

Influence of Female Sex Hormones on Periodontium

Running Title: Influence of Sex Hormones

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Abstract:

Periodontitis is a multifactorial disease with an inflammation of periodontium. The initiation and progression of disease is influenced by many factors like systemic, local and microbial factors. Eventhough the microorganisms initiate the disease, susceptibility of host is important. Many studies have proven that hormones modify the host susceptibility and play a role in the development and progression of disease. This review focuses on the effects of female sex hormones on periodontal diseases during various phases of their life including puberty, menopause and pregnancy.

Keywords: Microorganisms, Periodontitis, Hormones, Pregnancy, Menopause.

Introduction:

Hormones can be classified into four groups based upon their chemical structure including steroids, glycoproteins, polypeptides and amines.⁽¹⁾ Sex steroid hormones have potent effects on the nervous and cardiovascular system and on major determinants of the development and integrity of the skeleton and oral cavity including periodontal tissues.⁽²⁻⁶⁾ Steroidal female sex hormones exerting influence on the periodontium mainly are oestrogen and progesterone. These hormones have been demonstrated in the gingiva, periodontal ligament cells, osteoblastic cells, scattered fibroblasts in the lamina propria. In the gingiva, these hormones induces cellular proliferation, differentiation and growth. Estrogens are naturally found in three forms; estradiol, estrone and estriol in which estradiol is the most potent estrogen which is secreted by ovary, placenta and also by the peripheral tissues⁽⁷⁾. It acts on the tissues through two distinct subtypes of Estrogen Receptors (ER alpha and beta). Progestones are also known as luteal hormones, luteoids, gestogens or progestins. They are secreted by the corpus luteum, the adrenal cortex and the placenta⁽⁸⁾. Progesterone synergistically acts with estrogen to control the menstrual cycle.

Periodontium is one of the target tissues in oral cavity for these hormones which has been demonstrated by the localisation of Estrogen Receptor (ER) and Progesterone Receptor (PgR) in the

human periodontium⁽⁹⁾. ER alpha is predominantly found in the tissues of ovaries, mammary gland and endometrium whereas ER beta found in the periodontal ligament⁽¹⁰⁾ gingival epithelium⁽¹¹⁾, salivary glands⁽¹²⁾. This review explains the effects of female sex hormones on women during their various phases of life including pregnancy, puberty, menopause.

Influence on periodontium during pregnancy:

Pregnancy is accompanied by remarkable endocrine alterations due to the increased production of Estrogen and progesterone hormones by the corpus luteum. These hormones reach their peak plasma levels, by the end of third trimester and the potential biological impact of these hormones take place in periodontal tissues during this period.⁽¹³⁻¹⁵⁾ Some of the gingival and periodontal alterations occurs during pregnancy are increased bleeding on probing, increased GCF flow, increased probing depth, tooth mobility and another alteration is the pyogenic granuloma which is an exaggerated proliferative fibrovascular inflammatory reaction located in the gingiva. On the other hand, poor oral hygiene leads to complications in child birth including preterm birth and low birth weight. The first study to report the influence of poor oral hygiene on the low birth weight and preterm infants was performed by Offenbacher and colleagues.⁽¹⁶⁾ Pregnancy gingivitis is extremely common and affects 30-100% of all pregnant women.⁽¹⁷⁾ It is characterised as dark red, swollen, smooth, bleeds easily and sometimes it may develop into localized gingival enlargements. If the local irritants are eliminated, the gingival changes usually resolve within a few months of delivery.⁽¹⁸⁾ The most prominent histological changes in the gingiva and oral mucous membranes during pregnancy were a loss of surface keratin, hydropic alteration of the stratum spinosum, hyperplasia of the stratum germinativum, and inflammatory changes in the lamina propria.⁽¹⁹⁾

