Review Article

Crosstalk between hormones and oral health in the mid-life of women: A comprehensive review

Chander Mohan Grover, Vanita Parshuram More[1], Navneet Singh[2], Shekhar Grover[3]

Department of Pedodontics, MNDAV Dental College, Solan, Himachal Pradesh, [1]Department of Pedodontics and Preventive Dentistry, Mahatma Gandhi Vidyamandir's Karmaveer Bhausaheb Hiray Dental College and Hospital, Nashik, Maharashtra, [2]Departments of Orthodontics and Dentofacial Orthopaedic and [3]Preventive and Community Dentistry, Maulana Azad Institute of Dental Sciences and Research, New Delhi, India

Corresponding author (e-mail: <navneetsingh938@yahoo.in>)
Dr. Navneet Singh, Department of Orthodontics and Dentofacial Orthopaedic, Maulana Azad Institute of Dental Sciences and Research, New Delhi, India.

Abstract

Oral health is constantly shaped by the cross-talk between behavioral, biological, and social forces. Menopause is that time in a woman's life when menstrual cycles cease by reduced secretion of the ovarian hormones, such as, estrogen and progesterone. Diseases of the mouth itself are the most common reasons for pain and discomfort in the mouth. However, there are certain situations where oral symptoms are caused as a result of systemic diseases. This review article has emphasized on the diverse oral presentations of postmenopausal women by descriptive analysis of various underlying mechanisms associated with these conditions. Dentists should be aware of the possible association of menopause and various oral health problems.

Key words: *Estrogen, hormones, menopause, oral health*

INTRODUCTION

There is a considerable difference between the oral health needs of women and men. Hormonal fluctuations are said to have a strong influence on oral health, such as, puberty, menses, pregnancy, and menopause-all these factors influence a woman's oral health.[1] Menopause is a physiological process, typically occurring in the fifth decade of life in women, indicating the end of the fertile phase of a woman.[2] During menopause women go through a series of biological and endocrine changes, especially in their sex steroid hormone production, affecting their overall health. As the oral mucosa contains estrogen receptors, variations in hormone levels directly affect the oral cavity. The principal peri- and postmenopausal oral symptoms are xerostomia, sensation of painful mouth (PM) of numerous causes, and burning mouth syndrome (BMS).[3] This review article has discussed the various effects of various hormones and systemic factors that affect the oral health of post menopausal women.

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SELECTION OF DATA

We retrieved pertinent literature on oral health in the menopausal stage of women, selected references and internet services using the PubMed and Medline databases. We conducted a comprehensive literature search related to menopause and oral health using the keywords, 'Menopause and oral cavity;' 'Oral diseases and menopause;', and 'Hormones and oral disorders'.

Stages of menopause

The World Health Organization (WHO), has defined three age stages during the midlife age for women:

(1) Menopause is the year of the final physiological menstrual period retrospectively designated as one year without flow (unrelated to pregnancy or therapy) in women aged ≥ 40 years. (2) Premenopause begins at ages 35 to 39 years; during this stage, decreased fertility and fecundity appear as the first manifestations of ovarian follicle depletion and dysfunction, despite the absence of menstrual changes. (3) Perimenopause includes the period of years immediately before menopause and the first year after menopause.[4] Stages of the Reproductive Aging Workshop (STRAW) developed a model to describe the seven stages of reproductive aging.[5] Climacterium consists of the transition period from fertility to infertility, of which menopause (the last menstruation) as well as perimenopause and postmenopause are parts. It is characterized by several symptoms, such as, night sweats and hot flushes, which are observed in 75-80% of all women in the menopausal age. Other symptoms that are commonly linked to the climacteric stage are mood swings, urogenital dryness, tiredness, joint and muscle pains, dizziness, irritability, and insomnia.[6-8] In addition to the general manifestations of menopause (i.e, psychological alterations and hot flush) oral symptoms are also observed. Increased incidences of xerostomia, lichen planus, pemphigoid, Sjogren's syndrome, burning mouth syndrome (BMS), and periodontal disease are observed during menopause.[2]

