Effect of hormone replacement therapy (HRT) on periodontal status of postmenopausal women

Giuseppe Pizzo1, Rosario Guiglia1, Maria E. Licata1, Ignazio Pizzo1, Joan M. Davis2, Giovanna Giuliana4

1 Section of Oral Sciences, University of Palermo, Palermo, Italy
2 Department of Dental Hygiene, College of Applied Sciences and Arts, Southern Illinois University, Carbondale, IL, U.S.A.

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Summary

Background: The risks/benefits balance of hormone replacement therapy (HRT) is controversial. The aim of this study was to assess the periodontal status of a postmenopausal women group receiving HRT and to determine the effects of HRT on clinical measures of periodontal disease.

Material/Methods: Ninety-one postmenopausal women, 52 taking HRT (HRT+) and 39 not taking HRT (HRT–), completed the study. Clinical parameters measured included visible supragingival plaque, probing pocket depth (PD) and clinical attachment level (CAL). Gingival status was recorded as gingival bleeding on probing (BOP). Previous oral contraceptive use and current and past smoking status were also assessed.

Results: Data indicated that PD and CAL were not significantly different between HRT+ patients and HRT– patients (P=0.8067 and P=0.1627, respectively). The HRT+ group exhibited significantly lower visible plaque levels compared to the control group (P<0.0001). The percentage of gingival sites with positive BOP was significantly lower in the HRT+ group compared to the HRT– group (34.85% vs. 65.15%; P=0.0007). Plaque accumulation was also tested in ANCOVA as a possible explanatory variable for the differences observed in gingival bleeding. The ANCOVA showed no significant differences in gingival bleeding between HRT+ and HRT– women (P=0.4677). No significant differences in past smoking status and oral contraceptive use were detected between HRT+ and HRT– women (P=0.9999 and P=0.0845, respectively).

Conclusions: These findings indicated that long-term HRT was not associated with relevant effects on periodontal status and clinical measures of periodontal disease, thus suggesting that HRT may not confer protection against periodontitis in postmenopausal women.

key words: hormone replacement therapy • postmenopause • periodontitis • gingivitis • female

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Author’s address: Giuseppe Pizzo, Section of Oral Sciences, Università di Palermo, Via del Vespro 129, 90127 Palermo, Italy, e-mail: giuseppepizzo@unipa.it
**Background**

Chronic periodontitis is an inflammatory disease initiated by microbial pathogens that elicit a host immune response with subsequent loss of connective tissue attachment and supporting alveolar bone [1]. Although bacteria are the causal agents of periodontitis, individual susceptibility to disease may be influenced by systemic factors [2]. Recently, estrogen deficiency has received increasing attention in relation to susceptibility to chronic periodontitis in postmenopausal women [3,4]. The production of estrogens changes drastically at menopause, leading to osteoporosis in skeletal bones, characterized by the loss of bone mass and reduction of bone density, and with a consequent increase in bone fragility and susceptibility to fracture [5]. Total skeletal mass reduction in postmenopausal women may include the mandible [6–9].

A number of studies have shown that bone changes in osteoporosis are associated with loss of periodontal attachment, loss of teeth, and height of residual ridge [10–15]. Based on these findings, it has been hypothesized that osteoporosis may be a risk factor for the progression of periodontitis. Both osteoporosis and periodontitis, in fact, are bone resorptive diseases sharing common etiologic agents/risk factor (e.g., sex, cigarette smoking, alcohol consumption, systemic diseases, heredity) that may either affect or modulate the process of both diseases [3,5].

In the past decade HRT was recognized as an effective treatment of menopausal signs and symptoms [16–19]. This therapy leads to a reduction of bone mass loss, and therefore has a significant role in the primary and secondary prevention of postmenopausal osteoporosis [20–22]. It has also been suggested that HRT may be beneficial in optimizing periodontal status in postmenopausal women [23,24]. Some clinical studies showed that HRT had a positive effect on alveolar bone density and tooth retention [11,25–29]. Similarly, estrogen administration in rats was found to prevent alveolar bone loss resulting from an estrogen-deficient state [30,31]. Periodontal health in postmenopausal women taking HRT, however, has been addressed only in a limited number of studies [23,32,33]. It has been reported that women treated with HRT exhibited lower gingival bleeding than estrogen deficient women [29,32], but conflicting results were found when the effects of HRT on attachment level and pocket depth were determined [23,32,33].

