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DENTAL TREATMENT AND ORAL  
MANIFESTATIONS IN MENOPAUSE

LEČENJE ZUBA I STANJE U USNOJ DUPLJI  
U MENOPAUIZI

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*Abstract*

Menopause is a physiological process typically occurring in the fifth decade of life in women, and involving permanent cessation of menstruation. Menopause is the consequence of hormonal changes that produce a series of general manifestations that have become increasingly important as a result of the increased female life expectancy in the industrialized world; indeed, such manifestations are observed throughout the last third of the female lifetime. However, oral symptoms are also found in addition to the more general manifestations of menopause (i.e., hot flush and psychological alterations). In this sense, an increased incidence of dry mouth (xerostomia), disorders such as lichen planus, benign pemphigoid, Sjogren's syndrome and burning mouth syndrome are observed, as well as a debated rise in the prevalence of periodontal disease.

The dental treatment of such patients involves a series of particularities that should be taken into account, including the use of salivary secretion stimulators or saliva substitutes in cases of hyposialosis. Nevertheless, correct prevention, with good control of bacterial plaque, contributes to reduce the risk of many infections within the oral cavity.

*INTRODUCTION*

Menopause is a physiological process typically occurring in the fifth decade of life in women, and involving permanent cessation of menstruation. The condition does not include situations of ovarian activity interrupted as a result of surgery. The cessation of menstruation occurs gradually over a prolonged period of time, with interruptions lasting one to three months and followed by resumed menstruation. In this context, an interruption of 12 months is generally accepted as a definition of menopause (1, 2).

The term climacterium is often used in reference to menopause, i.e., for defining the critical period in which menstruation ceases. However, menopause is not synonymous of climacterium.

In general, menopause should be considered as the date of the last menstruation, and as such it represents a brief and defined period of time, while climacterium implies a much longer period involving a series of events such as the loss of female reproductive capacity and the occurrence of important changes in sex hormone secretion that induce major modifications not only in the genital apparatus but also in other areas of the body (2).

*MECHANISM OF MENOPAUSE*

The most important aspect of the climacterium is the associated drop in plasma estrogen levels. The concentration of progesterone also decreases, while in contrast, androgen output increases (i.e., testosterone and particularly androstenedione). These androgens compensate for the estrogen deficit by transforming these into peripheral or adi-

pose tissue estrone; consequently, depending on the volume of adipose tissue present in the body, the extra production of these hormones will be more or less important. Therefore, obese women tend to suffer fewer climacteric symptoms than thin women. During the ovarian cycle, 17-beta-estradiol constitutes the most important estrogen, though in postmenopause its production decreases considerably - the most important hormone becoming estrone, with mean serum concentrations of 35 ng/ml (2, 3).

In general, the climacterium is fundamentally characterized by a decrease in progesterone and especially estrogen levels - the secondary endocrine alterations and clinical manifestations being a consequence of this decrease.

A number of endocrine alterations should be taken into account. Firstly, consideration should focus on hypophyseal-hypothalamic regulation. Estrogens exert a negative feedback effect upon gonadotropin release (both follicle stimulating hormone (FSH) and luteinizing hormone (LH)). The drop in plasma estrogens suppresses such negative feedback, giving rise to an important increase in FSH and LH - these hormones being largely responsible for the symptoms of the climacterium (particularly hot flush). At hypothalamic level, the lack of estrogenic stimulation induces an increased output of gonadotropin releasing hormone (GnRH).

As regards the adrenal cortex, androgen production increases (specifically, androstenedione and testosterone) - these hormones serving as substrate for the extraglandular formation of fatty tissue (or peripheral) estrogen. Androgen concentration is particularly high when the remaining ovarian parenchyma is scantily active, and in cases of artificial climacterium due to castration. The postmenopausal ovary produces only minimum amounts of estrogen - the adrenal cortex affording the greatest contribution to estrogen production via peripheral conversion of androgens into estrogens (1).

