific measures.
- If the patient has been in treatment less than 3 years, the risk when undergoing extractions or surgery appears to be minimal, although the patient should be warned in the informed consent of a remote possibility of ONJ.
- The use of other immunosuppressive medications such as steroids, antiangiogenic agents, or the presence of concomitant systemic diseases such as diabetes mellitus, increase the risk of ONJ before surgical action, although the patient has followed treatment for less than 3 years.
- The patient treated for more than 3 years has a higher risk of ONJ in case of surgical intervention. However, most cases of ONJ associated to oral BP according to the literature are found in patients treated over 10 years (14, 18).

Before any invasive procedure such as implant placement, most consulted authors recommend to make the intervention under antibiotic prophylaxis with penicillin, or metronidazole in combination with a quinolone (in the case of allergy to penicillin). Clindamycin alone is not recommended because it is ineffective against Eikenella corrodens, Actynomices and other similar species that frequently colonize the oral cavity. It is also recommended to perform chlorhexidine rinses at 0.12% twice a day for 15 days.

The possibility of stopping treatment with oral BP 2-3 months before the intervention and until the completion of osseointegration depends on the opinion of the professional who prescribes it, considering the benefit / risk for discontinuation of the drug. From our point of view, the withdrawal of the drug is not very useful, because the effect of BP on the bone is maintained for years. For this reason it is convenient to reach an agreement among dentists and specialists in maxillo-facial surgery, and the physicians who treat osteoporosis in patients (rheumatologists, endocrinologists, internists, family doctors, etc.) (20).

It has also been recommended the establishment of the level of carboxyterminal telopeptide of collagen type I (CTX) in blood, as this telopeptide is separated of the collagen molecule by osteoclasts during bone resorption, and its level in blood would be proportional to the degree of reapsortive osteoclastic activity, which could have a specific value for predicting ONJ in patients undergoing surgery or extractions (15):
- If the levels of CTX are equal to or greater than 150 pg / ml the risk of ONM in connection with surgical procedures is minimal.
- If the levels of CTX are less than 150 pg / ml, it is advisable to postpone the surgery, to assess the temporary withdrawal of the drug, and to repeat the determination of CTX in 4-6 months' time. If it continues being lower after this time, carry on without the drug, and repeat 3 months later.

However, there is insufficient scientific basis about the predictive ability of CTX, and therefore its use should be considered with caution and this information should be detailed in the informed consent.

Conclusions

Patients with osteoporosis have no contraindications to dental implant placement. The steps to take before starting a surgical implant will be no different from people without osteoporosis. Nevertheless, proper oral hygiene prior to intervention will be highly advised. Although the risk of ONJ in subjects treated with BP is very low, patients should be informed and must sign consent with the inclusion of this specific point.

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