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The Relation Between Osteoporosis and Periodontits: A Review

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ABSTRACT

Background: There has been increasing interest in the interrelationship between systemic osteoporosis, oral bone loss, tooth loss, and risk factors for these conditions. Because the severity of alveolar bone loss increases with age, it has been hypothesized, that it may, in part, be related to systemic conditions that also predispose the patient to osteoporosis / osteopenia. There is also evidence that therapies designed to influence bone mineral density, such as harmone replacement and bisphosphonate therapy, may be associated with less tooth loss and a slower loss of alveolar bone, respectively. This paper reviews the possible relationship between systemic osteoporosis and periodontitis, and the treatment modalities for osteoporosis.

Keywords: Osteoporosis, Osteopenia, Periodontitis.

INTRODUCTION

Osteoporosis and osteopenia are characterised by reduction in bone mass and may lead to skeletal fragility and fracture. In most women, bone mass reaches its peak in the third decade of life and declines thereafter. with the onset of menopause the decline in bone mass is accelerated. Loss of bone mass, per se, does not cause symptoms. However pain, loss of function fracture does occur and in some cases, deformity may result. Hence osteoporosis before fracture is termed as "Silent disease".[1]

Periodontitis is an inflammatory disease characterised by loss of connective tissue and alveolar bone. Similar to osteoporosis, periodontitis is a silent disease, which does not cause symptoms until late in the disease process when mobility of teeth, abscesses and tooth loss may occur. The etiologic agent in periodontitis is pathogenic bacterial plaque in a susceptible patient, osteoporosis and periodontitis have several common risk factors.The relation between periodontitis, osteopenia and oral bone loss is important and has significant public health impact. Both osteoporosis and periodontal disease are major health problems and their impact will be more profound as the population ages. Determination of the relationship between these two diseases as well as identification of risk factors, common and uncommon to these diseases will be increasingly important in the prevention of morbidity and mortality released to these disorders.[2]

Risk Factors Associated With Osteoporosis

Primary Risk Factors:

History of fracture as an adult, Race, history of fracture in a first degree relative, low body weight (< about 127 pounds), current smoking, use of corticosteroid therapy for more than 3 months, genetics and advancing age.

Secondary Risk Factors

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At an early age (< 45 years)Impaired vision,Estrogen deficiency,, excessive alcohol or caffeine intake, low calcium intake (lifelong), poor health frailty, recent falls, low physical activity, dementia, lack of physical activity.

Risk Factors for Periodontal Disease:

Age, occurrence of pathogenic bacterial plaque, immune dysfunction, nutritional deficiencies, use of steroids / other medications, gender, stress, cigarette smoking, genetics and systemic conditions including neutrophil disorders, diabetes, pregnancy and other occurrences of hormonal alteration and osteoporosis.There are numerous risk factors which are common to both periodontal disease and osteoporosis including cigarette smoking, nutritional deficiencies, increasing age and immune dysfunction. Clear understanding of the influence and mechanism of action for these factors may assist us in better modelling our understanding of these procedures.[3]

Diagnostic Guidelines for Interpretation of bone mass measurements according to WHO:

1. Severe Osteoporosis:

Bone mineral density (BMD) more than 2.5 SD below the value of peak bone mass in young normal women and the presence of fractures.[4]

2. **Osteoporosis** :

BMD more than 2.5 SD below the mean value of peak bone mass in young normal

Women.[4]

3. **Osteoporosis (Low bone mass):**

BMD between 1 and 2.5 SD of the mean value of peak bone mass in young women.[4]

4. **Normal:**

BMD not more than 1 SD below mean value of peak bone mass in young normal

Women.[4]

Methods for Assessment of Bone

Systemic Bone

Absorptiometry[5]

Single Photon Absorptiometry

- Uses gamma source such as I^{128}
- Assesses bone mass and mineral content in peripheral areas

Dual photon absorptiometry

- Isotopes with 2 gamma - ray energies - gadollium^{172}can be used.
- Thicker body parts with overlying soft tissues can be scanned.

