Evaluation of Periodontal Response to Nonsurgical Therapy in Pre- and Post-menopausal Women with Periodontitis

Abstract
Context: The influence of sex steroid hormones on periodontium can be lowered with good plaque control. Aims: The aim of the present study was to evaluate periodontal status in pre- and post-menopausal women with periodontitis following nonsurgical therapy.
Settings and Design: Interventional pre–post clinical trial. Subjects and Methods: Periodontal status was measured by periodontal index (PRI), and oral hygiene status was measured by plaque index (PI). Both the parameters were measured at baseline, i.e., before scaling and root planing and after 3 months intervals posttreatment. Statistical Analysis Used: IBM SPSS version 21.
Results: The mean PRI scores in premenopausal group were $5.68 \pm 0.64$ and $2.53 \pm 0.13$ and PI scores were $1.84 \pm 0.17$ and $0.91 \pm 0.13$, respectively, at baseline and 3 months. The mean PRI scores in postmenopausal group were $6.08 \pm 0.47$ and $2.54 \pm 0.12$ and PI scores were $1.86 \pm 0.25$ and $1.00 \pm 0.24$, respectively, at baseline and 3 months. Conclusions: There was more desirable response to nonsurgical periodontal therapy in both the groups but not much variation in between two groups.

Keywords: Inflammation, menopause, nonsurgical therapy, periodontitis, plaque

Introduction
Endocrine system is very complex and plays an important role in promoting periodontitis (PD), which is characterized by inflammation of the supporting tissues of the teeth, including the gingiva, alveolar bone, and periodontal ligament. PD is a chronic inflammatory process that occurs in response to a predominantly Gram-negative bacterial infection originating in dental plaque.[1] Periodontitis leads to progressive and irreversible loss of bone and periodontal ligament attachment, as inflammation extends from the gingiva into adjacent bone and ligament. Signs and symptoms of progressing periodontitis include red, swollen gums that may appear to have pulled away from the teeth, persistent bad breath, pus between the teeth and gums, and loose or separating teeth.[2] Menopause archetypically occurs in the fifth decade of life in women.[3] Menopause in women is a physiological state that gives rise to adaptive changes at both the systemic and oral level. Menopause literally means “without estrogen” and by definition, it is the time at which cyclic ovarian function, as manifested by menstruation ceases.[4] The oral alterations noted at menopause are frequently related to hormonal changes although physiological aging of the oral tissues also plays a contributing role.[5] Gingival epithelium becomes thinner and more prone to inflammatory changes during menopause.[6] At the same time, salivary flow rate and composition may also be altered and contribute to the development of several oral conditions.[7] Sudden decrease in estrogen production during menopause stage is the main cause of primary osteoporosis, which also affects jawbones.[8] It has been suggested that this reduction in bone mineral density could contribute to periodontal disease progression.[9] In conjunction with its effect on bone, estrogen also interferes with other periodontal tissues (gingiva and periodontal ligament) and influences host immune-inflammatory responses.[10] In this study among pre and postmenopausal women, scrutiny was directed to what was influencing periodontal treatment.

Subjects and Methods
This interventional pre–post clinical trial was carried out in the outpatient Department of Periodontology. The study sample
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within group I. The mean PRI levels have reduced from 5.68 ± 0.64 at baseline to 2.53 ± 0.13 at 3 months after treatment. The mean PI levels have reduced from 1.84 ± 0.17 at baseline to 0.91 ± 0.13 at 3 months after treatment. There is statistically significant difference between baseline and 3 months posttreatment for all the parameters (P < 0.001) [Table 1].

There was also a statistically significant reduction in the mean values of all the parameters from baseline to 3 months within Group II. The mean PRI levels have reduced from 6.08 ± 0.46 at baseline to 2.55 ± 0.12 at 3 months after treatment. The mean PI levels have reduced from 1.86 ± 0.24 at baseline to 1.00 ± 0.24 at 3 months after treatment. There is statistically significant difference between baseline and 3 months posttreatment for all the parameters (P < 0.001) [Table 2].

The inter group comparison of these values from baseline to 3 months has shown no significant difference [Table 3 and Chart 1].

### Discussion

Periodontal disease is initiated by microbial pathogens that elicit a host immune response with subsequent tissue destruction of the periodontal structures, including breakdown of alveolar bone.[2] Although bacteria are a necessary factor in the equation, the reaction of the host’s immunoinflammatory system is responsible for most of the destruction found in periodontal disease. Thus, it makes sense that a

### Table 1: Comparison of periodontal parameters within Group I (premenopausal group)

| Parameter          | Group I (premenopausal group) | Group II (postmenopausal group) | Mean Difference (95% CI) |
|--------------------|-------------------------------|---------------------------------|--------------------------|
| Periodontal index  | Baseline 30 5.68±0.64          | 3 months 30 2.53±0.13           | t 26.91 df 29 P <0.001*  |
| Plaque index       | Baseline 30 1.84±0.17          | 3 months 30 0.91±0.13           | t 32.20 df 29 P <0.001*  |
| SD=Standard deviation, CI=Confidence interval, * is significant

