Impact of Osteoporosis and Its Treatment on Oral Health

Sukumaran Anil, BDS, MDS, PhD, Reghunathan S. Preethanath, BDS, MDS, Hani S. AlMoharib, BDS, Kavitha P. Kamath, BDS, MDS and Pradeep S. Anand, BDS, MDS

Abstract: Osteoporosis has emerged as a major health problem affecting middle-aged and older individuals. It is characterized by a reduced bone mass and strength, resulting in increased susceptibility to fractures. The disease is associated with several risk factors, and increasing evidence suggests that it may be associated with oral health conditions such as periodontal disease, reduced jaw bone density and tooth loss. Besides the effects of osteoporosis on oral health, bisphosphonate-related osteonecrosis of the jaws is a major concern to the dentist. Bisphosphonate-related osteonecrosis of the jaws is a recently described adverse effect of bisphosphonate therapy. The exact mechanisms by which these drugs cause necrosis of the jaws remain unclear, and a true cause-and-effect relationship between osteonecrosis of the jaw and bisphosphonate use has not yet been established. Hence, any form of invasive dentoalveolar treatment should be performed with caution in patients taking bisphosphonates. This review discusses current evidence on osteoporosis and its treatment implications as a risk factor in the development of various oral diseases.

Key Indexing Terms: Osteoporosis; Postmenopausal; Periodontal disease; Tooth loss; Bisphosphonates; Osteonecrosis. **[Am J Med Sci 2013;346(5):396–401.]**

Osteoporosis is a skeletal disorder characterized by low bone mass and microarchitectural deterioration with a resulting increase in bone fragility and susceptibility to fracture.[1] It is the most common type of metabolic bone disease, characterized by compromised bone strength. Osteoporosis is commonly seen in middle-aged and older individuals, which typically goes unnoticed until fractures occur. It is a complex, multifactorial, chronic disease that represents a severe public health problem because of the high risk of low and nontraumatic fractures, especially of the vertebrae, hip and forearm bones.[2] Osteoporosis can be characterized as either primary or secondary type. Primary osteoporosis includes the conditions in which the decrease in bone mass can be explained by changes of aging (senile types), as well as the hormonal changes of menopause. In contrast, the term secondary osteoporosis is used for the one caused by other diseases or medications.[3]

Primary osteoporosis can occur in both sexes at all ages, but often women experience more rapid bone loss following menopause, which places them at a higher risk for fractures. The incidence of osteoporosis in a population is dependent on gender, age, endocrine status, and lifestyle; however, the highest risk group being postmenopausal women above the age of 50 years. In most women, the main reason of osteoporosis is the decrease in estrogen that accompanies menopause. This decrease in estrogen levels is associated with an elevated rate of bone loss caused by the increase in several inflammatory cytokines, cooperatively stimulating osteoclast-mediated bone resorption. Production of all of these cytokines is either directly or indirectly suppressed or regulated by estrogen.[4]

From the Department of Periodontics and Community Dentistry (SA, RSP, HSA), College of Dentistry, King Saud University, Riyadh, Saudi Arabia; People's Dental Academy (KPK), Bhopal, India; and People's College of Dental Sciences & Research Centre (PSA), Bhopal, India.

Submitted June 16, 2012; accepted in revised form January 21, 2013.

The authors have no financial or other conflicts of interest to disclose.

Correspondence: Sukumaran Anil, BDS, MDS, PhD, Department of Periodontics and Community Dentistry, College of Dentistry, King Saud University, PO Box 60169, Riyadh 11545, Saudi Arabia (E-mail: drsanil@gmail.com).