Dual energy x-ray absorption (DAX)

- Uses x-ray source
- Measures bone density and mass in units of g/ cm^2
- May be used in central and peripheral sites

Quantitative computed Tomography (QCT)

- Trabecular or total bone density can be directly measured.
- Units are g/cm^2
- Relatively high radiation dose.

Measurements from radiographs[6]

- cortical thickness and other indices can be measured.
- Fractal dimensions

Intra Oral Sites

Adaptation Or Absorptiometry Or Dxa

Measurement From Panoramic Films

- Cortical thickness and other indices

Measurements From Intra Oral Films[7]

- Measurement of ridge / bone height
- Apparent bone density
- Digital subtraction radiography - change in bone height (mm) or density (mg/mm^2)
- Fractal dimension

Studies On The Relationship Between Osteoporosis, Oral Bone Loss, And Periodontal Disease

OsteoporsisAnd Oral Bone Loss:

Systemic loss of bone density leading to osteoporosis was suspected as a systemic risk factor for loss of oral bone, including loss of alveolar process associated with periodontal infection. Many studies using different populations and different methods to assess BMD have been done and most of them conclude that there is a relationship between systemic osteoporosis and reduced oral bone mineral density / oral bone loss .[8]

Kribbs et al (1983) in a comparison of 85 Osteoporotic women and 27 normal women found less mandibular bone mass and density and a thinner cortex at the gonion in osteoporotic women, than in normal women.[9]

Strekfus et al (1997) showed that postmenopausal women on estrogen therapy had more alveolar and second metacarpal density than premenopausal women. Alveolar bone densities strongly correlated to second metacarpal densities.[10]

Jonasson et al (2001) used an index to assess the alveolar trabecular patterns and found a significant correlation with skeletal BMD.[11]

Osteoporosis and Tooth Loss:

Krall and others studied tooth loss and skeletal bone density in 329 post menopausal women. Theremainingnumber of natural teeth were compared to the BMD of the lumbar spine and radius. The BMD of both the spine and the radius correlated well with the number of remaining teeth.He also studied the contribution of Osteoporosis to tooth loss in 208 women, aged 60-69 years who had either upper or lower full dentures. The current osteoporosis severity of the women and their smoking habits were compared. He found a strong association between smoking and edentulousness.This study although it strongly presents a role for smoking and osteoporosis in edentulousness, it does not prove relationship between these factors and the reason for edentulousness, which was presumed to be periodontal disease.In a limited number of studiestooth loss has been observed to be related to bone density in the oral cavity. When interpreting results in various regions, it is necessary to remember that tooth loss is highly influenced by local practices of the dental community as well as other factors related to oral health, not only by periodontal disease.[12]

Osteoporosis and Periodontal Disease

Several reports find a connection between advanced periodontal disease (as in tooth loss) and diminished systemic BMD.Hildebolt (2002) in a study of 135 women with atleast 10 teeth and no evidence of moderate or severe periodontal disease found that there was a weak correlation between attachment loss and vertebral / proximal femur bone density.[13]

Tezal et al (2000) in a study population of 70 post -menopausal women aged 51-78, assessed skeletal BMD by DXA. Clinical attachment level and inter proximal ABP represented periodontal disease severity. Mean ABL significantly related with systemic BMD. Correlation between clinical attachment level and BMD was found. In a 2 year longitudinal study, the density and alveolar bone height changes in 21 osteoporotic women compared with 17 women with normal lumbar spine BMD were studied. Osteoporotic women exhibited a higher frequency of alveolar bone height loss and crestal and subcrestal density loss relative to women with normal BMD.[14]

Diagnosis and Physical Examination:

The history and physical examination are insufficient for diagnosis of osteoporosis. However, they can be important in the screening process for osteoporosis and in directing the evaluation. The medical history will provide valuable information about factors that could influence bone mineral density, such as chronic conditions, behaviours, physical fitness, and the long term use of medications. The history should focus on the likelihood of fractures. The physical examination should be used to aid in the screening for osteoporosis.

Fractures are generally a late physical manifestation of osteoporosis. The forearm, vertebrae, femoral neck, and proximal humerus are common sites for fractures. dowager's hump (spinal curvature) in the elderly indicates the presence of a

decreased bone volume and multiple vertebral fractures.