The thyroid gland in turn undergoes a hyperfunctional reaction (climacteric hyperthyroidism), characterized by an increase in iodine-bound proteins and thyroxin binding protein in blood between 45 and 55 years of age. However, the most important aspect is the hypersecretion of thyrocalcitonin, a hormone that regulates calcium deposits in bone. A lack of this hormone is one of the causes of climacteric osteoporosis. According to some authors, the administration of thyrocalcitonin could be effective in treating osteoporosis in such cases (4).

The pancreas appears to have no direct relation to the climacterium. The diabetes sometimes seen in such situations does not seem to be a consequence of menopause but rather a phenomenon associated to senescence in general. Accordingly, some authors claim that no direct relation exists between the cessation of menstruation and the appearance of diabetes mellitus (5).

The parathyroid glands can also suffer alterations. In effect, due to the lack of estradiol the glands occasionally become hyperactive, thereby contributing to mobilization of calcium and phosphorus deposits in osteoporosis (1).

The mentioned hormonal changes induce a clinical condition with very inconstant symptoms, since many are psychosomatic - and patient subjectiveness contributes to

accounting for such variability (5). Mention will be made of the most important manifestations.

As regards cardiovascular problems, hypertensive episodes are common but tend to be moderate, and are frequently associated with the triggering of headaches (6). On the other hand, the risk of cardiovascular disease increases after menopause, coinciding with the estrogen deficiency (7). Other cardiovascular symptoms also appear, including tachycardia and arrhythmias that may occasionally disappear entirely once the clinical manifestations of menopause have been brought under control (8).

Hot flush is the most common symptom of the climacterium, affecting 50-85% of all postmenopausal women. Approximately 20-30% of females in the postmenopausal period develop hot flush serious enough to require medical care. This symptom is the menopause-related manifestation that most frequently leads to the seeking of medical help. The mechanism underlying hot flush is small blood vessel dilatation of vasomotor origin, though with an important neurovegetative component (9).

Osteoporosis, described by Albright (10), is another consequence of estrogen privation, which leads to the loss of bone mass and increased skeletal fragility. Although such diminished bone volume or osteopenia is a consequence of the climacterium, it takes a number of years to manifest. On the other hand, fractures in postmenopausal women constitute a major health care problem. Osteoporosis often produces no symptoms until hip or forearm fractures occur in late climacterium (11). One-fourth of all postmenopausal women are affected by osteoporosis - a figure that increases to 52% after the age of 65 years, though this proportion includes women with involutional osteoporosis not strictly related to the climacterium (12).

Psychosomatic alterations can also be observed. This period in the life of a woman commonly gives rise to psychological disorders. In this sense, the decadence in sexual activity is a source of important affective conflicts, while the diminished blood estrogen levels induce neuralgias, headaches, paresthesias, „restless legs” syndrome, pruritus, vertigo, sleep disorders and depression.

Urological disorders are occasionally observed as a result of estrogen dependency. The most frequent problem is interstitial cystitis, which manifests as micturition urgency, dysuria, pollakiuria, and suprapubic pain. Bladder capacity is diminished. The symptoms are progressive, and if left untreated can give rise to patient incapacitation (13). Incontinence is another common problem. In this context, Karafin and Coll (14) have observed urinary incontinence in 12-40% of postmenopausal women. The condition varies in magnitude from incontinence upon coughing, in response to major exertion, or as a result of stress.

#### *MENOPAUSE MANIFESTATION AND SYMPTOMS IN THE MOUTH*

A number of disorders affecting the oral mucosa can repeatedly develop in postmenopausal women. The most common or important alterations are described below.

A common oral problem in these patients is burning mouth syndrome, also known as glossodynia, glossopyrosis,

glossal-gia, stomatodynia and stomatopyrosis. The condition is characterized by intense pain and a spontaneous burning sensation affecting mainly the tongue and sometimes the lips and gums. However, despite the intense symptoms of pain and burning sensation, no appreciable organic lesions are generally observed. In addition to burning mouth, these patients refer alterations in taste (dysgeusia) and breath, dry mouth, swallowing difficulties and facial or dental pain (15).

Mean patient age at the onset of burning mouth syndrome is 50-60 years, with a marked (3:1) female predominance. This gender difference increases with age - suggesting that menopause plays an important role in the incidence of glossodynia.