Role of sex hormones and various cytokines

Sex hormones have been considered to play a significant role in periodontal tissues and periodontal disease progression from a long time. The role of various cytokines and sex hormones has been described below:

Estrogen and oral cavity

It is a well-established fact that estrogen reduces the osteoclast activity and increases their apoptosis. In the menopause stage, the estrogen levels decline rapidly, and lead to systemic bone loss. Estrogen receptors are also observed in the oral mucosa, gingiva, and salivary glands. Some investigators[1,3,9] have demonstrated a reduced salivary flow rate during menopause, whereas, others have failed to show a change in the quantity or flow rate of the saliva. Hence, we can presumably state that the salivary function of postmenopausal women can be investigated to explain the frequent complaint of oral discomfort, including dry and/or burning mouth.[9]

Cytokines, periodontitis, and skeletal bone loss

Estrogen deficiency leads to upregulation of immune cells (macrophages and monocytes) and osteoclasts, which are responsible for a greater production of bone-resorbing cytokines.[10,11] Lipopolysaccharide-released by-products related to periodontal tissues and bacterial plaque biofilm stimulate the production of inflammatory cytokines, which further activates the osteoclasts that resorb the bone. Inflammatory cytokines include interleukin 1 (IL-1), IL-8, IL-6, IL-10, tumor necrosis factor alpha, granulocyte-macrophage colony-stimulating factor (GM-CSF), and the granulocyte colony stimulating factor, which stimulate mature osteoclasts, alter bone-cell proliferation, and activate resorption of both the skeletal and alveolar bones, by triggering tissue proteinases and degradative enzymes, leading to destruction of the connective tissue, alveolar bone resorption, and finally tooth loss.[12,13]

Oral manifestations of menopause

Burning mouth syndrome

Patients typically describe the burning pain as having a bilateral symmetrical distribution, most frequently involving the anterior two-thirds of the tongue, the dorsum, the lateral borders of the tongue, the anterior hard palate, and the mucosa of the lower lip, often in more than one oral site. It is a common dysesthesia (distortion of a sense) usually described by the patient as a burning sensation in the oral cavity, in the absence of clinically apparent changes in the oral mucosa. BMS is reported most commonly by perimenopausal women, with onset of symptoms typically occurring between three years before menopause and 12 years after menopause; and it rarely manifests before the age of 30 years. Investigators have reported high female predilection, with the ratio between women and men ranging from 3:1 to 16:1. Oral mucosal changes vary from an atrophic pale appearance to *menopausal gingivostomatitis,* which is characterized by dry and shiny gingiva that bleeds easily, and a reduced salivary flow rate in the presence of the disease. The burning sensation seems to be like mouth burnt with hot coffee, but it does not go away. It usually happens in the tongue and is associated with the bitter taste sensation. The bitter taste ability located at the tip of the tongue inhibits the pain, and when it is gone, it leads to pain that is interpreted as burning mouth syndrome. The symptom typically gets worse over the day and it can extend to months or even years. The reason why burning mouth syndrome is common in post menopause women is directly related to the reduced estrogen production. There is also a relationship between anxiety and depression and burning mouth syndrome, although it is difficult to state which the precursor is; the psychological changes or the pain.[3,14]

Dry mouth

Xerostomia is defined as the subjective sensation of oral dryness and is usually associated with hyposalivation, but not always. Several research reports have demonstrated that xerostomia or dry mouth is experienced by 25 to 50% more women than men, regardless of age and intake of xerogenic medications.[15] The composition of saliva and decreased saliva flow seem to be estrogen-dependent, often leaving menopausal and postmenopausal women with a persistent feeling of dry mouth, as there is reduction of estrogen at the menopause stage. This can be accompanied by a bitter taste and bad breath (Halitosis). Medications are considered as a major reason for impaired salivary function.[16] Steroid hormones can be assessed in the saliva samples and their salivary concentrations are shown to correlate well with those in the blood serum. The prevalence of oral discomfort was significantly higher in perimenopausal and postmenopausal women (43%) than in premenopausal women (6%).[17] Association between the psychological symptoms in menopausal women and oral discomfort was also believed to be one of the prime reasons for altered salivary flow, indicating sympathetic activation due to psychological stress.[18,19] In contrast, there are no significant differences in the salivary flow rates between women using hormone replacement therapy (HRT) and non-users. Decrease in salivary flow is responsible for an increase in dental caries, candidiasis, and increase in dental plaque, which is again responsible for initiating gingivitis, thereby, providing a contributing factor for periodontitis in menopause.[20,21]