Bone density measurement

Conventional radiographs are not sensitive enough to diagnose osteoporosis until total bone density has decreased by 50%. Bone densitometry is useful for measuring bone density. For assessment of bone mineral density, the most widely used techniques are dual-energy X-ray absorptiometry and quantitative computed tomography. When compared to X-ray absorptiometry Single and dual photon absorptiometry have been used in the past providedmore radiation exposure, poorer resolution, less accurate analysis,.Dual-energy X-ray absorptiometry and quantitative computed tomography have precision error rates of 0.5-2 %.[8]

Among these methods, dual-energy X-ray absorptiometry is the most precise and the diagnostic measure of choice. Quantitative computed tomography is the most sensitive method but results in substantially greater radiation exposure than dual-energy X-ray absorptiometry.For assessment of the peripheral skeleton, smaller less expensive systems can be used. Dual-energy X-ray absorptiometry scans of the distal forearm or the middle phalanx or quantitative ultrasound measurements can be of use for monitoring therapy when compared with baseline scans.[15]

Laboratory Tests

Chemical analysis of serum is indicated when clinical history and physical examination indicate other clinical conditions influencing bone mineral density. Therefore to exclude secondary causes of osteoporosis laboratory tests are appropriate. Specific biochemical markers used in research can give information about the overall rate of bone formation and bone resorption. These markers include human osteocalcin and bone alkaline phosphatase.[16]

Therapy:

Therapy can be based on the classification of bone mineral density. Patients with normal density measurements need no further therapy. In osteopenic patients, emphasis should be on counseling and prevention of future bone loss. Follow up will be needed to monitor potential changes in bone mineral density. In osteoporotic patients, active therapy should be aimed at increasing bone density and decreasing fracture risk. Treatment of established osteoporosis, irrespective of the patient's age, is cost-effective. Therapies with proven rapid efficacy may offer important value to healthcare funders, providers, and patients. Correctly diagnosing, identifying, and treating patients at risk of fracture, before sustaining a fracture, will have a significant impact on the long-term burden of osteoporosis. The risk of the first fracture can be reduced from 8% to 2% and the 5-year fracture incidence can be reduced from approximately 34% to 10%. However, there is evidence suggesting that many women who sustain a fragility fracture are not appropriately diagnosed and treated for probable osteoporosis. Of the majority of individuals at high risk, a large proportion will experience a fracture before being diagnosed and treated, and they will have an inadequate or non existent prevention strategy. This highlights the importance of proper screening, early diagnosis, and the institution of appropriate prevention and treatment strategies.[8]

Prevention Strategies

It is important to identify risk factors for individual patients and develop prevention strategies for the specific situations of patients. The general principles and recommendations for prevention that have been formulated by the National Osteoporosis Foundation are:[8]

- Regarding the risk factors for osteoporosis counseling must be done for all women.
- Just as hypertension is for stroke,for fracture Osteoporosis is a 'silent' risk factor, one in two Caucasian women will have an osteoporotic fracture at some point in her lifetime.
- For the determination of the diagnosis and disease severity all postmenopausal women who present with fractures must be evaluated for bone mineral density.
- Bone mineral density testing is recommendedin postmenopausal women younger than 65 years

who have one or more risk factors for osteoporosis, in addition to menopause.

- Regardless of additional risk factors screening for bone mineral density in all women 65 years and older is recommended.
- Counseling must be done for all diagnosed patients to obtain an adequate dietary intake of calcium (at least 1200 mg/ day), including supplements if necessary.
- To reduce the risk of falls and fractures regular weight-bearing and muscle-strengthening exercises, are recommended.
- Patients should be advised against smoking and smoking cessation should be advocated. Alcohol intake should be at a moderate level (i.e., up to one drink per day for women and up to two drinks per day for men).
- All post-menopausal women who present with vertebral or hip fractures should be considered candidates for osteoporosis treatment.
- Initiate therapy to reduce fracture risk in women with bone mineral density T scores below -2 in the absence of risk factors and in women with T scores below -1.5 if other risk factors are present.
- Hormone replacement therapy, alendronate (Fosamax) and raloxifene (Evista) for prevention; and calcitonin (Calcimar are pharmacological options for osteoporosis prevention and treatment.

