

Research Article

The Contribution of Hormone Replacement Therapy in Postmenopausal Women to Prevent Periodontal Disease

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Abstract

Aim: We investigated the possible association of hormone replacement therapy (HRT) administration and periodontitis in postmenopausal women by testing of systematic inflammatory parameters.

Participants and Methods: 169 postmenopausal women participated in a prospective clinical study. They were divided into two groups: Group HRT (n=69) received HRT and Group no-HRT (n=100) did not receive HRT, but continued with body exercise and daily suitable natural food diet. We measured in the serum: Interleukin-1a (IL-1a); Interleukin-1b (IL-1b); Interleukin-6 (IL-6); Tumor necrosis factor (TNF- α); C-reactive protein of serum (CRP); Alkaline phosphatase (ALP); and Activin A. We also examined: oropharyngeal cavity microbial cultures; use of periodontal probe; depth of

pocket; and bone mineral density.

Results: The laboratory analyses showed statistical significant decrease of TNF-a ($p<0.001$), IL-6 ($p<0.001$), IL-1a ($p<0.001$), IL-1b ($p<0.001$), alkaline phosphatase ($p<0.001$) and CRP ($p<0.001$) in Group HRT compared to no-HRT. Activin A was also reduced but not statistically significantly ($p=0.549$). Oropharyngeal cavity cultures were all negative in Group HRT.

Conclusion: We conclude that post-menopausal women after administration of HRT are protected of oral cavity health problems periodontitis and other local symptoms,

Keywords: Hormone Peplacement Therapy; Periodontitis; IL-1a; IL-1b; IL-6; TNF- α ; CRP; Activin A

Introduction

Menopause is the permanent interruption of the woman's period which occurs during the climacterium [1]. To be considered a woman in menopause, the menstruation should be interrupted for a period of 12 months without any obvious physiological or pathological cause being responsible for it [2,3]. Most women feel fear and anxiety about this condition. In the first 2-3 years during which the hormonal changes of menopause occur, most women may experience a variety of symptoms. The menopausal symptoms are mainly due to estrogen deficiency and occur in 80% of women [2,3].

Post-menopausal estrogen deficiencies or/and decreased bone density show, according to recent studies, that menopause is associated with increased rates of tooth loss (periodontal disease) [4]. The effect of periodontal disease has been reported to have aggravating effects on the oral cavity of women in menopause. During this time of her life the woman may notice changes in her mouth, such as dryness, intolerance, burning sensation or even pain [4]. There may be changes in taste, especially in salty, sour or spicy dishes. One can also notice a condition in which the gums appear dry, easily bleed and have a pale or very red tint. In addition, bone loss is associated with periodontal disease and osteoporosis [4].

In practice, alveolar bone loss is the strongest indicator of tooth loss in women with menopause. This bone loss is associated with a lack of estrogen after menopause [5]. Because periodontal disease is a "silent disease", many women do not realize that they have advanced disease until periodontitis reaches an advanced stage [4,5]. For this reason, at any stage of her life the woman must take measures to protect her oral health. Hormonal changes that occur during menopause are an important factor in the development of periodontal disease [6,7]. During this period and due to hormonal changes, women are more susceptible to various diseases of the oral cavity [6,7]. Periodontitis is an inflammatory disease of the supporting dental tissues caused by interactions between the microbial biofilm and the immuno-inflammatory response of the host, leading to bone resorption. The symptoms of periodontitis are the following: gum bleeding during brushing, red, swollen or sensitive gums, tooth mobility, persistent mouth odor or bad taste, gum recession or gum detachment from the teeth, pine between the tooth and gums creating large gaps, relaxing, shaking or change in tooth position, changes in tooth closure. The early diagnosis of osteoporosis is possible with diagnostic tools that measure the bone mineral density (BMD) [8,9].

According to the literature, the low bone mass in women with estrogen deficiency affects the density of the alveolar bone, and therefore, constitutes an important factor in the progression of periodontitis and fractures of the upper and lower jaw [9-12]. The postmenopausal women with low BMD are more likely to develop clinical attachment loss, gum recession and inflammation [9-12].

The mechanism of bone loss in these diseases is the local or general increase of bone resorption due to increased osteoclastic activity and local effects of cells and cytokines [9-12]. Hormone Replacement Therapy (HRT) is successful in preventing symptoms in post-menopausal women[9-12].

The purpose of this study was to investigate the possible association of HRT administration in postmenopausal women and subsequent osteoporosis and periodontitis by measuring systematic inflammatory parameters. Oropharyngeal cavity pathogenic bacteria cultures were also detected which are responsible for the occurrence of periodontitis.

