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Osteoporosis and its implications in dentistry.

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ABSTRACT

Osteoporosis is a common disease in middle-aged and older individuals. Oral health maintenance for adults with Osteoporosis is important. Osteoporosis and related fractures are more common than coronary disease, stroke and breast cancer. Fractures resulting from Osteoporosis can affect a patient's quality of life severely, and fractures result in functional impairment and increased health care cost and mortality. Medical management of Osteoporosis includes diet control, with appropriate intake of calcium and vitamin D, weight-bearing exercise, discontinuation of tobacco and alcohol intake, and use of medications, including selective estrogen receptor modulators, calcitonin, anabolic agents and bisphosphonates. Bisphosphonates have been associated with the development of osteonecrosis of the jaws.

Keywords: Osteoporosis, dental implications, bisphosphonates, periodontitis, implants

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INTRODUCTION

Osteoporosis is a systemic skeletal disease manifested by reduced bone strength, decreased bone mineral density (BMD), and altered macrogeometry and microscopic architecture, and resultant increased risk of fractures. A recent report revealed that osteoporosis affects more than 10 million individuals aged 50 years or more; an additional 33.6 million are affected by osteopenia (low bone mass) and consequently are at risk for osteoporosis and its complications(1).

Osteoporosis is defined by the World Health Organization (WHO) as a bone mineral density (BMD) that is 2.5 standard deviations (SDs) below the young normal. Osteopenia is defined as a BMD between 1 and 2.5 SDs (Table 1) (2).

Table 1: World Health Organization criteria for defining osteoporosis and osteopenia

Normal	BMD ≤1 SD below the mean for a young, healthy adult (T ≥ –1.0)
Osteopenia	BMD >1 SD, but <2.5 SD below the mean for a young, healthy adult (–1.0 > T > –2.5)
Osteoporosis	BMD ≥2.5 SD below the mean for a young, healthy adult (T ≤ –2.5)
Established osteoporosis	BMD ≥2.5 SD below the mean for a young, healthy adult (T ≤ –2.5), with 1 or more fragility fractures

T score = 1 SD difference from the BMD in a young, healthy adult of the same gender. BMD, bone mineral density; SD, standard deviation; WHO, World Health Organization. Modified from Report of a WHO Study Group[2]

Risk factors for osteoporosis is not restricted by and may include: genetics, aging, early menopause, physical inactivity, heavy smoking, alcohol abuse, decreased calcium intake, and long-term use of certain medications (e.g., glucocorticoids, antiepileptic agents, gonadotropin-releasing hormone agonists, excessive thyroxine doses and anticoagulants). Several systemic diseases also present as risk factors (e.g., primary hyperparathyroidism, hypogonadism, multiple myeloma, leukemia, rheumatoid arthritis, celiac disease, gastrectomy, and chronic obstructive pulmonary disease), of which some factors can be modified(3).

Pathogenesis

Skeletal fragility can result from: (a) failure to produce a skeleton of optimal mass and strength during growth; (b) excessive bone resorption resulting in decreased bone mass and microarchitectural deterioration of the skeleton; and (c) an inadequate response to increased resorption during bone remodeling.

To understand how excessive bone resorption and inadequate formation result in skeletal fragility, it is necessary to understand the process of bone remodeling, which is the major activity of bone cells in the adult skeleton. The bone remodeling or bone multicellular units (BMUs) described many years ago by Frost and others (4) can occur either on the surface of trabecular bone as irregular Howship lacunae or in cortical bone as relatively uniform cylindrical Haversian canal. The process begins with the activation of hematopoietic precursors to become osteoclasts, which normally requires an interaction with cells of the osteoblastic lineage. Because the resorption and reversal phases of bone remodeling are short and the period required for osteoblastic replacement of the bone is long, any increase in the rate of bone remodeling will result in a loss of bone mass. Moreover, the larger number of unfilled Howship lacunae and haversian canals will further weaken the bone. Excessive resorption can also result in complete loss of trabecular structures, so that there is no

template for bone formation. Thus, there are multiple ways in which an increase in osteoclastic resorption can result in skeletal fragility. However, high rates of resorption are not always associated with bone loss; for example, during the pubertal growth spurt. Hence an inadequate formation response during remodeling is an essential component of the pathogenesis of osteoporosis.