Painful mouth (Stomatodynia)

Painful mouth has been accompanied with a reduced salivary flow rate. Mandibular dysfunction and also diffuse gingival atrophy or oral ulcerations can be present with oral dryness, causing pain in the mouth. Other possible causative factors are oral candidiasis, pernicious anemia, and some nutritional deficiencies.[3]

Osteoporosis

Osteoporosis is a reduction in bone mass density, with deformity, pathological fractures, and is sometimes associated with pain.[22] Osteoporosis is caused by an uncoupling of the bone resorption/formation process, with an exaggeration of resorption, reduction in bone formation or a combination of both. In most cases, postmenopausal osteoporosis is due to an abnormal increase in resorption or demineralization and not a decrease in bone formation or remineralization.[23] There is an established association between low estrogen levels and bone loss. Both bone-forming osteoblasts and bone-resorbing osteoclasts express estrogen receptors. Estrogen receptors observed on the bone-resorbing osteoclasts recognize the reduced estrogen and respond by enhancing their activity level. Although estrogen receptors on the bone-forming osteoblasts also recognize the paucity of estrogen, they respond by decreasing their activity level.[24] As the remodeling process continues, the rate of trabecular (cancellous) and cortical bone resorption exceeds that of trabecular and cortical bone formation. During this postmenopausal osteoporotic process, women lose 30 to 50% of the trabecular bone and 25 to 35% of the cortical bone mass that was present during the peak bone mass years-between the age of 20 and 30 years.[25] According to the WHO criteria, osteoporosis is diagnosed when bone mineral density is at least 2.5 standard deviations below the average value for young and healthy women (T-score < -2.5).[26] Osteoporosis is termed as a 'silent disease,' because the loss of bone mass does not cause symptoms. However, once a fracture does occur, pain, loss of function, and, in some cases, deformity may result.[27]

Periodontitis

Periodontitis is an inflammatory disease of bacterial origin that affects the supporting structures of the teeth.[28,29] It is a silent disease, similar to osteoporosis, which does not cause symptoms until in the latter stage of the disease process, such as, mobile teeth, abscesses, and tooth loss. Both periodontitis and osteoporosis are bone-resorptive diseases. Risk factors associated with periodontal disease include accumulation of dental plaque and host-response abnormalities, involving smoking and many systemic diseases.[30]

The homeostasis of the periodontium involves complex multifactorial relationships, in which the endocrine system plays an important role. Estrogen, progesterone, and chorionic gonadotropin, all affect the microcirculatory system, producing the following changes: Swelling of endothelial cells and pericytes of the venules, adherence of granulocytes and platelets to the vessel walls, formation of microthrombi, disruption of perivascular mast cells, increased vascular permeability, and vascular proliferation.[31-33] Fluctuation of sex hormones during menopause have been implicated as a factor for inflammatory changes in the human gingiva, hypertrophy or atrophy. Estrogen affects cellular proliferation, differentiation, and keratinization of the gingival epithelium. Hormone receptors have been identified in the basal and spinous layers of the epithelium and also in the connective

tissue implicating the gingiva and oral tissue.[34] When considering the relationship between osteoporosis and periodontitis, it is believed that osteoporosis is not an etiological factor in periodontitis, but may affect the disease severity in the pre-existing periodontitis. Systemic bone loss may be considered as a risk indicator for periodontal destruction and elevated rates of loss of bone mineral density after menopause are associated with greater risk of tooth loss.[35,36] Osteoporosis is observed to cause bone destruction in the alveolar processes of the mandible and maxilla, which provide a bony framework for anchorage of the tooth. Even though the association between systemic osteoporosis and oral health remains controversial, it has been suggested that tooth loss in menopausal and postmenopausal women might signal the onset of systemic osteoporosis. Edentulous women are referred to dental clinics with particular problems of ill-fitting dentures due to alveolar ridge regression. Women with fewer teeth had lower bone densities than women who retained teeth. However, some studies did not find an association between systemic osteoporosis and the parameters of poor mandibular bone quality.[37]