Participants and Methods

Participants

We report the results of a prospective, double-blinded observational clinical study on post-menopausal women conducted from March 2015 to June 2019 in the Department of Obstetrics and Gynecology of Democritus University of Thrace, Greece.

The study protocol was approved by the institutional ethical committee (Reference number 249/21.03.2016). Written informed consent was obtained from every participant. Participants completed a confirmation of participation form containing demographic and other symptom characteristics. In case of side effects, a form was completed by the investigators describing adverse reactions and possible concomitant medication administered.

All participants ($n=169$) were post-menopausal for more than two years, free of other illness, with estrogen deficiency symptoms. Among the participants, 69 (Group HRT; age 51.8 ± 1.5 years) received HRT, while the other 100 women (Group no-HRT; 52.1 ± 1.8 years) did not receive HRT but continued with body exercise and daily suitable natural food diet. Inclusion criteria were: post-menopausal status, no other disease, intact uterus, normal cervical-vaginal smear and mammography findings.

In Group HRT, Tibolone 2.5 mg was administered daily. Tibolone is a synthetic steroid molecule which is, in essence, a progestogen whose metabolites have estrogenic, progestogenic and androgenic properties.

Protocol Description

Blood samples were also taken to determine the following parameters in serum: Interleukin-1a (IL-1a); Interleukin-1b (IL-1b); Interleukin-6 (IL-6); Tumor necrosis factor (TNF- α); C-reactive protein of serum (CRP); Alkaline phosphatase (ALP); and Activin A. The following parameters were measured in the participants of both groups: oropharyngeal cavity cultures; use of periodontal probe; depth of pocket and also in a limited number of study participants we performed

additionally BMD measurements.

Also, sampling in dental plaque for identification of the following periodontal pathogens was made: *Neisseria catrhallis*, *Bacteroides* spp, *Candida* spp, *Streptococcus* spp, *Lactobacilli* spp, (gram + bacteroides) *Streptococcus mitis*, *Enterococcus* spp, *Neisseria* spp, *Peptostreptococcus* spp, *Escherichia coli*, *Staphylococcus aureus*, *Bacteroides forsythus*, *Streptococcus orallis*, *Streptococcus tholaltensis*, *Fusobacterium* spp, *Haemophilus influenza*, *Enterococcus* spp, *Rothia mucilaginosa*, *Neisseria sicca*, *Porphyromonas gingivalis*, *Actinomycetes rothia*, *Enterobacter aeroganes*, *Propionibacterium*, *Corynebacteria*, *Actinobacillus*, *Actinomycetemcomitans*, *Bacteroides forsythus*, *Rothia dentocariosa*, *Corynebacteria*, *Facklamia*, *Streptococcus hominis*, *Tholaltensis*, *Porphyromonas* spp, *Neisseria elongate*, *Streptococcus gordonii*, *Streptococcus pneumonia*, *Streptococcus sanguinis*, *Haemophilus* and *Prevotella* spp.

Sampling was performed by a special dentist using a sterile scraper. 500 μ L of Phosphate Buffered Saline (PBS) x1 was placed on the scraper, under aseptic conditions, and a sample from the patient's oral cavity was taken in patients with periodontitis. The samples containing cells of dental plaque were transferred to the laboratory and stored at -20°C until analysis. The scraper with the 500 μ L PBS and the detached cells was transferred with a pipette to an Eppendorf tube and centrifuged for 10 min at 7500 rpm. Finally the clinical evaluation of periodontitis grade in oral cavity was performed by an experienced dentist based on gum clinical symptoms and also on measuring the depth of tooth pocket.

Statistical analyses

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 19.0 (IBM). The normality of quantitative variables was tested with Kolmogorov-Smirnov test. Alkaline phosphatase, TNF-a, activin A and IL-6 levels were expressed as mean value \pm standard deviation (SD), while CRP, IL-1a and IL-1b were expressed as median value and the interquartile range (25th to 75th percentile). To assess differences in demographic and clinical characteristics between participants of Group HRT and Group no-HRT, the Student's t-test and Mann-Whitney U test were used. Receiver operating characteristic (ROC) analysis was used to provide the ability of the laboratory parameters studied herein to classify subjects according to the use of HRT. The area under the ROC curve (AUC), sensitivity, specificity, positive and negative predictive values were calculated, while Cohen's kappa was used to assess agreement. The optimal cutoff values were derived according to Youden Index. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by means of logistic regression analysis as the measure of association of participants' classification according to the laboratory parameters with the initial HRT classification (use of HRT or no-use of HRT). All tests were two tailed and statistical significance was considered for p-values <0.05.