All postmenopausal women and men of older age should be aware of their risk for developing osteoporosis and be familiar with the range of non-pharmacological approaches to maintain bone health, bone mineral density, and to prevent osteoporotic fractures. Clinicians, including dentists, should be a source of this information and motivation to make and sustain lifestyle changes relating to exercise, tobacco, diet, and alcohol use, and approaches to fall prevention. Adequate intake of calcium and vitamin D is probably the easiest lifestyle modification. The National Academy of Sciences as well as National Osteoporosis Foundation, as well as the recommends a daily intake of 1200 mg dietary calcium and 400-800IU of vitamin D. Well-balanced nutrition to ensure this is preferred; however, supplements should be suggested if diet alone cannot provide the recommended daily intake. Tobacco use should be discouraged and current smokers should be encouraged to quit on their own or participate in a smoking cessation program. Excessive alcohol consumption adversely impacts bone health. Counseling and treatment should be offered to patients with excessive alcohol consumption as part of the lifestyle modifications to prevent osteoporosis.[17]

Physical activity and the beneficial effects of weight-bearing exercise have been well studied in a multitude of randomized, controlled clinical trials. Postmenopausal women participating in aerobic, stretching exercises, weight-bearing, strength-training, and, who received calcium and vitamin D supplements, showed an increased lumbar spine bone mineral density by 1.3%, compared with a 1.2% decrease in the control group. Motivation of currently sedentary women to exercise and increase physical activity is a difficult challenge. The average older woman is not likely to exercise to the level needed to actually build bone. Additional benefits of exercise are strengthening of muscles, improvement of balance, and prevention of falls. On a weekly basis, a minimum exercise program should include three sessions lasting from 30 to 60 minutes each.[18]

Pharmacological Intervention

Several pharmacological strategies are available to increase bone mineral density and therefore treat or prevent osteoporosis and reduce the risk of fractures. They include hormone replacement therapy, bisphosphonates, calcitonin, selective estrogen receptor modulators, parathyroid hormone or combinations of these medications.There is sufficient evidence in the literature to demonstrate that treatment reduces the risk of vertebral fracture by 30-65% and of non-vertebral fractures by 16-53%, depending on the drug and the patient population. On the other hand, poor compliance of patients with drug therapies for osteoporosis over a year leaves them at risk for fractures and higher healthcare costs.[19]

Hormone replacement therapy

Rapid loss of bone density is observed because of estrogen deficiency in the early postmenopausal years. The rationale for hormone replacement therapy is to delay this bone loss. Estrogen therapy can have a dual effect that results in increased bone density. It can inhibit osteoclast formation and function and can also extend the lifespan of osteoblasts and osteocytes.[20]

A meta-analysis evaluated data on all estrogen therapy and hormone therapy trials performed up to 1999 . The main focus was the impact of hormone replacement therapy on bone density and fractures. The combined data of this analysis suggest a strong impact of hormone replacement therapy on bone density at both trabecular and cortical sites after 1 and 2 years of therapy. A dose-response in bone density with hormone replacement therapy, in particular for the lumbar spine and femoral neck, was observed. There was a significant difference in 2 years between low-dose estrogen, defined as equivalent to 0.3 mg of Premarin, and high-dose estrogen, equivalent to 0.9 mg Premarin.. All the trials studied the effect of two, three or four doses of estrogen therapy and hormone therapy against placebo on bone mineral density. These studies in general found similar increases in spine bone mineral density for estrogen therapy and hormone therapy as reported in the meta-analysis.[21]