Certain microorganisms (*Candida albicans*, staphylococci, streptococci and anaerobes) have also been implicated in the etiology of burning mouth syndrome, together with xerostomia (associated to Sjogren's syndrome, anxiety and medication), nutritional disorders related to vitamin B complex or iron, anemia (pernicious or ferropenic), climacteric hypoes-trogenemia per se, diabetes mellitus, certain mechanical traumatism (abnormal oral habits, chronic denture-induced irritation) and other idiopathic factors (16).

Psychological disorders appear to play a fundamental role, including depression, anxiety, cancerphobia and other psychogenic alterations (17, 18). In this sense, Trikkas et al. (19), in a group of 25 subjects with burning mouth syndrome in the 52-75 years age range, found disorders such as hostility - particularly in introverted individuals - anxiety, phobias and depression to constitute an important component of the psychological profile of patients with this syndrome.

Wardrop et al. (20), in a study of postmenopausal women aged 30 to 63 years and who were receiving treatment for control of the symptoms, observed that 33% had oral manifestations - including burning mouth - though no evidence was observed of organic lesions capable of accounting for such alterations. The prevalence of oral symptoms was found to be significantly greater in peri- and postmenopausal women (43%) than in premenopausal females (6%). An association was also observed between the oral symptoms and psychological alterations of these patients. Approximately two-thirds of the study subjects who presented oral symptoms but no evident clinical manifestations were seen to improve with hormone replacement therapy.

The diagnosis of burning mouth syndrome is based on the compilation of a detailed case history, the absence of findings in the physical examination and laboratory tests, and the exclusion of other possible oral disorders. In general, a clinical diagnosis is established without difficulty, though the factors underlying the symptoms are either difficult or impossible to identify (16).

The treatment of burning mouth syndrome also poses difficulties. When the underlying cause is attributable to nutritional deficiencies, replacement therapy is effective. In patients wearing dentures, a careful evaluation of denture fit and the underlying tissue status is indicated, since denture adjustment or replacement may contribute to eliminate chronic irritation. Treatment with topical clotrimazole or nystatin sometimes yields satisfactory results when fungal culture proves positive. In those cases where the symptoms

are attributable to drug use, the physician should be consulted about the possibility of prescribing some alternative medication. Since most patients with burning mouth syndrome do not correspond to any of these categories where a culprit factor amenable to elimination can be identified, treatment is usually a complicated matter.

The dental professional should provide support and offer an explanation for the disease, without promising easy solutions or expressing undue optimism - since the patient must accept the condition and learn to live with it. On the other hand, the patient can be consulted on the convenience of psychological counseling, since as has been mentioned above, the condition can also have a neurological origin (16).

Based on a study of postmenopausal women, Volpe et al. (21) found that 12 out of 22 patients improved of their oral symptoms with estradiol-based treatment. Moreover, 7 of 10 patients administered conjugated estrogens also experienced in improvement symptoms. These findings again point to estrogen deficiency as a possible cause of the oral symptoms in some postmenopausal women, and suggest that estrogen replacement therapy might subjectively improve these symptoms.

Posterior research has likewise revealed a relation between these oral alterations and steroid hormones, though only in some postmenopausal women. Moreover, hormone replacement therapy has been shown to improve the symptoms in such patients. On the other hand, the presence of estrogen receptors has been established at oral epithelial level in most patients who respond to replacement therapy, while patients failing to derive benefit from such therapy lacked estrogen receptors. This observation implies that the identification of estrogen receptors in the oral mucosa may contribute in selecting those patients capable of deriving benefit from hormone treatment (22).

Xerostomia is another frequent symptom in postmenopausal women. In this context, although an association to menopause exists, salivary flow is known to decrease with age -though not necessarily so.

A number of studies have evaluated salivary function in postmenopausal women, in an attempt to explain the association between dry mouth and the climacterium. In this sense, some authors (23, 41) have found a decrease in salivary flow associated to menopause, while other investigators have been unable to identify changes in either salivary volume or composition (24).