ANTI-RESORPTIVE AGENTS

NSAIDs

Inflammation-induced bone resorption is mediated mainly by arachidonic acid metabolites, like prostaglandins and COX-2. These substances are increased in areas of inflammation, mostly in the gingiva of periodontitis patients, and they stimulate bone resorption by enhancing expression and potentiating the effects of RANKL(6-8). NSAIDs inhibit the production of the inflammatory mediators and therefore are used to inhibit osteoclast formation and hence decrease oral bone loss(9, 10). Williams and colleagues (11) studied the effects of flurbiprofen on naturally occurring periodontitis in a canine patient. In this study, beagle dogs were treated with either surgical or nonsurgical periodontal therapy in combination with either flurbiprofen or placebo. For up to 12 months, flurbiprofen significantly decreased the rate of radiographic ABL; this same result did not occur in the placebo group. A human case-control study of 22 patients taking NSAIDs for other medical conditions (e.g., arthritis) found that these patients, when compared with matched controls, displayed lower Gingival Index (GI) scores and shallower pocket depths(12). A 3-year longitudinal trial (13) assessed the effects of NSAIDs on periodontal disease progression in 44 adult patients with advanced periodontitis. Following periodontal therapy, patients self-administered 50 mg flurbiprofen or placebo twice daily (bid) for 24 months. After 3 years, there were 33 compliant patients available for follow-up. Flurbiprofen significantly arrested the progression of bone loss in these patients when compared with controls. Use of these drugs for prevention of oral bone loss has decreased in recent years because of the need for long-term systemic administration and the resultant side effects, (14) although local-delivery applications are being pursued with some success(15).

Bisphosphonates:

Bisphosphonates inhibit bone resorption through multiple mechanisms, although the main mechanisms involve inhibiting the formation and resorptive capabilities of osteoclasts and promoting osteoclast apoptosis(16). Chemically they are similar to pyrophosphate which is an endogenous regulator of bone resorption (17-19). Bisphosphonates decrease the metabolic activity and numbers of osteoclasts, and accelerates their apoptosis. It also inhibits osteoclast recruitment and concentrates in lacunae around the osteoclasts. There are 2 major groups, one of which is a Non-Nitrogen containing Group. The Non-Nitrogen group enters phosphate of ATP which inhibits cell functions and hastens apoptosis. In physiological doses bisphosphonates have an affinity for bone, deposit in new bone in close proximity to and in osteoclasts, and will remain in bone for many years (up to a decade).(20) Bisphosphonates also downregulate levels of several MMPs, including MMP-1, -3, -7 through -9, and -12 through -14, even in the periodontal ligament cells. (21) Some bisphosphonates also have anti-inflammatory properties and inhibit the release of inflammatory mediators such as IL-6, TNF-α, and IL-1Beta. The histological appearance of 20 samples of bisphosphonate affected bone has been reported. (22) Generally, the bone showed reduced osteoclastic and reversal line activity. The vascularity of the connective tissue was intact but congested with red blood cells contributed to the slightly lower level of mineralization and an apparent normal number of osteocyte lacunae in the presence of osteomyelitis. Current etiologic possibilities for bisphosphonate necrosis are centered upon the effects of bisphosphonates on the inhibition of angiogenesis (23) and osteoclastic action. (24)

It has been suggested that the bisphosphonates produce ischaemic changes in the maxilla and mandible. The unique environment of the oral cavity could explain why the maxilla and mandible are solely involved. It can be hypothesized that patients who have received long-term bisphosphonate therapy may have a compromised blood supply to their maxilla and mandible. When dental extractions are performed on this group of patients, the open bony wound with a compromised healing ability cannot cope with the presence of oral microflora. (25) The extraction wound then becomes infected and progresses into osteomyelitis due to the poor healing ability of the tissues. It then develops into osteonecrosis. (25) It should be noted that all other bones in the skeleton are well enclosed in the soft tissue and thus protected from a resident microflora.

ANABOLIC AGENTS

Estrogen and Selective Estrogen Receptor Modulators (SERMs)

Estrogen functions to maintain bone mass, and its withdrawal leads to accelerated bone resorption, increased osteoclast activity, and subsequent bone loss. The loss of bone mass associated with estrogen deficiency may also occur in the oral cavity. Many studies have linked features characteristic of oral bone loss (tooth loss, decreased oral bone density, and crestal ABL) to both osteoporotic and estrogen-deficient states. Hormone replacement therapy (HRT) using estrogen is well established as a first-line treatment for osteoporosis and is being studied as a way to prevent oral bone loss. SERMs, a class of drugs modified from estrogen, have been developed to provide the specific therapeutic effects of estrogen therapy without unwanted side effects. In terms of treating oral bone loss, the therapeutic goals include blocking cytokine production to decrease osteoclast resorption, which results in increased bone mass. In one study (26) evaluating the effects of Hormone Replacement Therapy [HRT] on the periodontium, patients who received HRT had decreased probing depths, less tooth mobility, and less dental pain compared with controls.