Localized gingival enlargement resembling pyogenic granulomas also known as pregnancy tumor / pregnancy epulis/ epulis gravidarum have been described as a painless, exophytic mass also has an increased incidence in pregnant women at a prevalence of 0.2-9.6%.⁽²⁰⁾ It occurs during the second and third month of pregnancy which mostly involves gingiva followed by tongue, lips, buccal mucosa and the palate.^(17,21) It develops as an exaggerated inflammatory response to local irritants which may be sessile or pedunculated and range from red to purple in colour with minute fibrin spots.⁽¹⁴⁾ Kornman and Löesch reported that increased levels of estrogen and progesterone paralleled the proportions of P.gingivalis and P.intermedia in the gingiva during pregnancy.⁽²²⁾ Yokoyama and co-workers showed in their in vitro studies that estradiol is able to increase the growth of C. rectus, which is another potential periodontal pathogen.⁽²³⁾

Influence of periodontium during puberty:

Puberty is a complex process which has an increased levels of steroid sex hormones, testosterone in males and estradiol in females.⁽²⁴⁾ Many studies have shown that increased sex-hormone levels correlate with an increased prevalence of gingivitis.⁽²⁵⁾ Puberty gingivitis is clinically characterised by the onset of inflammation of the marginal and adjacent attached gingiva, especially in the interdental papillae with increased gingival bleeding during puberty. This gingival enlargement, is found primarily on the facial surfaces, with the lingual surfaces remaining unaltered. Many studies have reported that there is a significant increase in gingivitis during puberty and pubertal

period.^(1,25,26) There also is an increase in the quantity of plaque and other species including spirochetes, Capnocytophagia sp., Actinomyces sp., and Eikenella corrodens.^(27,28) There is a higher incidence of black-pigmented Bacteroides in the subgingival microflora compared with healthy sulci in puberty.⁽²⁹⁾

Influence of periodontium during menstrual cycle:

Menstrual cycle is divided into two phases: a follicular or proliferative phase and a luteal or secretory phase, corresponding to pre- and post-ovulatory events in the ovaries. Lindhe and Attström⁽³⁰⁾ have reported that on the day of ovulation there is a gradual increase of the gingival exudation is observed in all females, whereas in the secretory phase the gingival exudation is gradually decreased. Also he reported that women without clinical gingivitis showed no increase in gingival fluid, whereas those with gingivitis showed increase in gingival fluid. Holm-Pedersen and his colleagues have reported that during menses there is a minor increase in tooth mobility.⁽³¹⁾ Holm-Pedersen and Loe showed no correlation existed between the condition of the gingiva and the different phases of the menstrual cycle in clinically healthy gingiva, whereas a remarkable deterioration of pre-existing gingivitis was observed during the day of menstruation.⁽³¹⁾ Apart from gingival and periodontal changes, most of the women experiences few other significant changes. During the secretory phase of the cycle, when progesterone reaches its highest concentration, intraoral recurrent aphthous ulcers, herpes labialis lesions and candida infections may also occur in women.^(32,33)

Influence of oral contraceptives on periodontium:

Oral contraceptives acts to increase the hormonal levels of pregnancy and these are one of the most widely utilised drugs. Current oral contraceptives consist of low doses of estrogens (50mg/d) and progestins (1.5 mg/d). Many studies have reported that gingival changes also occurs as a result of the use of oral contraceptive agent. Kaufman⁽³⁴⁾ and Lynn⁽³⁵⁾ concluded that oral contraceptives induced gingival enlargement in healthy females with no history of gingival hypertrophy or hyperplasia. Gingival overgrowth was reversed in all the cases, when the oral contraceptives were discontinued. Jensen and colleagues⁽³⁶⁾ demonstrated a 16-fold increase in the population of Bacteroides species in women taking contraceptives, whereas Klinger and colleagues⁽³⁷⁾ reported that P.gingivalis and A.a. were not detected and there was a 4.8% increase in P.intermedia in women receiving a contraceptive containing 0.02mg ethinyl estradiol and 0.15mg desogestrel after a 20-day use of this contraceptive.

Conclusion:

Endogeneous female sex hormones alter the periodontal tissue responses to microbial plaque, and thus indirectly contribute to periodontal disease. They can influence the periodontium at different phases of life including puberty, menstruation, pregnancy and postmenopause.

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