

Influence of climacteric hormonal changes on buccal tissues

Influência das alterações hormonais advindas do climatério nos tecidos bucais

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ABSTRACT

During the climacteric period, when female gonads cease their function, estrogen deficiency, especially estradiol, causes important changes in the oral cavity, interfering in inflammatory mechanisms, salivary secretion, collagen metabolism, among others. Through a literature review, this study aimed to see the influence of the hormonal changes from the climacteric period in the oral tissues, providing the dentist surgeon with information regarding the consequences and care related to this phase of the woman's life. In this period, women become more susceptible to changes such as: osteopenia and osteoporosis of the jaws, hyposalivation, periodontal diseases, among others. Preventive treatment through removal of plaque, adequacy of the buccal environment and orientation before and during climacteric are the best means of minimizing oral problems arising from this phase of a woman's life.

Keywords: climacteric; gonadal steroid hormones; estrogens; oral health.

RESUMO

Durante o climatério, período em que as gônadas femininas cessam sua função, a deficiência de estrógenos, especialmente do estradiol, provoca alterações importantes na cavidade bucal, interferindo em mecanismos inflamatórios, secreção salivar, metabolismo do colágeno, entre outros. Por meio de uma revisão de literatura, esse estudo teve como objetivo, ver a influência das alterações hormonais advindas do período de climatério nos tecidos bucais, proporcionando ao cirurgião dentista informações em relação às consequências e cuidados relacionados a esta fase da vida da mulher. Nesse período, as mulheres tornam-se mais suscetíveis a alterações tais como: osteopenia e osteoporose dos maxilares, hipossalivação, doenças periodontais, entre outros. O tratamento preventivo por meio de remoção de placa, adequação do meio bucal e orientação antes e durante o climatério são os melhores meios de minimizar os problemas bucais advindos dessa fase da vida da mulher.

Palavras-chave: climatério; hormônios esteroides gonadais; estrogênios; saúde bucal

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INTRODUCTION

Humans undergo several systemic changes during life that may be physiological caused by aging or pathological. Many of these changes occur in the hormonal system. In the male reproductive system, testosterone predominates, and in the female, estrogen (estradiol, estrone and estrinol), and its deficiency or excess promotes important changes¹.

During life, women go through periods of sexual evolution such as puberty and maturity reaching senectude¹. In these phases have different levels of concentration of sex hormones: estrogen and progesterone. These hormones act in different functions of the body and their low concentration during climacteric causes important systemic changes, including affecting the tissues of the oral cavity and favoring the appearance of tooth loss²⁻⁵ gingival scaling and retraction^{2,3,6,7}, periodontal problems^{2,3,5,6}, among other disorders⁸⁻¹⁷ highlighting osteopenia and osteoporosis of the jaws^{2,6,8,18,19} and menopausal gingival stomatitis^{3,7,20}.

Estrogens may minimize or inhibit the inflammatory response^{2,3}. In addition, they inhibit the release of substances that favor osteoclast activity and act on collagen metabolism. Its deficiency during climacteric favors the production of proinflammatory cytokines² such as interleukins⁴ 1 and 6 that are involved in promoting bone resorption, favoring the inflammatory response and relating to the oral disorders mentioned above.

When studying the relationship between climacteric and dental tissues, a study attributed to estrogen deficiency the reduction of dentinogenesis in rat lower incisors. Significant reduction in odontoblast-specific proteins was found and a reduction in the pre-dentin layer in these elements²¹.

Given the above, this study aimed to see the influence of hormonal changes arising from the climacteric period in the oral tissues, providing the dentist with information regarding the consequences and care related to this phase of women's life.

METHODS

This is a systematic literature review study, where the research question was: what do studies in the literature show about the influence of hormonal changes during climacteric on oral tissues and what would be the role of the dental surgeon in these cases? The search for articles was performed in the electronic databases, SciELO, PubMed and Google Scholar using the keywords in Portuguese and English selected according to the classification of Descritores em Ciências da Saúde (DeCS/Health Sciences Descriptors): menopausa/menopause, climatério/climateric, saúde oral/oral health, hormônios esteroides gonadais/gonadal steroid hormones, estrógenos/estrogens, and search in the article references. Thus, 52 studies were found in the databases, after the selection criteria were 29 articles in Portuguese and English that were considered useful to the study. Regarding the selection

criteria, we first analyzed the abstracts of the articles in order to select only those that really added knowledge to the established question. Original articles and literature reviews published between 2000 and 2016 were included in studies conducted in Brazil and abroad. Articles prior to the year 2000, those that did not answer the question proposed by our study and those with similar parameters were excluded. The Table 1 shows the list of articles by theme and their main conclusions. At the end, all selected articles were read in full and analyzed.