Parathyroid Hormone (PTH):

PTH is an endogenous hormone with potent anabolic and catabolic actions in bone. Clinically, it increases BMD and prevents osteoporotic fractures, and consequently, it is used in the treatment of osteoporosis. (27, 28) Although the effects of PTH on the oral cavity are largely unknown, animal studies suggest that oral bone structure is responsive to the anabolic actions of PTH. (29)

A study (30) of patients with hyperparathyroidism revealed that these patients did not have an increase in periodontal disease as measured by attachment levels, but they had a higher prevalence of tori and exostoses, indicating an increased level of osseous activity. These findings suggest that the oral cavity is not adversely affected by increased circulating levels of PTH. In fact, the oral cavity may respond more favorably than other areas of the body to PTH therapy.

Osteoporosis and oral bone loss

Dentate patients stimulate the jaw bone metabolism on a daily basis. Consequently osteoporosis is not always visibly obvious on jaw radiographs (31-38). But since bite-wing radiographs often are taken with check-ups on a regular annual basis, changes can be detected by comparison indicating marrow changes, also seen in panoramic radiographs. Diagnosis by CT is feasible. (35) More typical of Osteoporosis is the development of localized Osteoporosis defects, which may be confused with other bone pathology, such as simple bone cyst, giant-cell-granuloma, ossifying fibroma, osteosarcoma, aneurysmal bone cyst and others(32). A biopsy for histopathology investigation is always necessary and will differentiate and/or confirm the diagnosis (34). Accordingly while focal osteoporosis marrow defects are not commonly found in both the maxilla and mandible, they do occur in these bones (33-37). With OP, edentulous jaws will show thinner cortical plates, loss of alveolar bone, a thin mandibular ridge and less dense medullary bone (38).

Periodontitis

Gingivitis affects over 90 percent of the population, but only 8-12 percent of people develop periodontitis. Nearly all periodontitis is mediated through stagnated biofilms which change their invasive destructive capacity over time. Although bacterial plaque is the primary cause of periodontitis, host susceptibility is believed to play a major role in the initiation and progression of tissue destruction. While some forms of aggressive periodontitis affect young people and diabetics due to systemic predisposing dysfunctional metabolic factors, most chronic forms of periodontitis affect middle-aged and older people. Osteoporosis becomes prevalent in seniors, particularly females but also later males, and consequently when seniors suffer from osteoporosis and periodontitis, there is a tendency for periodontitis to be more aggressive, rapid and destructive of supporting alveolar bone. Both osteoporosis and periodontitis are bone-resorptive, host-dependent, multifactorial diseases, and the bone loss in both diseases is exaggerated, either systemically or locally, by the activity of cytokines (e.g., IL-1 and IL-6).

Implants and osteoporosis

Osteoporosis results in decreased bone quality and therefore may affect the outcome of dental implant therapy. In an animal study (39) evaluating the effect of glucocorticoid-induced osteoporosis on implant osseointegration, animals received intramuscular injections of glucocorticoids (7.5 mg/kg) for 8 weeks before, along with, or after implant placement, with a fourth group serving as the control. Although there was no difference in interfacial strength between the test and control groups, bone-to-implant contact (BIC) was significantly lower in the osteoporosis groups (range, 24%±16% to 42%±16%) compared with the control group (49%±10%). The result of this study implies that although osseointegration of implants in osteoporotic bone is possible, the long-term stability of the implants may be compromised by the disease. Several studies (40-42) in humans have reported successful implant placement in osteoporotic individuals, although 1 case report (43) revealed that 5 implants failed in a patient 6 months after diphosphonate therapy was initiated. A retrospective study (44) analyzing 16 osteoporotic patients who received implant therapy showed an overall implant survival rate of 97% in the maxilla and 97.3% in the mandible with a follow-up time of 6 months to 11 years. In addition, the marginal bone loss observed was consistent with that in other studies conducted in non-osteoporotic patients, indicating that osteoporosis does not adversely affect implant success.

General Therapy and Management

Therapy and management involves (1) dietary modification, (2) behavior changes (3) moderation of OP through medication (4) oral and dental implications (45-51).

Diet and nutrition as therapy and control of Osteoporosis

Because low calcium intake and diets are implicated in development of osteoporosis, dairy products are promoted as high sources of calcium containing foods (52). Dairy products include, milk (high or low fat), cream, cheese (egg: Mozzarella), yoghurt, skim milk, milk shakes, ice-creams. Whole cow's milk (3.7G total fats), is about 88 percent water, but the solids contain essential nutrients of skeletal growth. Besides calcium, phosphates and magnesium, (all nutrients essential for healthy bone growth), bovine milk also contains: proteins, potassium, sodium carbohydrates (lactose), Vit-A, Vit-D, Thiamine, Riboflavin, Niacin, Vit B-6 , Folic acid, Vit-B12, Pantothenate and Zinc(53).