In a randomized clinical trial as part of the Women's Health Initiative trial, those women randomly assigned to receive conjugated estrogens, with or without a progestin, 33% reduction in hip fracture was noticed. Hormone replacement therapy increased total hip bone mineral density and reduced the risk of fractures at the hip, vertebrae, and wrist. When studying women with a hysterectomy in the estrogen-alone component of the Women's Health Initiative, a reduced rate of hip fracture was found. Measurable bone loss results due to discontinuation of estrogen , although it is not certain whether discontinuation results in a greater fracture risk than continuation. Until recently, hormone replacement therapy was considered the primary therapy for postmenopausal women with osteoporosis. In 1999, it was used for approximately 38% of postmenopausal women in the USA. Forty-six million prescriptions were written in 2000 for conjugated estrogen. That made it the second most frequently prescribed medication in the USA. With long-term use of estrogen recently, concern has been raised about the non-skeletal risks associated. Evidence of an increased risk of breast cancer and of cardiovascular outcomes during the course of the estrogen plus progestin trial of the Women's Health Initiative prompted early termination of this trial in 2002. In 2004, an increased risk of stroke and failure to lower the incidence of coronary heart disease led to the early termination of the estrogen-alone trial.[22]

This has lead to a re-evaluation of the role of hormone replacement therapy in the treatment and prevention of osteoporosis. It should not be recommended for prevention of osteoporosis in postmenopausal women unless the woman is at significant risk of osteoporosis and other osteoporosis medications are unable to be considered. Since the publication of the Women's Health Initiative findings in 2002 about the risks of combined estrogen / progestin, a substantial decline has been observed in women receiving hormone replacement therapy. The result of this could be an increase in the incidence of osteoporosis in women who discontinued hormone replacement therapy and did not start another form of anti-resorptive therapy; especially when data concerning the rate of bone loss after withdrawal of estrogen therapy are considered. An accelerated rate of bone loss is observed, resulting in reductions in bone mineral density of up to 4.5% at the lumbar spine and up to 3.3% at the hip, during the first year after therapy discontinuation. When comparing women who had never used hormone replacement therapy to women who had discontinued hormone replacement therapy during the previous 5 years, the rate of hip fracture was 65% higher.Therefore it is important that women discontinuing hormone replacement therapy receive appropriate screening for their risk for complications of osteoporosis and should be counseled regarding alternative forms of therapy to prevent fracture.[23]

Selective estrogen receptor modulators

To provide the benefits of estrogen therapy without its unwanted side effects Selective estrogen receptor modulators were developed. Their mechanism of action, such as that of raloxifene, is

similar to that of the estrogens. Although less potent than conjugated equine bisphosphonates and estrogens, the selective estrogen receptor modulators decrease bone turnover. Raloxifene increases spine bone mineral density slightly and decreases the risk of vertebral fracture by 40% in women with osteoporosis, but it has no effect on the risk of non-vertebral fracture.The Multiple Outcomes of Raloxifene Evaluation trial in 7705 women with postmeno- pausal osteoporosis evaluated the efficacy of raloxifene. 4 years of therapy with raloxifene with high and low doses, the risk of vertebral fracture was reduced by 43% and 36%, respectively. Reduction in fractures was observed in the first year of treatment but no effect was found on the risk of non-vertebral fractures. Hot flashes and leg cramps were the adverse events . Similar to estrogen therapy, an increase in the incidence of deep vein thrombosis was observed. A reduction in the risk of breast cancer is observed with long-term use of raloxifene. The drug, however, is not approved for this indication.New selective estrogen-receptor modulators are being under research and may be available in the near future.[24]

Bisphosphonates

Bisphosphonates, analogs of pyrophosphate, bind selectively to bone mineral. They are taken up by osteoclast, resulting in osteoclast deactivation and apotosis. Increased in bone mass, improving bone strength, and a reduction in fractures resulted from Bone resorption suppression, followed by a secondary mineralization. Bisphosphonates are often considered the first-line therapy for the treatment of post-menopausal osteoporosis. They are the most widely prescribed antiresorptive agents. Randomized trials of alendronate and risedronate, two second-generation bisphosphonates, demonstrated increased bone mineral density in post-menopausal women with osteopenia or osteoporosis. A reductionof nearly 50% was found in the incidence of vertebral, and non vertebral fractures, hip.[25] Of concern to the dental community is the occurrence of osteonecrosis of the jaws. Within the last 34 years, reports in the literature have described osteonecrosis of the jaw as a potentially serious complication which is suspected of being associated with the use of intravenous bisphosphonates.