RESULTS

We found 52 articles by searching the databases. Of these, 13 were excluded because the summary did not match the purpose of our study. Of the remaining 39, 4 had similar parameters and 8 had been published before 2000. Thus, 27 articles were selected for full reading. During their analysis, the references were consulted and 2 more articles that fit the proposal and the selection criteria of our study were selected.

DISCUSSION

Estrogens develop genitals, breasts and determine female secondary sexual characteristics until woman evolves to climacteric phase¹.

Systemically, estrogens also interfere with the functioning of skeletal muscle and, according to Vasconcelos and Rodrigues-Garcia⁸, act as muscular adductor and strengthen skeletal muscle. Their results showed higher bite force during estrogen peak and lower force during lower estrogen levels, in agreement with the study by Brown et al.¹⁰. A study by Bell et al.⁹ found a negative correlation between estrogens and the rate of muscle strength production when the combined male and female genders were evaluated. When evaluated individually, women showed a negative correlation between estrogen and muscle stiffness, in agreement with the above studies.

Regarding the association of estrogens with nociception, a study¹¹ carried out in rats attributes an antinociceptive effect, another¹² a pro nociceptive effect. In contrast, human studies^{13,14} concluded that there was no association between pain threshold and estrogen concentration, as well as between this and the effect of local analgesia used in dentistry.

When analyzing oral health, it is common the appearance of gingival desquamations (collagen metabolism is also affected)^{3,7} and the aggravation of periodontal diseases due to previous periodontal changes. Periodontal disease has a chronic and infectious character and occurs through the exposure of the protective or support periodontal to periodontopathogens that adhere to the dental element through the bacterial plaque. These produce lipopolysaccharides and toxins that result in an

inflammatory response. Inflammation causes production of cytokines and mediators that cause destruction of microorganisms and healthy tissue⁷.

The fall of sex hormones favors the adhesion of bacteria and modifies the tissue metabolism in relation to the inflammatory and immunological response^{2,3}, since estrogen has anti-inflammatory effect, its deficiency only when there is bacterial plaque becomes an aggravating development of gingivitis: inflammation of the gums showing signs of bleeding and reversible edema. Gingivitis is the first stage of periodontal disease^{2,7}.

When the support periodontium is reached, periodontitis occurs, also resulting from the local accumulation of bacterial biofilm that may result in loss of dental insertion, increased probing depth, showing periodontal pockets and mobility⁷, leading to tooth loss, that during this period, could increase about 4 times^{3,6}.

Moreover, in relation to the inflammatory response, estrogens cause an inhibition of leukocyte chemotaxis and decrease the production of proinflammatory cytokines² such as interleukins⁴ 1 and 6: cytokines that are involved in stimulating bone resorption and promoting tissue degradation². Thus, its deficiency during climacteric would be directly associated with bone resorption and onset of osteoporosis in women^{1,2}, as its low concentration also decreases calcium absorption^{1,7}, increasing urinary excretion in the urine¹.

Osteoblasts produce a growth factor called TGF-beta that favors osteoblastic activity. When producing TGF-beta, osteoblasts

deposit it in the bone matrix and osteoclasts release it when they perform their resorptive activity. Upon release, TGF-beta stimulates osteoblastic proliferation and differentiation⁴. According to the literature, estrogens would induce gene transcription to produce this factor⁵ and also anticipate their release from the bone matrix^{4,5}.

When estrogens bind to their specific receptors on osteoblasts, they inhibit the release of substances that favor osteoclast activity and stimulate factors that inhibit these cells⁵. Studies associate higher bone mineral density with less tooth loss^{3,6,7}.

The appearance of root caries may also be characteristic of this period. Caries is a disease of multifactorial etiology (plaque, diet, saliva), infectious and transmissible. Contagion occurs through the action of Mutans microorganisms through enzymes present in plaque and acquired enamel film that metabolize fermentable carbohydrates in the diet, especially sucrose⁷.

With the susceptibility that they are exposed to developing gingival retractions due to bone resorption, the incidence of root exposure that culminating in a diet rich in sucrose and poor hygiene becomes more risky, favors the onset of the disease. In addition, a condition known as menopausal gingival stomatitis may be common, characterized by pain, burning, altered taste, dryness of the mouth, and a peculiar coloration of the gums that may range from pale pink to deep red^{3,7}.