Pathogenesis

In living bone tissue, there is a fine balance between bone formation by osteoblast and bone resorption by osteoclast. Osteoporosis is bone reduction resulting from imbalance between resorption and bone formation, with resorption tending to increase. This disorder leads to demineralization of bones, which begins to manifest clinically in the fourth and fifth decades of life. Several risk factors for the development of osteoporosis have been identified, and these have been broadly classified as nonmodifiable and modifiable.[5] The nonmodifiable risk factors include age, sex, genetic factors and early menopause, while the modifiable risk factors include inadequate calcium consumption, lack of exercise and behavioral factors such as smoking and alcoholism. Besides these, other factors that can contribute to the development of osteoporosis include certain endocrine diseases such as hyperparathyroidism, chronic renal and hepatic disease, malabsorption and drugs like oral glucocorticoid therapy.[5,6]

The role of estrogen in the development of osteoporosis is well documented. Studies have shown that sex steroids, particularly estrogen, are important in developing peak bone mass, and estrogen deficiency is a major determinant of bone loss in both sexes.[7,8] In females, bone loss occurs most rapidly following menopause due to fall in estrogen levels and this observation led to the concept that estrogen deficiency is critical to the pathogenesis of osteoporosis. Although bone remodeling is accelerated at menopause, this accelerated bone remodeling is associated with increased bone loss and impaired bone formation.[4] Estrogen deficiency may enhance the rate of bone loss by stimulating synthesis of several inflammatory cytokines that regulate osteoclast generation, such as interleukin 1 (IL-1), IL-2, IL-6, and prostaglandin E_2.[9]

Genetic factors also contribute significantly to the risk of osteoporosis. Genetic factors influence the peak bone mass and heritability of bone mineral density (BMD) ranges from 50% to 90% in human populations.[10,11] Although numerous molecular association or linkage studies aiming to identify genes for BMD determination have been performed, to date, no clear consensus has been reached.[11]

A recent study among Swedish women has identified previous history of fragility fractures and low BMD as important factors contributing to increased hip and fragility fracture in older women.[12] Another similar study conducted in United States revealed that several factors such as age, self-reported health, weight, height, self-reported physical activity, history of fracture after 54 years, parental hip fracture, current smoking, current corticosteroid use and treated diabetes could be useful predictors of hip fractures.[13] Factors associated with increased risk for osteoporosis in men include glucocorticoid treatment, hypogonadism, excessive alcohol consumption,

anticonvulsant use, osteomalacia, severe hyperthyroidism or bone marrow neoplasia.[14]

OSTEOPOROSIS AND ORAL HEALTH

Several studies have been conducted over the last few decades to determine the relationship between osteoporosis and oral health. Majority of these investigations have studied the association between osteoporosis and periodontal disease, tooth loss and jawbone density.[5,15–19] According to the current concept, osteoporosis due to the estrogen deficiency represents a variety of conditions in relation to the stability of the structure of the jawbones. Given the evidence that alveolar processes provide the bony framework for teeth support, the loss of systemic bone density in osteoporosis, including that of the oral cavity, can be a negative consequence on tooth stability. It has also been found that the decline of skeletal mass can be correlated with an increased risk of oral bone loss, resulting in a host system that is increasingly susceptible to infectious destruction of periodontal tissues. In spite of these findings, osteoporosis may cause alteration in the mineral content of the alveolar bone and thus can predispose to the progression of periodontal disease[6] (Figure 1).

Tooth Loss

An association between tooth loss and osteoporosis has been reported in the literature.[20–24] Among postmenopausal women on hormone replacement therapy, the risk of tooth loss was relatively less. Increased alveolar ridge resorption and greater alveolar crestal height loss was reported in subjects with osteoporosis and osteopenia.[19,25,26]

Periodontal Disease

Recent literature suggests a possible association between osteoporosis and periodontal disease among postmenopausal females and showed a positive association between the 2 diseases.[27] Payne et al[28] in their 2-year longitudinal study evaluated the effect of osteoporosis and cigarette smoking on alveolar bone height in postmenopausal females. They reported that both smoking and osteoporosis had a negative impact on alveolar bone height. Jabbar et al[29] evaluated the relationship between periodontal disease and plasma cytokines, vitamin D and BMD in postmenopausal women with and without osteoporosis. They reported that periodontal disease was more common in women with osteoporosis and is associated with lower vitamin D and higher concentrations of receptor activated nuclear factor kappa B ligand and suggested that raised cytokines may play an important role in the association between these 2 conditions. Mohammad et al[19] in their cross-sectional study on postmenopausal women compared various periodontal parameters in individuals with high and low bone and spine density. They reported that parameters such as gingival recession and clinical attachment level were significantly different in both the groups.