### Table 2: Comparison of periodontal parameters within Group II (postmenopausal group)

| Parameter          | Group I (premenopausal group) | Group II (postmenopausal group) | Mean Difference (95% CI) |
|--------------------|-------------------------------|---------------------------------|--------------------------|
| Periodontal index  | Baseline 30 6.08±0.46          | 3 months 30 2.55±0.12           | t 42.29 df 29 P <0.001*  |
| Plaque index       | Baseline 30 1.86±0.24          | 3 months 30 1.00±0.24           | t 16.55 df 29 P <0.001*  |
| SD=Standard deviation, CI=Confidence interval, * is significant

### Results

There was statistically significant reduction in the mean values of all the parameters from baseline to 3 months intervals.

### Inclusion criteria

- Patients aged between 40 and 60 years, and suffering from chronic moderate periodontitis (≥4 mm pocket depth or ≥3 mm loss of attachment) were selected for the study
- Patients should have at least 15 natural teeth remaining
- Nonsmokers
- Systemically healthy from the past 6 months.

### Exclusion criteria

- Present or past smokers
- Below 40 years of age
- With gross oral pathology or tumors
- Patients on long-term steroid medication
- Pregnant women or planning for pregnancy
- Those who have received periodontal therapy in the preceding 6 months
- Those that are under medication in the preceding 6 months
- Any systemic disorders or any medication that affects the periodontal status.

Periodontal parameters such as periodontal index (PRI) (Russell’s 1956),[1] and plaque index (Silness and Loe 1964)[2] were measured and included in this study. All these parameters were measured at base line, i.e., before scaling and root planing and at 3 months intervals.

### Statistical analysis

Statistical analysis was performed using IBM SPSS version 21 software (Armonk, NY: IBM corp). Intergroup comparison and percentage decrement was done using independent sample t-test and intra group comparison was done by paired t-test. The value of P < 0.05 is considered as statistically significant.

### Inclusion and exclusion criteria are same for both groups.

- Group I–30 premenopausal women with chronic periodontitis
- Group II–30 postmenopausal women with chronic periodontitis.

### Patients aged between 40 and 60 years, and suffering from chronic moderate periodontitis (≥4 mm pocket depth or ≥3 mm loss of attachment) were selected for the study

### Patients should have at least 15 natural teeth remaining

### Nonsmokers

### Systemically healthy from the past 6 months.

### Periodontal parameters such as periodontal index (PRI) (Russell’s 1956), and plaque index (Silness and Loe 1964) were measured and included in this study. All these parameters were measured at base line, i.e., before scaling and root planing and at 3 months intervals.

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### There was statistically significant reduction in the mean values of all the parameters from baseline to 3 months intervals.
number of environmental and acquired factors may modify a patient’s risk of developing periodontal disease. Menopause triggers a wide range of changes in women’s body, and the oral cavity is also not an exception.[13] Estrogen deficiency, which systemically affects the sequence of bone resorption and formation, has received increasing attention in relation to the stability of alveolar bone structure in postmenopausal women.[14] With the estrogen deficiency at menopause, the anti-inflammatory effect of this hormone on the periodontium is lost and the periodontium gets compromised. Another sex hormone which also plays an important role in bone metabolism during the pre and post menopausal phase is progesterone. Effects of estrogen and progesterone function is different on different organ systems. Estrogen can influence the cyto differentiation of stratified squamous epithelium, synthesis and maintenance of fibrous collagen. In addition, estrogen receptors in osteoblast-like cells and receptors in periosteal fibroblasts provide a mechanism for direct action on bone as well as periodontal tissues.[15] These together affect the micro circulatory system by producing the following changes: swelling of endothelial cells and pericytes of the venules, adherence of granulocytes and platelets to vessel walls, formation of micro thrombi, disruption of the perivascular mast cells, increased vascular permeability, and vascular proliferation.[4] Steroid hormones have been shown to directly and indirectly exert influence on cellular proliferation, differentiation and growth in target tissues, including keratinocytes and fibroblasts in the gingiva.[16] Two theories were explained about the actions of hormones on the cells: (1) change of the effectiveness of the epithelial barrier to bacterial insult and (2) effect on collagen maintenance and repair.[17] These hormones have also been shown to increase the rate of folate metabolism in oral mucosa. Since folate is needed for, tissue maintenance, marked increase in metabolism can deplete folate stockpiles and affect tissue repair.[18] Estrogen is responsible for alterations in blood vessels of target tissues in females.[19] In contrast, progesterone has been shown to have little effect on the vasculature of systemic target tissues.[20] On the other hand, in gingiva and other nonperiodontal intraoral tissues, more evidence has accumulated for progesterone affecting the local vasculature than for estrogen. In addition, progesterone has been shown to reduce corpuscular flow rate, allowing for accumulation of inflammatory cells, increased vascular permeability, and proliferation.[21]