Table 1: List of articles by subject and main conclusions.

Main subject	Articles	Study type	Main conclusions
Periodontal and bone disorders	5	4 literature review 1 original article	Changes in sex hormone concentration have modulatory effect on inflammatory response when periodontal disease occurs; More studies are necessary; Lower lumbar bone mineral density, lower teeth in postmenopausal women.
Muscle	3	1 thesis 2 original article	Hormonal fluctuations of female sex hormones influence muscle properties.
Nociception	4	1 dissertation 3 original articles	Pain sensitivity and anesthetic parameters were not different at different sex hormone concentrations; Estrogens facilitate spinal cord nociception transmission in rats; In humans, unlike experimental animals, changes in estrogen levels have little influence on nociception.
Salivary gland	3	2 literature reviews 1 original article	Ovariectomy does not morphologically alter the salivary gland, but delays the glandular regenerative process in its initial phase; The consequences of salivary flow changes should be analyzed and appropriate treatment evaluated.
Implant osseointegration	3	1 literature review 1 thesis 1 original article	Osteoporotic individuals have a higher rate of implant loss, but there is no final conclusion to be made at this time; Ovariectomy-induced estrogen deficiency negatively affected preexisting and newly formed bone around titanium implants inserted into rat tibia.
Dental tissue	3	3 original articles	Estrogen deficiency reduces dentinogenic capacity and calcium deposition in rat incisors.
Bisphosphonate use	4	2 literature reviews 1 original article	The type, administration and time of use of bisphosphonates influence the development of jaw osteonecrosis, the most involved being intravenous zolendronate and pamidronate and oral alendronate.
Oral care in menopause	5	5 literature reviews	Preventive treatment, oral hygiene care guidelines, periodic dental evaluations, periodontal instrumentation; History and clinical examination are important for diagnosis.

The role of female sex hormones in the salivary glands is not yet well established, but the presence of estrogen and progesterone receptors in these structures has been identified¹⁵. Other work also attributes estrogen deficiency during climacteric as one of the possible causes of atrophic changes in the oral epithelium²⁰.

Colombo et al.¹⁵, studying the role of female sex hormones in parotid gland regeneration in rats, concluded that ovariectomy delayed the initial phase of the gland regeneration process, and the unregenerate ones exhibited secretion granules that would lead to ovariectomy decreased salivary flow in agreement with another study¹⁶ that found a significant decrease in salivary flow in hysterectomized patients.

Regarding the role of estrogens in dental tissues, estrogens increase the 25-HCC hormone hydroxylation, interfering with dentin remodeling¹. This fact is in agreement with studies conducted in agreement with each other^{21,22}. One of the authors attributed estrogen deficiency to reduced dentinogenesis in rat lower incisors. In the present study, they found a significant reduction in odontoblast-specific proteins, as well as a reduction in the predentinal layer in these incisors, culminating in reduced compressive strength and calcium content²¹. When the pulp was studied, a lower level of blood supply was found in the presence of low estrogen concentration and a significant increase in high concentration²², in agreement with a study by Wang et al.²³ that also verified a decrease in odontogenic differentiation in the pulp stem cells when there is estrogen deficiency.

All of these disorders directly affect the different dental treatments. The prevalence of hyposalivation/psyloquesis¹⁵ culminating in a possible deficient dentinogenesis^{1,21,22} may predispose to the onset/progression of carious lesions and the difficulty of retention and adaptation of removable prostheses. Saliva plays an important protective role, highlighting its buffering effect¹ against enamel demineralization processes, in addition to the importance of surface tension for adhesion of prostheses. In addition, the risk of opportunistic oral infections such as candidiasis increases because some enzymes/proteins capable of inhibiting *Candida* growth are present in saliva, the yeast involved in the etiology of the infection¹⁷.

Given the high incidence of osteoporosis due, among others, to estrogen deficiency in climacteric women^{24,25}, many physicians have opted for bisphosphonate therapy and among them, nitrogenous bisphosphonates such as sodium alendronate. These in turn work in inhibiting bone remodeling initiated by osteoclasts, thereby inhibiting bone resorption and turnover index²⁶.