To ensure stable calcium for bone formation the range of calcium intake is 200 mg-to over 1000 mg/day. The FAO/WHO minimum requirement is close to the minimum requirement, which is low for ideal health. However, the recommended calcium per day for adults is at least 800 mg and 1200 mg+ for teenagers and seniors over 55 years. People consuming less protein will remain in calcium balance with lower levels of calcium intake. Only one quarter of calcium intake from cow's milk is retained. Milk is a ubiquitous source of calcium, though a varied diet is easier to sustain.

Sodium

A Total of 2G sodium is needed per day. Consuming excess >2Gper day will reduce bone density. High sodium intakes may disrupt stable metabolism and induce hypertension. Sources from salted foods and table salt added to food to enhance flavor (53).

Vitamin-C

A daily intake of 60 mg a day is considered adequate. This is double the RDA of Vit C needed for bone synthesis. Excess intake of Vit-C may have pharmacological effects unrelated to the function of the vitamin. Sources are broccoli, parsley, guava, citrus, rose hips and fresh fruits and vegetables (53).

Phosphorous

The Phosphorous requirement is at least 1:1 for Ca: P, and probably needs more Phosphorous. The average Calcium intake per day is 400-1300 mg/d and Phosphorous 800-1500 mg/d. Sources are vegetables, meats and fruits (53).

Behavior modifications

Exercise, and particularly weight bearing activities, slows development of Osteoporosis. Exercise forces the body to support full weight. This stimulates bone formation and modeling. Brisk daily exercise is needed for 30 minutes. Exercise at least three times weekly is the desirable minimum. Making exercise part of a daily routine is beneficial in the long run. Playing sports is one pleasurable form of securing benefits of exercise, such as climbing stairs, playing ball games, (like racket ball, tennis, squash) dancing, and jogging. Daily walk for a vigorous 30-45 minutes is recommended (53).

Dental therapy and management of Osteoporotic dental patients

Changing, modifying or stopping Osteoporosis medication should not be done without communicating with the patients controlling physician. For Dentate Patients with Osteoporosis, most standard procedures can be successfully performed on Osteoporosis patients. Smokers, especially females, are more prone to complications, such as dry sockets post-extraction, and delayed healing after minor dento-alveolar or periodontal surgery. Smokers have a higher prevalence of severe periodontitis and are more resistant to periodontal treatment. Severity of alveolar bone loss increases when periodontitis presents in elderly female individuals suffering from estrogen deficiency. General alveolar ridge resorption is accelerated in women without hormone replacement therapy. Extraction sockets do not heal. Bony ridge protuberances and mylohyoid ridges are affected, particularly in edentulous jaws (54-56). Non-vital bone protrudes into the mouth and frequently loses its mucosal covering.

In cases with the above mentioned conditions, and on high doses of Bisphosphonate therapy (BPT), these patients are not ideal patients for major invasive periodontal or dento-alveolar surgery. BPT persists in the system for years, and should extractions or major periodontal infections require treatment, these should be done and stabilized whenever possible before implementing anti-resorptive therapy by BPT. New invasive oro-dental therapies should be thought of, but non-vital bone must be removed to avoid developing osteomyelitis. Care of general nutrition is similar to management of patients suffering from cancer.

Summary

Both osteoporosis and periodontitis are common bone-resorptive, host-dependent, multifactorial diseases that generally affect older patients. Both diseases are stimulated by bone-resorptive proinflammmatory cytokines such as IL-1 and TNF-α, but the end result of this stimulation differs in the 2 diseases. Osteoporosis results in bone loss that is generalized throughout the skeleton, whereas periodontitis results on bone loss that is localized to the alveolus.

There are 2 types of chemotherapeutic agents for the treatment of systemic/oral bone loss: anti-resorptive agents (which inhibit bone loss) and anabolic agents (which increase bone formation). Anti-resorptive agents include NSAIDs, bisphosphonates and RANKL. Anabolic agents include SERMs and PTH. Longitudinal studies have demonstrated reduction in risk of tooth loss with hormone replacement therapy. There is limited amount of evidence that calcium supplementation may be beneficial. In clinical trials, bisphosphonate Aldendronate has been found to reduce the risk of progressive loss of alveolar bone.

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