Marx and Migliorati Wang at the University of California, San Francisco reported similar findings in a new set of patients. The clinical aspects and behavior of the osteonecrotic lesions in these patients showed a striking resemblance to osteoradionecrosis with exposed bone, sequestration, and questionable delayed response to conventional surgical management. Many of the initial observations point the potential role of intravenously administered bisphosphonates, such as zoledronate andpamidronate, in the development of this condition. In a detailed paper, the findings in an additional 63 patients were outlined. 56 patients had received intravenous bisphosphonates for bone metastasis and 7 had undergone chronic oral bisphosphonate treatment for osteoporosis.[26] In a 2004 editorial, Greenberg further underscored the importance of this largely unrecognized destructive lesion, and alerted oncologists and dentists of its potential association with intravenous bisphosphonates.[27] 119 patients who had bisphosphonate-related bone exposure after being treated with intravenous bisphosphonates for approximately 1 year were described. Common findings were periodontitis (84%), dexamethasone use (59.7%) and other maintenance chemotherapies. The most common identifiable precipitating events were tooth extraction (37.8%) and periodontitis (84%), with approximately one-quarter of bone exposures occurring spontaneously in patients with edentulous mandibles.[28]

Calcitonin

Calcitonin is an inhibitor of osteoclast activity. Nasal calcitonin and subcutaneous calcitonin are available for treatment of postmenopausal osteoporosis. . Nasal calcitonin has been shown to reduce the incidence of vertebral fractures in the treatment of women with osteoporosis with, in a single randomized study, by 33% when compared with placebo.Calcitonin is not a first-line treatment for osteoporosis and it is now considered preferable to treat osteoporosis with more potent agents.[29]

CONCLUSION

The prevalence of osteoporosis in the general population is increasing rapidly, and fractures associated with this disease can have devastating consequences for the patients. Therefore, diagnosis of osteoporosis in its early stages is important. It is recommended that physicians and dentists collaborate to improve early detection of patients at risk of experiencing, or who already have early osteoporosis. As a health care provider, the dentist could serve as a pre-screener of patients with the potential for osteopenia or osteoporosis. Familiarity with the risk factors could help identify these individuals and aid in earlier diagnosis.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. RameshA, Mahajan K, Thomas B, ShenoyN, Bhandary R. Alveolar bone mass in pre- and postmenopausal women with serum calcium as a marker: A comparative study.Indian J Dent Res2011;22:878.
2. KodugantiRR, Gorthi C, ReddyPV, Sandeep N.Osteoporosis: A risk factor forperiodontitis.J Indian SocPeriodontol 2009;13:90-6.
3. EdwardsBJ, MiglioratiCA.Osteoporosis and its implications for dental patients. JADA 2008; 139:545-52.
4. Kanis JA, Melton LJ , Chriastiasen C, Johnson CC, Khaltaev N. The diagnosis of osteoporosis. J. Bone Mineral Res 1994; 9: 1137-41.
5. Kribbs PJ, ChesnutCH. Relationships between mandibular and skeletal bone in an osteoporotic population. J Prosthet Dent; 62: 703-707; 1989.
6. Hausmann E, Christersson L, Dunford R, Wikesjo U, Phyo J, Genco RJ : Usefulness of subtraction radiography in the evalvation of periodontal therapy. J. Periodontol1985 ;56 : 4-7.
7. WendeJW, GrossiSG, Trevisan M,GencoRJ. The role of osteopenia in oral bone loss and periodontal disease. J. Periodontol1996;6:1076-84.
8. GeursNC. Osteoporosis and periodontal disease. Periodontology 2000 2007; 44 : 29-43.
9. Kribbs PJ, Smith DE, Chesnut CH Jr. Oral findingsin osteoporosis. Part II: relationship between residualridge and alveolar bone resorption and generalizedskeletal osteopenia. J Prosthet Dent 1983: 50: 719–724.
10. Streckfus CF, Johnson RB, Nick T, Tsao A, Tucci M. Comparisonof alveolar bone loss, alveolar bone density andsecond metacarpal bone density, salivary and gingivalcrevicular fluid interleukin-6 concentrations in healthy premenopausal and postmenopausal women on estrogen therapy. J Gerontol A BiolSci Med Sci 1997: 52: 343–51.
11. Jonasson G, Bankvall G, Kiliaridis S. Estimation of skeletalbone mineral density by means of the trabecular patternof the alveolar bone, its interdental thickness, and thebone mass of the mandible. Oral Surg Oral Med OralPathol Oral RadiolEndod 2001: 92: 346–52.
12. Krall EA, Dawson-Hughes B, Papas A, Garcia RI. Tooth loss and skeletal bone density in healthy postmenopausalwomen. OsteoporosInt 1994: 4: 104–109.
13. Hildebolt CF, Pilgram TK, Yokoyama-Crothers N, VannierMW, Dotson M, Muckerman J, Armamento-Villareal R,Hauser J, Cohen S, Kardaris EE, Hanes P, Shrout MK,Civitelli R. The pattern of alveolar crest height change inhealthy postmenopausal women after 3 years of hormone/estrogen replacement therapy. J Periodontol 2002:73: 1279–84.
14. Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, DunfordR, Genco RJ. The relationship between bone mineraldensity and periodontitis in postmenopausal women.JPeriodontol 2000: 71: 1492–98.
15. Watts NB. Fundamentals and pitfalls of bone densitometry using dual-energy X-ray absorptiometry (DXA).Osteoporos Int 2004;15: 847–854.
16. Jeffcoat MK. Osteoporosis:A possible modifying factor in oral bone loss. J. Periodontol Annals.1998; 3 : 312 -21.
17. Krall EA. The Periodontal-Systemic Connection: Implications for Treatment of Patients with Osteoporosis and Periodontal Disease.Ann periodontol 2001;6:209-213.
18. Kemmler W, Engelke K, Lauber D, Weineck J, Hensen J,Kalender WA. Exercise effects on fitness and bonemineral density in early