Duarte et al.¹⁸ studied about the impact of estrogen deficiency and its different therapies on bone tissue around implants. The results showed that estrogen replacement therapy and alendronate were able to prevent the negative influence of estrogen deficiency on the bone around the implants, and only alendronate was able to prevent the progression of bone loss from induced periodontitis

by agreeing with another study²⁷ which demonstrated that therapy with 70 µg/kg sodium alendronate (Teiroc; Teijin, Osaka, Japan) injected subcutaneously twice a week resulted in increased implant removal torque in ovariectomized rats and influenced positive way in the process of repairing these.

Still, the risk of developing jaw necrosis at implant placement or any ruthless procedure in patients using this drug exists and is well established in the literature through numerous reports and case series where the only common denominator among patients is the use of the medicine. In a review study²⁸, the author points out that this is not an absolute contraindication, but should be guided above all by rigorous oral hygiene and constant evaluation by the dentist (especially in continuous use for more than 3 years), paying attention to several factors such as time and form of administration.

The literature also presents work by Robert Marx et al.²⁹ that evaluating the risk of mandibular osteonecrosis in osteoporotic patients using bisphosphonates, concluded that in addition to the frequency with which the drug is used, the form of administration also influences the risk. The use of intravenous alendronate seems to increase the chances of developing osteonecrosis, whereas in oral use the risks are lower, but exist. The use of a marker for fasting C-terminal telopeptide bone suppression in the morning, according to the author, becomes an important complementary exam for the dentist in this situation, indicating high, medium and low risk patients to develop necrosis. Such study seems to emphasize the need to individualize the therapy adopted for each patient, evaluating several important and characteristic factors of each one, such as the presence of comorbidities, time and form of drug administration and urgency of the surgical procedure to be performed.

Thus, in view of the oral tissue manifestations caused by estrogen deficiency, the knowledge and performance of the dental surgeon in this area is essential. Prior to any conduct, the importance of anamnesis and detailed physical examination is emphasized, where there may be a bad interaction between the gynecologist and the dental professional.

Silva et al.¹⁷, in a literature review, it was found that the prescription of artificial saliva, diet with foods that stimulate salivary production, ingestion of water and fresh drinks and use of xylitol chewing gum for dentate patients can bring some comfort, but they are aware that the best conduct is to treat the causa. The professional may also resort to manipulation of the salivary glands, associated with the history/systematic physical examination and a possible sialometry test to diagnose the present hyposalivation.

Faced with the need to install implants or any surgical procedure in a patient with this condition, professional knowledge regarding complementary exams to be performed, such as the fasting C-terminal telopeptide bone suppression marker, is

essential²⁹. Thus, the dental surgeon could identify patients at high, low and medium risk of developing osteonecrosis and, together with the clinical and physical examination, get to a correct diagnosis and therapy²⁸.

The oral hygiene, diet and habits of these women should also be guided by the dentist. Poor hygiene of teeth, gums, tongue and prosthetics, a diet rich in sucrose and harmful habits such as smoking further increases the risks to the development of all the aforementioned disorders, such as periodontal, bone, hyposalivation, among others^{3,7}.

The importance of hygiene through the different types of brushes (unitufo, bitufo and interproximal if necessary), the use of fluoride toothpastes and flossing daily is emphasized. Also, the use of 0.12% chlorhexidine-based mouthwashes (10mL after day and night brushing), which assist in the control of bacterial plaque and caries prevention due to their action reducing the *Streptococcus mutans* flora, is also valid. Attention should be paid to the importance of professional follow-up due to possible adverse effects such as teeth staining and transient loss of taste³⁰.

Sub and supragingival prophylaxis and scraping for plaque removal and calculus should also be performed, showing

removal of bacteria and pathogens. Therefore, the application of fluoride varnishes and gels should also be performed when necessary³⁰.

Prevention^{3,7,17,28}, strict control of plaque and oral health education in the periods of female life prior to and during climacteric is the best way to minimize most oral problems, highlighting the tooth loss arising from all other disorders⁷.

CONCLUSION

Estrogen deficiency in the climacteric period negatively influences female oral health, interfering among others with bone, calcium and collagen metabolism and inflammatory events. Consequently, these women become more susceptible to changes such as: hyposalivation, osteoporosis/jaw osteopenia, menopausal gingival stomatitis, problems with dental remodeling, periodontal disease, and tooth loss. Preventive treatment by removing sub and supra gingival plaque, adequacy of the oral environment and hygiene and dietary guidance before and during the climacteric are the best ways to minimize the oral problems arising from this phase of a woman's life.

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