The aims of this cross-sectional study were to assess the periodontal status of a group of postmenopausal women receiving HRT, and to evaluate the association between HRT and clinical measures of periodontal disease including attachment level, pocket depth and gingival bleeding.

**Material and Methods**

**Study population**

A total of 91 Caucasian postmenopausal women, being at least 5 years past their last menstrual period (age range 50 to 62 years; mean age±SD: 55.12±3.81), volunteered to participate in this clinical study. The women enrolled in the study were selected from a pool of 195 subjects attending the Obstetrics and Gynecology Unit of the University of Palermo Medical Center (Palermo, Italy) on the basis of the following criteria: being dentate with at least 9 natural teeth in the posterior sites (with the exclusion of third molars); having no history of early menopause (ie, occurring before age 45 years); having no cancer or active or chronic parathyroid diseases; and having no pharmacological history of steroidal or non-steroidal anti-inflammatory drug use or use of immunosuppressants. Subjects who were current smokers and those who had a surgically- or chemically-induced menopause were not enrolled in the study. Moreover, no woman included in the study had received periodontal therapy and/or used antimicrobial mouthrinses in the preceding 6 months.

Previous oral contraceptive use and past smoking status were recorded. Screening and selection of volunteers were carried out by a single investigator who explained the study and obtained witnessed and signed consent to participate. The study was performed between October 2005 and September 2008 at the Department of Oral Sciences, University of Palermo. The study design was approved by the local Ethics Committee and was found to conform to the requirements of the “Declaration of Helsinki” as adopted by the 18th World Medical Assembly in 1964 and subsequently revised [34].

The subjects were divided into 2 groups on the basis of HRT use. Women who reported current HRT supplementation (n=52) for at least 5 years were assigned to the HRT+ group. The control group (HRT−) (n=39) consisted of the remaining women.

The mean age for both groups was similar, 55.67±3.36 (range 50–62 years) for HRT+ group, and 54.38±4.26 (range 50–62 years) for the control group. No significant differences in age were found between groups (P=0.1107).

**Oral examination**

Volunteers were given an oral examination performed by a single investigator. The following oral health variables were measured: Plaque Index (PI), recorded on 4 sites in each tooth (mesio-buccal, mid-buccal, disto-buccal, mid-lingual) [35]; Bleeding on Probing (BOP), recorded on 4 sites in each tooth (mesio-buccal, mid-buccal, disto-buccal, mid-lingual) [36]; Probing Depth (PD) and Clinical Attachment Level (CAL) recorded on 6 sites in each tooth (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual). PD was measured from the free gingival margin (MG) to the base of the pocket, for CAL assessment, according to Ramfjord’s technique, probing depth from the free gingival margin to the base of the pocket was measured; the distance from the gingival margin and the cemento-enamel junction (CEJ) was also recorded. The difference between the 2 obtained values indicated CAL [37]. The following considerations were observed when measuring CAL: 1) calculus that obscured the CEJ or interfered with the correct placement of the probe was removed with a curette; 2) when the margin of restoration was apical to the CEJ, the position of CEJ was estimated using adjacent landmarks and dental anatomy; 3) when the CEJ could not be estimated, the examiner excluded the site; 4) when the natural tooth was missing, the site was excluded; 5) partially erupted teeth and root tips were excluded.
Results

Mean PI, PD and CAL for both HRT+ and HRT– groups are shown in Table 1. Mean PI were significantly lower in HRT+ women than in HRT– women (P=0.0001). Conversely, no significant differences were found for PD and CAL between groups (P=0.8067 and P=0.1627, respectively). The percentage of gingival sites with positive BOP was significantly lower in the HRT+ group compared to the control group (34.85% vs. 65.15%; P=0.0007) (Table 1).

Plaque accumulation was tested in ANCOVA as a possible explanatory variable for the differences observed in gingival bleeding. The ANCOVA showed that this covariate was significantly different between groups (P=0.0001) (data not shown). After the effect adjustments, no significant differences in gingival bleeding were found between HRT+ and HRT– women (P=0.4677) (data not shown).

No significant differences in women who smoked and those who used oral contraceptives were detected between HRT+ and HRT– subjects (P=0.9999 and P=0.0845, respectively) (data not shown).

Discussion

The physiological changes associated with menopause can cause some women to experience uncomfortable symptoms such as hot flashes and night sweats, vaginal dryness and dyspareunia, disturbed sleep and irritability/depression [5,38]. Moreover, estrogen deficiency arising from menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease [5,38]. Moreover, estrogen deficiency arising from menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5]. Until recently, HRT was considered the single most effective treatment of menopause, in association with age-related factors, has been shown to increase the risk of developing cardiovascular disease, including coronary heart disease and stroke, colorectal cancer and osteoporosis [5].