In a longitudinal study, Ship et al. (25) did not observe significant differences in salivary flow volume in premenopausal women versus postmenopausal females. Likewise, no important differences were recorded in terms of salivary flow between postmenopausal women receiving estrogen treatment and postmenopausal females without treatment of any kind. These authors concluded that none of the healthy women participating in their study showed signs of burning mouth, xerostomia or alterations in salivary output.

Ben Aryenh et al. (26) found 45% of menopausal women without general symptoms to suffer oral manifestations, while 60% of the patients with general alterations also had oral problems. No differences were recorded in salivary flow

or composition between the two groups. Nevertheless, the concentration of salivary IgA and total proteins was significantly higher among these subjects than in healthy young women - a phenomenon attributed to the psychological stress to which these patients may be exposed.

Other alterations of the oral mucosa can also be observed. Accordingly, in addition to xerostomia and burning mouth syndrome referred to above, a number of other less important disorders can develop, including bad taste, viscous saliva or burning sensations - usually complicated with atrophy of the oral mucosa. An increase in certain mucosal disorders such as lichen planus, benign mucosal pemphigoid, or Sjogren's syndrome has also been documented (27, 40).

Periodontal problems can also be observed. In this sense, the association of menopause, osteoporosis and diminished blood estrogen levels may be related to the appearance of periodontal disorders - though no direct association has been firmly established to date. The main problem is the fact that both osteoporosis and periodontal disease are multifactor processes with etiologies that continue to pose uncertainties. As a result, it is generally unclear whether one condition enhances the other or vice versa, and in what way. In any case, estrogen concentration seems to be the single factor capable of exerting the greatest influence upon the development of periodontal disease - even more than the presence or absence of concomitant osteoporosis (28).

In this sense, Hildebolt et al. (29) analyzed the association between osteoporosis and periodontal attachment loss, examining vertebral and long bone density, and relating it to tooth and attachment loss. These authors found attachment loss to be related to tooth loss, but not to vertebral or long bone density. In this same study they related periodontal attachment loss to patient age at menopause and tobacco smoking - a direct association being observed between estrogen deficiency and attachment loss among smoking women. In a more recent study (30, 43), these same investigators analyzed the relation between the distance from the cemento-enamel line to the alveolar crest and bone density in postmenopausal women. They concluded that this distance is influenced by parity, skeletal bone density and also cigarette smoking.

Some studies have been made of the association between osteoporosis and periodontal disease (31-33), though no direct relation has been reported between attachment loss or the tendency towards active periodontitis and osteoporosis or bone mineralization levels.

More recent studies such as those conducted by some authors (34, 42) have concluded that the loss of skeletal bone density is related to periodontal support in interproximal zones, analyzed as clinical attachment loss, and that postmenopausal osteopenia is an indicator of the risk of periodontal disease in Caucasian females. In this sense, another study attempting to relate alveolar bone morphological measurements via digital dental X-rays to bone density of the femur and dorsal spine in postmenopausal women without periodontitis (or with only slight involvement) found no clear correlation between these two factors (35,44).

Recent research has attempted to confirm the influence of estrogen therapy upon osteoporosis and periodontal disease (36). It was concluded that estrogen treatment is associated with a reduction in gingival inflammation and in periodontal attachment loss in postmenopausal and osteoporotic women. In this same sense, a study involving 81 postmenopausal women with good oral health and subjected to hormone replacement therapy found periodontal status to show a highly dynamic turnover, with sporadic changes in periodontal attachment or alveolar bone height that usually remitted without difficulty (37, 46).

Another important aspect requiring consideration is the question of whether menopause is implicated in any way with the prognosis of implant therapy. In a population of 116 postmenopausal patients aged 50 years on average and treated with a total of 450 implants, hormone replacement therapy did not seem to be related to the outcome of implant treatment - though tobacco smoking significantly increased the failure rate (38).

### *MENOPAUSE IN DENTAL TREATMENT*

As has been seen above, although endocrine alterations are more or less directly related to the oral problems of postmenopausal women, many of these disorders can be attributed to physiological aging of the oral tissues.

The treatment modalities proposed for these oral problems basically center on the use of sexual steroids, though some authors (39, 47, 49) point out that patient response to conventional therapy (i.e. artificial saliva) is not substantially modified by the administration of such hormones.