Results

No statistically significant differences were found in the demographic (age) and clinical characteristics of participants of Group HRT and Group no-HRT. Statistically significantly higher values ($p < 0.001$) were observed for all parameters (except Activin A) measured in serum in Group no-HRT compared to Group HRT participants, i.e., IL-1a (higher by 43.2%), IL-1b (higher by 245.3%), TNF-a (higher by 643.9%), IL-6 (higher by 205.6%), CRP (higher by 183.3%), and alkaline phosphatase (higher by 30.6%) (Table 1). Activin A levels were very slightly higher in Group no-HRT ($p = 0.541$)

(Table 1).

	HRT	no-HRT	Difference (%)	P value
ALP, U/L	44.51 ± 11.58	58.15 ± 19.24	+30.6	<0.001
CRP, mg/Dl	0.30 (0.21 - 0.58)	0.85 (0.25 - 3.75)	+183.3	<0.001
TNF-a, pg/mL	10.28 ± 2.69	76.47 ± 19.58	+643.9	<0.001
IL-1α, pg/mL	1.76 (1.25 - 2.52)	2.52 (1.66 - 3.17)	+43.2	<0.001
IL-1β, pg/mL	1.79 (1.27 - 2.20)	6.18 (5.97 - 6.45)	+245.3	<0.001
Activin A, pg/mL	135.42 ± 13.50	137.00 ± 20.01	+1.2	0.541
IL-6, pg/mL	8.73 ± 4.31	26.68 ± 6.75	+205.6	<0.001

ALP, TNF-a, Activin A and IL-6 were expressed as mean ± SD; CRP, IL-1α and IL-1β were expressed as median (25th – 75th percentile)

Table 1: Measurements of laboratory parameters in relation to the use of HRT

Table 2 presents the area under the ROC curve (AUC) for all the above laboratory parameters, which was calculated for the evaluation of their ability to discriminate the use of HRT. This analysis showed statistically significantly lower levels of TNF-a (AUC=1.000; p<0.001), IL-6 (AUC=0.998; 95% CI=0.996 – 1.000; p<0.001) and IL-1b (AUC=0.986; 95% CI=0.957 – 1.000; p<0.001) in Group HRT. Three more parameters, alkaline phosphatase (AUC=0.732; 95% CI=0.658 – 0.807; p<0.001), CRP (AUC=0.702; 95% CI=0.624 – 0.779; p<0.001) and IL-1a (AUC=0.681; 95% CI=0.602 – 0.761; p<0.001) had AUC close to 0.700, which indicates a high discrimination significance of lower levels in Group HRT. Inferior results, statistically non-significant, were obtained for activin A levels (AUC=0.527; 95% CI=0.440 – 0.614; p=0.549).

ROC analysis was also used to determine cut-off points for all laboratory parameters in order to classify participants according to the use of HRT (Table 2). In particular, the optimal cut-off point of 23.8 pg/mL for TNF-a yielded perfect sensitivity (100%), specificity (100%), positive and negative predictive values (100%). Moreover, the optimal cut-off points of 16.85 pg/mL for IL-6 and of 4.29 pg/mL for IL-1b yielded very high sensitivities (IL-6: 97%; IL-1b: 100%) and specificities (IL-6: 98.6%; IL-1b: 98.6%), as well as very high positive (IL-6: 99%; IL-1b: 99%) and negative (IL-6: 95.8%; IL-1b: 100%) predictive values. The cut-offs for the other three laboratory parameters (alkaline phosphatase, CRP and IL-1a) yielded substantial sensitivities (38% to 49%) and high specificities (87% to 97.1%).

The overall agreement of participants' classification according to TNF-a, IL-6 and IL-1b with the initial HRT classification (use of HRT or no-use of HRT) was 100% for TNF-a, 97.6% for IL-6 and 99.4% for IL-1b, while Cohen's kappa coefficient indicated excellent agreement for TNF-a (kappa = 1.000, p<0.001), IL-6 (kappa = 0.951, p<0.001) and IL-1b (kappa = 0.988, p<0.001). Substantial overall agreement for the other three laboratory parameters (alkaline phosphatase, CRP and IL-1a) was noticed (ranging from 59.2% to 68.6%), with kappa values ranging from 0.248 to 0.415

(all p<0.001) (Table 2).