postmenopausal women: 1-yearEFOPS results. Med Sci Sports Exerc 2002; 34: 2115–2123.
19. Delmas PD, Rizzoli R, Cooper C, Reginster JY. Treatment of patients with postmenopausal osteoporosis is worthwhile.The position of the International OsteoporosisFoundation. Osteoporos Int 2005; 16: 1–5.
20. Manolagas SC. Birth and death of bone cells: basic regulator mechanisms and implications for the pathogenesis and treatment of osteoporosis. Endocr Rev 2000; 21: 115–137.
21. Lees B, Stevenson JC. The prevention of osteoporosisusing sequential low-dose hormone replacement therapy with estradiol-17 beta and dydrogesterone. Osteoporos Int 2001; 12: 251–258.
22. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ,Kooperberg C, Stefanick ML, Jackson RD, BeresfordSA, Howard BV, Johnson KC, Kotchen JM, Ockene J,Writing Group for the Women's Health Initiative I. Risksand benefits of estrogen plus progestin in healthy postmenopausalwomen: principal results From the Women'sHealth Initiative randomized controlled trial. J Am MedAssoc 2002; 288: 321–333.
23. Yates J, Barrett-Connor E, Barlas S, Chen YT, Miller PD, Siris ES. Rapid loss of hip fracture protection after estrogen cessation: evidence from the National Osteoporosis Risk Assessment. Obstet Gynecol 2004: 103: 440–446.
24. Riggs BL, Hartmann LC. Selective estrogen-receptor modulators – mechanisms of action and application to clinical practice [erratum appears in N Engl J Med 2003: 348: 1192]. N Engl J Med 2003: 348: 618–629.
25. Tenenbaum HC, Shelemey A, GirardB, ZoharR, FritzPC. Bisphosphonates and Periodontics : Potential applications for regulation of bone mass in the periodontium J. Periodontol2002; 7:813-22.
26. Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Osteonecrosisof the jaws associated with the use of bisphosphonates: a review of 63 cases. J Oral Maxillofac Surg2004; 62: 527–534.
27. Greenberg MS. Intravenous bisphosphonates and osteonecrosis.Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004; 98: 259–260.
28. Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. J Oral Maxillofac Surg 2005; 63: 1567–1575.
29. Chesnut CH, Silverman *S,* Andriano K. A randomised trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis. PROOF Study Group. Am J Med.2000; 109: 267-76.