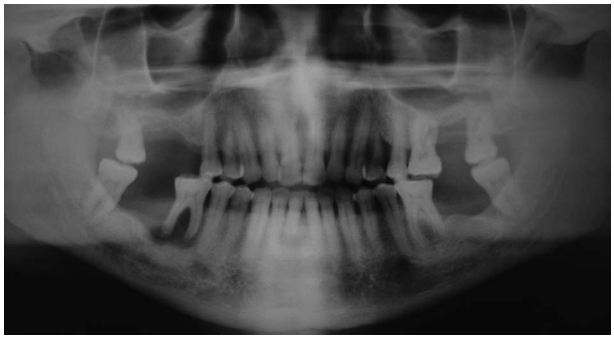

FIGURE 1. Orthopantomogram of a 60-year-old patient with osteoporosis. Note the area of low bone density, alveolar bone loss and tooth loss.

Both osteoporosis and periodontal diseases are bone resorptive diseases. Osteoporosis is characterized by reductions in bone mass and may lead to skeletal fragility and fracture. Periodontitis is characterized by resorption of the alveolar bone and is a major cause of tooth loss in adults. Because loss of alveolar bone is a prominent feature of periodontal disease, severe osteoporosis could be suspected of being an aggravating factor in the case of periodontal destruction. Therefore, it has been hypothesized that the breakdown of periodontal tissue may, in part, be related to systemic diseases, including osteoporosis. In addition, literature has proposed the role of osteoporosis in the onset and progression of periodontitis and tooth loss. Bando et al[30] reported that lower spinal BMD was positively correlated with tooth loss. In a study to determine the risk factors for tooth loss in elderly people, Xie and Ainamo[31] found that tooth loss was associated with a history of bone fracture that was used as an indicator of osteoporosis.

Loss of Bone Density

Osteoporosis also results in loss of BMD throughout the body, including the maxilla and the mandible. The resulting low density in the jawbones leads to increased alveolar porosity, altered trabecular pattern and more rapid alveolar bone resorption following invasion by periodontal pathogens. The systemic factors affecting bone remodeling may also modify the local tissue response to periodontal infection, such as increased systemic release of IL-1 and IL-6. However, chronic infection around multiple teeth could contribute significantly to elevated production of cytokines associated with periodontal diseases. This could accelerate systemic bone resorption by modulating the host response. Proinflammatory cytokine IL-6, produced by osteoblasts, may play a pivotal role in this potential mechanism. In normal bone homeostasis, IL-6 production stimulates osteoclastic activity resulting in bone resorption.[32] Many of the effects on BMD may also be modulated through IL-6.[33] Animal studies have proved that elevated levels of IL-6 were found in the serum and gingival tissue adjacent to deep periodontal pockets.[34] Therefore, it is at least theoretically possible that chronic periodontitis may contribute to the development or progression of osteoporosis. However, clinical reports have failed to find this correlation.[33]

ORAL IMPLICATIONS OF OSTEOPOROSIS THERAPY

Several medications are available to increase BMD, which include hormone replacement therapy, bisphosphonates (BPs), calcitonin, selective estrogen receptor modulators, recombinant human parathyroid hormone (teriparatide of ribosomal DNA origin: Forteo, Eli Lilly and Company, Indianapolis, IN) or combination of these medications.[6] Recently, a new bone antiresorptive agent Denosumab (Prolia, Amgen Inc, Thousand Oaks, CA) has been approved by Food and Drug Administration in the treatment of osteoporosis and metastatic cancer to the bones. Denosumab targets and binds to RANK ligand, inhibiting osteoclast formation, function and survival.[35] There is sufficient evidence in the literature to demonstrate that most of the medications used for the treatment and prevention of osteoporosis have the potential to reduce systemic as well as oral bone loss.[15] It has been shown that estrogen used in