	ALP	CRP	TNF-a	IL-1a	IL-1b	IL-6	Activin A
AUC	0.732	0.702	1.000	0.681	0.986	0.998	0.527
95% C.I.	0.658 – 0.807	0.624 – 0.779	1.000 – 1.000	0.602 – 0.761	0.957 – 1.000	0.996 – 1.000	0.440 – 0.614
P value for AUC	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.549
Cut-off	≥55.5 U/L	≥1.05 mg/Dl	≥23.8 pg/mL	≥2.945 pg/mL	≥4.29 pg/mL	≥16.85 pg/mL	≥149.5 pg/mL
Sensitivity (%)	47.0 (37.0-57.2)	49.0 (38.9-59.1)	100.0 (95.4-100.0)	38.0 (28.6-48.3)	100.0 (95.4-100.0)	97.0 (90.8-99.2)	29.0 (20.6-39.1)
Specificity (%)	87.0 (76.2-93.5)	97.1 (89.0-99.5)	100.0 (93.4-100.0)	89.9 (79.6-95.5)	98.6 (91.1-99.9)	98.6 (91.1-99.9)	91.3 (81.4-96.4)
PPV (%)	83.9 (71.2-92.0)	96.1 (85.4-99.3)	100.0 (95.4-100.0)	84.4 (69.9-93.0)	99.0 (93.8-99.9)	99.0 (93.6-99.9)	82.9 (65.7-92.8)
NPV (%)	53.1 (43.5-62.5)	56.8 (47.3-65.7)	100.0 (93.4-100.0)	50.0 (40.9-59.1)	100.0 (93.3-100.0)	95.8 (87.3-98.9)	47.0 (38.4-55.8)
Overall agreement (%)	63.3	68.6	100.0	59.2	99.4	97.6	54.5
Cohen's kappa	0.309	0.415	1.000	0.248	0.988	0.951	0.177
P value for kappa	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.001
OR (95% C.I.)	5.91 (2.65-13.20)	32.19 (7.47-138.60)	n.a.	5.43 (2.25-13.08)	101.91 (14.37-710.07)	n.a.	4.29 (1.67-11.00)

AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; OR, odds ratio.

Table 2: Results of ROC analysis for the evaluation of ability of ALP, CRP and TNF-a to discriminate HRT and non-HRT participants

Regarding the participant oropharyngeal cavity culture sampling, in the Group no-HRT abnormal findings were found, mainly gram-anaerobic bacteria, such as Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans and Bacteroides forsythus, while in Group HRT the oropharyngeal flora was normal.

Using the periodontal probe measurements, toothpick depth of more than 0.4 mm was noticed in Group no-HRT, while in Group HRT this parameter was less than 0.4 mm (normal value).

Discussion

Frequent menopausal vasomotor symptoms, including night sweats and hot flushes, persist in more than half of women for more than five years. After consideration with the responsible gynecologist, the recommended therapy modus is HRT. HRT is an effective treatment for typical menopause-related symptoms, and so, it presents research interest [13,14].

Continuous combination therapy is used to increase tolerance, minimize hemorrhage, or establish complete amenorrhea. There is no general agreement on the duration of treatment. Some claim that it should be applied until the symptoms have subsided. The menopausal woman has an increased rate of bone loss due to a negative bone balance, a misalignment of osteoclastic and osteoblastic activity, and therefore, an increased risk of osteoporotic fracture. During the menopausal period, due to the drastic reduction of estrogen, gingivitis, dry mouth, burning sensation in the mouth or taste alteration are observed. Often, they report that their gums bleed easily or that they have a pale or bright red color. All of the above symptoms are related to the so-called menopausal ulostomatitis, which subside as soon as the women starts taking HRT [15,16].

Regarding the relationship between menopause and periodontitis, it should be mentioned that in some women osteoporosis begins along with menopause. Osteoporosis is also likely to affect the bones of the jaws, resulting in loss of bone support in the teeth, and over time some teeth may become motile or begin to migrate and even disappear. Systematic loss of bone density due to osteoporosis provides a host system with high sensitivity to periodontal tissue infections, local increase in cytokines, inflammatory mediators leading to local response of periodontal connective tissue, responsive retinal detachment, and other infections. HRT formulations inhibit bone-induced bone resorption by osteoclasts [17,18].