Nevertheless, a very important consideration in these more or less elderly women is the minimization of bacterial plaque, since excess plaque can facilitate the development of odontologic infections. Mechanical control of bacterial plaque is therefore essential, complemented where necessary by the use of some pharmacological product such as chlorhexidine - the most effective chemotherapeutic agent known for combating oral microorganisms. However, despite its acknowledged efficacy, chlorhexidine must be used with caution in these individuals, since many mouthwashes contain variable proportions of alcohol (6-29%) that can dry and irritate the oral tissues, thereby exacerbating the signs and symptoms of patients with dry mouth. Chlorhexidine is able to reduce bacterial plaque, improving periodontal disorders and largely eliminating the presence of *Streptococcus mutans*, i.e., preventing dental caries - especially root caries, which is more frequent in elderly subjects.

<b>Basic dental treatment protocol in menopausal patients</b>
<b>Case history</b>
a) Medical: Evaluation of systemic diseases (allergies, drug consumption, use of drugs causing dry mouth). b) Dental: Thorough exploration of the mucosa, dental status, periodontal condition and salivary flow (quantity and quality). 2. Consultation with other specialists (where applicable)
<b>Possibility of systemic steroid therapy</b>
3. Dental treatment: a) Prevention: Bacterial plaque: - Mechanical control - Chemical agents (chlorhexidine) Root caries: - Fluorides (gels and varnishes) Xerostomia: - Salivary substitutes or stimulators - Artificial saliva (where applicable) b) Periodontal treatment: Etiological phase: meticulous and reevaluation Corrective phase: evaluation of previous maintenance c) Conservative/rehabilitating treatment:
<b>Periodic reevaluations</b>
<b>Evaluation of bone quality before implant therapy</b>

The prevention of caries can also be facilitated by the use of fluorides - the most frequently employed vehicles being toothpastes, varnishes, gels or tablets. Low-dose but frequent administrations of Fluor involving daily tooth brushing or mouth washing are very useful for the prevention of root caries. Xylitol or fluoride tablets are easy to administer and ensure protection as good as that afforded by mouthwashes; furthermore, they stimulate saliva secretion in patients who may have a diminished salivary flow.

As has already been mentioned, postmenopausal women may show a high prevalence of dry mouth, in proportion to the number of xerostomizing drugs used, the existence of background illnesses or radio therapeutic sessions, among other factors. The use of salivary flow stimulators and even saliva substitutes is essential in dealing with dry mouth. When dryness is nearly total and stimulation no longer suffices, artificial salivas become necessary (27, 48).

As regards oral surgical interventions or the corrective phase of periodontal treatment, consideration should first focus on the physical condition of the patient. In the event of patients with important intercurrent disease, prior medical consultation is advised. In any case, and as a general norm, advanced patient age and menopause are not contraindications for advanced treatments (where necessary), and do not constitute reasons for compromising the quality of such therapy (40, 50).

### Sažetak

Menopauza je fiziološki proces koji se obično dešava kod žena u petoj deceniji života i podrazumeva trajni prestanak menstruacije. Menopauza je posledica hormonskih promena koje dovode do serije opštih manifestacija koje su dobile na značaju jer utiču na povećanje dužine života u industrijski razvijenim zemljama; u svakom slučaju, te promene se dešavaju u poslednjoj trećini života žena. I promene u usnoj duplji su takođe deo opštih manifestacija menopauze (na pr. vrući talasi i fiziološke promene). U sklopu tih promena, primećena je povećana učestalost suvih usta (xerostomia), oboljenja kao što su lihen planus, benigni pemfigoid, Sjogrenov sindrom i sindrom usta koja gore, kao i diskutabilan porast učestalosti periodontalnih bolesti.

Lečenje zuba kod takvih pacijenata ima niz specifičnosti koje treba razmotriti, uključujući stimulare lučenja pljuvačke ili zamenu za pljuvačku u slučaju hiposijaloze. U svakom slučaju, odgovarajuća prevencija i dobra kontrola stvaranja bakterijskih plakova doprinosi smanjenju rizika

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