Lichen planus

Lichen planus is an immunologically mediated disease in which the basal cell layer of mucosa and/or skin is attacked. All forms are seen mostly in patients older than 40 years and have a predilection for females, with the ratio being 3:2.[38] Although there is no direct relationship between lichen planus associated to menopause, it is hypothesized that it may be due to the effect of the various drugs that are given for the treatment of menopause.

Neurological disorders

Trigeminal neuralgia (TN), an archetype of orofacial neuralgia, which follows the anatomical distribution of the fifth cranial nerve, is frequently observed in postmenopausal women, which may be due to the compression of any one of the branches of the trigeminal nerve or superior cerebellar artery.[39] It is characterized by severe unilateral, searing, stabbing or lancinating pain, usually in the middle and lower third of the face. In addition to TN, other neurological disorders, such as, atypical facial pain/neuralgia, and Alzheimer's disease may affect postmenopausal women. Such disorders have a tendency to influence impression-making procedures, recording jaw relations, and denture retention.[40] Thus, strategic protocols are suggested to menopausal women to reduce anxiety and stress during treatment procedures.

Eating disorders

An eating disorder is a condition characterized by abnormal eating habits that may involve either insufficient or excessive food intake to the detriment of an individual's physical and mental health. Psychological stress may lead to eating disorders in menopausal women. Oral changes may result from self-induced vomiting or regurgitation of gastric contents in the oral cavity. Menopausal women having eating disorders may suffer from smooth erosion of enamel, perimolysis, increased tendency to use pen and combs to induce vomiting, enlarged parotid glands, angular cheilitis, dehydration, erythema, and trauma to the oral mucosa and pharynx resulting from use of fingers.[40]

Effects of bisphosphonates

Osteonecrosis of the jaws is usually observed in patients treated with bisphosphonates (BPs). These drugs are endogenous pyrophosphate analogs that have the ability to affix to the bone, inhibiting osteoclast function, and thereby reducing the bone turnover and disturbing the active remodeling in those areas, characterized by excessive bone reabsorption.[41,42]

Although the risk of osteoporosis is very low in maxillary osteonecrosis patients, the following criteria must be met in order to establish a diagnosis of maxillary osteonecrosis: Current or past treatment with BPs; the presence of one or more ulcerated lesions on the alveolar mucosa, with the exposure of maxillary or mandibular bone, necrotic appearance of the exposed bone; spontaneous presentation of the lesions, or more frequently, manifestation after dental–alveolar surgery; and the absence of healing for a period of at least six weeks.[43]

Dental management of menopause

A vigilant and comprehensive evaluation of the oral mucosal membranes, the periodontal, dental conditions, and salivary flow, along with a detailed clinical history is imperative in all postmenopausal women, along with other pertinent tests, such as, radiographs, periodontal probing, and sialometry. It is imperative to maintain proper oral hygiene, with application of several measures, such as, brushing, interproximal brushes, and dental floss, together with the use of mouth washes, such as, chlorhexidine or Listerine to the lower the dental plaque levels, which improves the overall periodontal health and prevents caries.[44,45]

CONCLUSION

Hormones influence oral health by directly affecting the oral tissues, as well as affecting a multitude of other body systems that in turn produce effects in the oral cavity. Oral discomfort like dry mouth, altered taste, and burning sensation are the common and chief complaints among menopausal women in dental clinics. On account of this high risk of dental and gum problems, it is deemed necessary that women approaching or traversing the menopausal transition are aware of the signs and symptoms of these oral disorders. Dentists should conduct a thorough examination of the oral cavity and rule out other systemic diseases before arriving at any definitive diagnosis related to hormonal changes. In future, more randomized controlled trial studies should be conducted to understand the association between menopause and oral health.

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