HRT has also been associated with decreased levels of gingival bleeding [23,32]. It has been suggested that estrogen may have an inhibitory effect on gingival inflammation by inhibiting mediators (IL-1, TNF-a, IL-6, IL-8) and cellular mechanism of inflammation (PMN recruitment, lymphocyte activation) [54–57]. Similarly, estrogen supplementation may modulate the rate of breakdown of periodontal tissue through a mechanism involving down-regulation of matrix metalloproteinases (MMP-8 and MMP-13) and cytokines involved in bone resorption [45,57–59]. Conflicting results exist on the effects of HRT on probing pocket depth and attachment level [23,32,33]. Furthermore, the risk of tooth loss was found to be lower in women who used HRT...
than those who did not [26,29,52,60,61]. Tooth loss, however, could not be used as a surrogate evaluation for periodontal disease, since reasons for tooth loss could include caries or trauma. Moreover, the extent of periodontal destruction around the remaining teeth was not taken into account in this analysis.

The aim of this study was to evaluate the periodontal status of postmenopausal women and to determine the effect of HRT on standard clinical measurements of periodontal disease. In the present study, HRT+ women had lower inflammatory gingival scores than HRT- women, as indicated by the lower percentage of bleeding sites (P=0.0007). The level of supragingival plaque accumulation was found to be significantly lower in HRT+ women than in HRT– women (P<0.0001). To account for factors that are known to be associated with gingivitis, it was of great importance to adjust for the difference in plaque level in the final analysis between groups. The findings of initial statistical analysis were not confirmed after correcting for plaque accumulation by those women on HRT having less gingival bleeding (ANCOVA, P=0.4677). Women taking HRT had fewer bleeding sites than did HRT– women, but this finding may be related to the lower level of supragingival plaque than to the effect of HRT. These results are in contrast with previous reports linking the use of HRT with the reduction of bleeding sites [23,32]. In those studies, the percent of gingival sites with bleeding was significantly lower in HRT+ women compared to HRT– women, despite the levels of plaque accumulation.

The results of the present study showed no detectable differences in CAL between groups. CAL is an important measure of periodontitis progression because of its relationship with alveolar bone loss. Due to the known beneficial effects of HRT on osteoporosis, it may be expected to significantly lower values for CAL in the HRT+ group. Ronderos et al. [24] found the mean CAL differences observed between postmenopausal females who reported the use of estrogen supplementation for more than 5 years and those who never used estrogens were significant, although quite small (1.74 vs. 1.56) [24]. Other previous studies reported lower values of CAL in women using HRT, but the difference found between HRT+ and HRT– patients was not significant [23,32].

In the present study, no significant difference was detected in the mean PD between the 2 groups of women. This finding is in agreement with previous studies [23,32], with the exception of the study by Lopez Marcos et al. [33], who evaluated the differences in PD values between HRT+ and HRT– groups at the beginning of the therapy and then re-evaluated over 6 months to 1 year after the beginning of the HRT. Lopez Marcos et al. [33] reported the PD variable for patients not receiving HRT evolved to worse stages, whereas patients receiving HRT showed a significant improvement in PD. It must be noted, however, that these results cannot be compared with those of the present study because of the different study designs. Moreover, in the study of Lopez Marcos et al. [33], CAL was not assessed and other clinical measures of periodontitis (dental pain of periodontal origin, gingival recessions) did not show significant improvement in the HRT+ group. Thus, the decrease of PD values in patients receiving HRT could be related to the reduction of gingival inflammation due to the estrogen action rather than to an effective gain of attachment [33].

**Conclusions**

The findings of the present study indicate that, in postmenopausal women, long-term HRT was not associated with significant effects on periodontal status and clinical measures of periodontitis, thus suggesting that HRT may not confer protection against periodontitis. Periodontitis may be primarily related to the presence of plaque and to a lesser extent to hormonal changes such as estrogen deficiency. However, the possibility exists that the decreased estrogen levels associated with the postmenopausal period may contribute to the progression of periodontal disease by affecting the oral bone mass [3,10–12,15,23,28,50]. Thus, postmenopausal women with periodontal disease should undergo periodontal examinations in order to detect changes in their periodontal status and support them with periodontal treatment.

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