The above action is due to estrogen-induced growth factor and cytokines mobilization. Estrogens also regulate the movement of calcium ions within the renal infiltration by increasing absorption and limiting excretion [19-22]. Estrogens also suppress the age-related increased production of parathormone in post-menopausal women. Estrogens reduce the risk of fractures to a greater degree than expected based on reduced bone density. Regarding progesterone, its action ranges between enhancing the above action of estrogen and the absence of any effect [19-22]. Estrogens also suppress the age-related increased production of parathormone in postmenopausal women. Estrogens reduce the risk of fractures to a greater degree than expected based on reduced bone density [19-22].

Careful examination of the periodontium (gums) and proper oral hygiene are crucial parameters for menopausal women. Because prevention is the best ally of health in general and oral health in particular, it is best for women to have regular dental checkups by their dentist [19-22].

Periodontitis is one of the most common diseases and about 95-100% of the human population is affected by some form of it, according to life expectancy. Gram-anaerobic bacteria are the main causative agents of periodontal disease and among them, *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans* and *Bacteroides forsythus* are hypothesized to be the main pathogenic bacteria. We confirm these also in our study in Group no-HRT [19-22].

Estrogen deficiency increases osteoclastogenesis by activating the production of macrophage colony stimulation factor by investment of osteomyelic cells, which is controlled by IL-1 and TNF- α (23). IL-1 levels, which are a potent activator of osteoclastic bone resorption, are increased in estrogen deficiency through increased IL-1 production and inhibition of the IL-1 receptor antagonist (IL-1ra) [23]. In the present study, IL-1a and IL-1b in the serum were at statistically significantly

higher levels in Group no-HRT.

The loss of alveolar bone and the systematic reduction of BMD in adult mice with oophorectomy were accompanied by increased activity of gum collagenase. Interestingly, the severity of both osteoporosis and bone destruction decreased with non-antimicrobial, chemically modified tetracycline in mice [24,25].

In addition, IL-6, a potent mediator of inflammation, seems to be involved in the pathogenesis of both periodontitis and osteoporosis due to increased age-related IL-6 levels [26]. However, Keller et al. [26] showed that the differentiation of IL-6 levels is not the key mechanism by which estrogen deficiency coordinates bone loss. Serum IL-6 levels were tested as a prognostic indicator of bone loss in a study of 137 postmenopausal German women [27]. Epidemiological data suggest that serum IL-6 levels were a prognostic indicator of bone loss in the femur in postmenopausal women, but the prognosis was limited to the first 10 years after menopause [27].

The onset and progression of periodontal disease may be affected by the increased sensitivity of the host to the infectious challenge (28). It is biologically possible that part of the periodontal damage is affected by generalized bone loss. We also confirm the above-mentioned results concerning IL-6 based on the comparison of our two groups of participants [29-31].

Bone mass and endurance decrease in menopause due to increased bone resorption activation and decreased osteoblast ability to produce bone. Recent data support the key role of estrogen in controlling bone resorption through estrogen receptors ER α and ER β in the cytoplasm of osteoblasts and osteoclasts. These receptors limit the pathway of osteoclast activation by osteoblasts, reduce the formation of osteoclasts by their precursors, and inhibit the osteoclastic action of osteoclasts [29-31]. In addition, estrogen can control the function of prostaglandin E2, which is a potent stimulant of bone resorption and osteoclast formation by inhibiting cytokines that stimulate cyclooxygenase-2. Although estrogen deficiency increases the expression of IL-1 and TNF- α , attempts to correlate serum levels of these cytokines with osteoporosis have resulted in conflicting results [29-31].

According to our results, the symptoms of participants in the oral cavity were reduced and disappeared completely at the 2nd follow up, 6 months after the beginning of HRT administration. The tolerability of this regimen was also excellent. No serious side effects were observed in any participant.

Our results agree with recent studies which found that HRT has favorable efficacy, safety profile and long-term health benefits. On the other hand, there are studies in which the use of HRT was not associated with a significant positive effect on gingiva and oral cavity. The-inflammatory parameters IL-1a, IL-1b, TNF-a, IL-6, CRP, ALP in Group no-HRT were statistically elevated compared to Group HRT. A possible explanation is the pathological association between sexual steroid hormone—deficiency in menopause period with subsequent improving osteoporosis and beginning local inflammation in mouth cavity and gum area. This is confirmed by Golub [25] who proposed a "two-stroke" model that links osteoporosis, among other systemic diseases, to loss of alveolar bone. Periodontal germs provide the first "hit" in the sequence of destructive events of periodontitis and the second "impact" comes from the systemic inflammatory response

caused by various pathological disorders. Even a small increase in serum IL-1, IL-6, and TNF- α levels may trigger the cytokine-prostaglandin-metalloproteinase binder axis of the RANKL B-factor activator receptor in periodontal tissues [25].