Menopause and the lack of ovarian steroids are known to promote important changes in connective tissue. The mechanisms involved in this influence are not completely understood, but it is thought to be related to the action of estradiol on the connective tissue.[22]

During menopause, estrogen deficiency is one of the most frequent causes of osteoporosis in women and a possible cause of bone loss and insufficient skeletal development in men. During bone growth, estrogen is needed for proper closure of epiphyseal growth plates both in females and in males. Estrogen deficiency leads to increased osteoclast formation and enhanced bone resorption. In menopause, estrogen deficiency induces cancellous as well as cortical bone loss.[23] These hormones may alter immunologic factors and responses, including antigen expression and presentation, and cytokine production, as well as the expression of apoptotic factors, and cell death.[24] Several studies have focused on the observation that immune system components have been identified as possessing sex steroid receptors.[16] Progesterone in particular has been shown to stimulate the production of the inflammatory mediator, prostaglandin E2 and to enhance the accumulation of polymorphonuclear leukocytes in the gingival sulcus.[25] In addition, sex steroid hormones seem to modulate the production of cytokines,[26] and progesterone has been shown to down regulate IL-6 production by human gingival fibroblasts to 50% of that of control values.[27]

The steroid metabolites may also contribute to nutritional requirements of the pathogens, or enable synthesis of matrices associated with host evasion mechanisms.[28]

Culture supernatants of these micro-organisms have been shown to enhance the expression of 5a-reductase activity in human gingiva and in cultured gingival fibroblasts,
resulting in the formation of 5α-dihydrotestosterone (DHT) from androgen substrate.[29] The DHT can influence protein synthetic activity in these pathogens, for which there is a variety of applications. Some of these functions are: (a) the formation of surface capsular protein contributing to their evasion of host elimination mechanisms, such as phagocytosis, by preventing opsonisation, (b) persistence and dissemination with the host, and (c) interspecies aggregation and energy generation as a result of the electron transfers involved in these enzyme activities.[28] 5α-reductase activity can be activated in a phospholipidic environment. Increased amounts of phospholipases A2 and C are synthesized by periodontal pathogens (e.g., spirochaetes) during inflammatory episodes in the periodontium. Phospholipase C is also released from leukocytes during cell lysis and in addition to degrading gingival crevicular epithelium it is also known to stimulate 5α-reductase activity.[29]

Several studies have concluded that there is a relation between the risk of postmenopausal tooth loss and estrogen replacement. Decrease in estrogen levels have been linked to inflammation of gingiva and reduced levels of clinical attachment.[30] Many authors demonstrated a potential correlation between ovarian dysfunction and an increased incidence of periodontal disease.[31] There is no published data regarding evaluation of periodontal status in pre- and post-menopausal women with periodontitis following nonsurgical therapy. Till date no such study has been done. As per my knowledge, this is the first study comparing pre- and post-menopausal periodontal status. Since both pre- and post-menopausal conditions have disproportion of hormones and imbalance of host inflammatory as well as other functional cells, both conditions are thought to be inflammatory conditions that lead to destruction of other body parts including oral cavity.[32,33] However, these hormones by themselves do not have sufficient influence to produce changes in the gingiva. They may however alter responses of periodontal tissue to microbial plaque and thus be indirectly responsible for severity of periodontal disease.[34] In this study, both groups showed good results from nonsurgical periodontal treatment. This shows proper oral hygiene maintenance and plaque control might counteract the effects of hormonal dysfunction. Treatment of periodontal disease has been primarily directed toward a microbiological etiology.[25,35-39] Prevention of bone loss by modulating the host response to infection could be a new adjunctive method for the management of periodontitis.[40,41] Apart from maintenance of meticulous oral hygiene, several studies have indicated that estrogen therapy builds up mandibular bone mass and diminishes the severity of periodontal disease in postmenopausal women.[31,42]

Limitations
1. Short sample size
2. Longitudinal studies conducted on larger sample size might provide more precise results
3. Identification of inflammatory markers would have been more specific.

Conclusions
This study emphasizes the effects of pre- and post-menopause on periodontal disease progression. It is also clear that not all patients and their periodontium respond in the same way to similar amounts of circulating sex hormones. There was better response to nonsurgical periodontal therapy in premenopausal women when compared to that of postmenopausal women with chronic periodontitis suggesting that even severe inflammatory conditions which are exaggerated by other influencing factors become less intense with nonsurgical periodontal therapy. With these results we can put forward that the influence of sex hormones can be minimized with good plaque control. Prevention and early management of oral disorders is priority in women’s health research. Physicians caring for postmenopausal women should be wakeful and embolden their patients to seek regular dental checkups.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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