The Activin A levels were similar in the two groups. This finding is associated to post-menopausal status in all study participants due to ovary function inactivity. Also, when there is an infection with Gram-negative microbes, estrogen deficiency has been reported to have a synergistic effect on bone metabolism with lipopolysaccharides, leading to increased bone resorption in female mice [32-35]. While in Group HRT the oropharyngeal cultures were normal, in Group no-HRT pathological findings were found in most participants based on destruction of periodontal tissue due to menopause hormone reduction.

Recent research suggests that periodontal condition is associated with osteoporosis, nationality, the depth of the follicle, sex, CRP and levels of *Parvimonas micra*, *Prevotella intermedia*, *Tannerella forsythia*, and *Streptococcus mutans* [36-38]. In addition, in an animal study, increased expression of IL-6, NF- κ B, ALP and bone osteocalcin suggests a potential role for these molecules in the pathogenesis of osteoporosis [36-38].

Hormone replacement therapy is often used to prevent bone loss as well as other signs and symptoms in women with osteoporosis. Additional estrogen therapy has been associated with reduced urinary bleeding in relation to a control group [36-38] and has been shown to be beneficial in preventing tooth loss, although not without risk for other systemic disorders [36-38].

The effect of estrogen on alterations in the alveolar bone was examined in a one-year study in which estrogenically adequate postmenopausal women showed BMD gain in the alveolar bone, while estrogenically deficient women showed loss [40-41]. Estrogen replacement therapy has also been linked to decreased gingivitis and a reduced incidence of clinical adhesion loss in early menopausal osteoporotic women [40-41] as well as increased density of the alveolar bone and improved dental health [40-41]. Finally, Hildebolt et al. in 2004 [42] reported that osteoporotic women treated with estrogen and/or calcium and vitamin D showed a significant increase in jaw bone density, which was higher during the first 3 years in a five-year treatment period.

Taguchi et al. [41,43] reported that the density in the lumbar spine correlated with the density of the mandibular cortex in early menopause and with the density of both the cortex and cancellous bone in later menopause. Estrogen deficiency had a higher frequency of sites with a net loss of alveolar bone density at follow-up. Furthermore, estrogen-deficient women undergoing supportive periodontal therapy following treatment of moderate to severe periodontitis had three times more sites of losing more than 0.4 mm of interproximal alveolar bone height.

According to Cummings et al., who support the above view, BDM in the proximal femur determines the risk of fracture in the hip joint better than measurements in other anatomical positions, such as the forearm or spine. Bone mineral density (BD) is closely related to bone strength and because bone strength is a determining factor in vulnerability to fracture in a

particular traumatic violence, it implies that BMD is also associated with fracture risk. The relative risk of fracture is increased by a factor of 1.5-3 or more for each standard deviation of BMD reduction, depending on the location of the measurement and the technique used.

Although the effectiveness of combining BMD measurements in various anatomical positions has not yet been adequately demonstrated, population measurements immediately after menopause in the spine, hip joint, or wrist appear to be good indicators of fracture risk for any anatomical position. The choice of location for the measurement, therefore, depends on the clinical assessment. Clinical examination and history have an important role in the diagnosis and differential diagnosis of the diseases that cause a decrease in bone mass.

Osteoclast activity inhibitors are:

The classic action of estrogens involves their binding to specific receptors on the cytoplasm, the hormone-receptor complex migrating to the nucleus of the target cell, where it binds to specific sites in DNA (genetic action). It is possible that non-genomic actions have a complementary effect to genomic actions, and in some cases, lead to DNA transcription. It is the most popular type of treatment in the pre- and post-menopausal period. A similar type is combination therapy without a break. The cyclical addition of progestogen usually results in escape bleeding that occurs either during the progesterone phase or after both types of treatment resulting in premenopausal women with a steady menstrual cycle not resisting this effect. In addition, women with abnormal cycles benefit from the fact that progesterone normalizes unwanted abnormal cycles. In contrast, many women who start HRT a few years after menopause consider the return of menstruation as a treatment for the disadvantage and discontinuity.

Conclusions

We conclude that post-menopausal women who received HRT present lower systematic inflammatory parameters, associate to better oral cavity health and low risk of hygiene periodontitis. HRT appears to have a positive effect on the jaws, suggesting that the alveolar bone may be prone to periodontitis.

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