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Influences of estrogen and progesterone on periodontium - A review

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Abstract:
Hormones exert significant influence in body physiology throughout life. Women in particular, experience hormonal variation under either physiological and non-physiological conditions, such as menstrual cycle or the use of oral contraceptives. Endocrine disturbances and hormone fluctuations affect periodontal tissues directly; they modify the tissue response to local factors and produce anatomic changes in the gingiva that may favor plaque accumulation and disease progression. Here is a brief review which focuses on hormonal influences reflected in the periodontium as they affect the physiology of host-parasite interactions in oral cavity.

Keywords: Steroid hormones, estrogen, progesterone, periodontium, pregnancy gingivitis, menopausal gingivostomatitis.

Introduction:
Hormones are specific regulatory molecules that modulate reproduction, growth and development and the maintenance of internal environments as well as energy production, utilization and storage. Homeostasis of the periodontium involves complex multifactorial relationships, in which the endocrine system plays an important role. The clinical changes seen in plaque-induced gingivitis are accentuated by circulating levels of the female sex hormones via mechanisms such as partial immune suppression, increased fluid exudation, stimulation of bone resorption and stimulation of fibroblast synthetic activity.

It is also observed that gingivitis is mild and reversible and is unclear whether pregnancy is related to higher risk of periodontitis, which is a more severe state of periodontal disease, and other clinical periodontal parameters. These clinical observations coupled with tissue specificity of hormone localization, identification of hormone receptors, as well as the metabolism of hormones have strongly suggested that periodontal tissues are targets for estrogen and progesterone. A better understanding of the periodontal changes to varying hormonal levels throughout life of women during puberty, menstrual cycle, pregnancy, menopause, and oral contraceptive use can help the general practitioner in diagnosis and treatment of periodontal diseases.

Effects of estrogen and progesterone on periodontium:

Microbial Changes:
1. Increased ratio of anaerobe to aerobe (P/E)
2. Increased numbers of Prevotella intermedia (P/E)

Vascular Changes:
1. Dilated gingival capillaries
2. Increased venule and capillary permeability.

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Cellular Changes:
1. Stimulated endothelial cells (P)
2. Decreased keratinization
3. Increased epithelial glycogen (P/E)
4. Altered polymerization of ground substance (P/E)
5. Increased collagen production (P)
6. Increased folate metabolism (P/E).

Immune Changes:
1. Depressed neutrophil chemotaxis and phagocytosis (P/E)
2. Depressed antibody response (P/E)
3. Depressed T cell response (P/E)
4. Stimulated prostaglandin synthesis in macrophages (P/E)

P: effect of progesterone, E: effect of estrogen.

Changes in the gingiva during puberty\textsuperscript{5-10} (Fig 1).
Puberty is frequently accompanied by an exaggerated response of the gingiva to local irritation. Pronounced inflammation, bluish red discoloration, edema and enlargement result from a degree of local irritation that would ordinarily elicit a comparatively mild gingival response. Pronounced anterior overbite aggravates the gingival changes in these cases because of the complicating effects of occlusal disharmony, and food impaction on the labial aspect of the mandibular teeth and palatal aspect in the maxilla. As adulthood is approached the severity of the gingival recession diminishes even when the local irritation has not been removed. Complete return to normal does not occur without treatment. Although the prevalence and severity of gingival disease is increased in puberty, gingivitis is not a universal occurrence during this period; many patients present no notable gingival disease during puberty.

Clinical and microbial changes during puberty include:
• Increase gingival inflammation without accompanying an increase in plaque levels\textsuperscript{17,18}.
• Increased prevalence of certain bacterial species such as Prevotella intermedia and Capnocytophaga species.
• Enhanced blood circulation in the end terminal capillary loops and associated increased prevalence of gingivitis/bleeding tendency.

Effect of menstrual cycle on periodontium\textsuperscript{11-13}:
Menstrual cycle is not generally accompanied by notable gingival changes. Minor gingival changes such as the periodic appearance of ‘bleeding gums’ or a bloated congested feeling in the days preceding the menstrual flow, are occasionally encountered.
• Oral changes that may accompany menses include swollen erythematous gingival tissues, activation of herpes labialis, apthous ulcers, prolonged hemorrhage following oral surgery, and swollen salivary glands.
• Some females are not aware of any gingival changes at all, while others complain of bleeding and swollen gums in the days preceding the onset of menstrual flow. These changes usually resolve once menses begin. In addition, an increase in gingival exudate caused by inflamed gingiva has been observed during the menstrual period and is sometimes associated with a minor increase in tooth mobility.
• In some women, postoperative hemorrhage occurs more frequently during menses than at other times and also increases in gingival exudate is seen during this period.

Changes during pregnancy\textsuperscript{13-17}:
(Fig 2 & 3).
During pregnancy there is a tendency toward excessive vascularity in the response of the gingiva to local irritation. This exaggerated response to local irritation accounts for the differences in the appearance of gingival disease in pregnant and nonpregnant individuals. Pregnancy itself does not cause gingival disease. The gingiva in pregnancy presents no notable clinical changes in the absence of local irritation. The commonly used term pregnancy gingivitis is misleading because the gingivitis is caused by local irritants; pregnancy is a secondary modifying factor. Gingival changes usually appear about the third or fourth month of pregnancy. It is quite common for a patient with slight chronic gingivitis, which had attracted no particular attention, to become aware of her gingiva at that time because the previously inflamed areas become excessively enlarged and edematous and more noticeably discolored. Patients having chronic marginal gingivitis with a slight amount of bleeding before pregnancy become concerned about the increased tendency to bleed. Approximately two months after parturition, the severity of the gingivitis subsides but does not disappear completely unless the local irritants are removed.
• Increased tendency for gingivitis and larger gingival probing depths and periodontitis.
• Increased susceptibility to infection.
• Decreased neutrophil chemotaxis and depressed antibody production.
• Increased numbers of periodontopathogens (especially Porphyromonas gingivalis and Prevotella intermedia).
• Increased synthesis of PGE\textsuperscript{2}.
Post-menopausal gingivitis\(^{18}\): (Fig 4 & 5):
This occurs during the menopause or in the postmenopausal period. Mild signs and symptoms sometimes appear associated with the earliest menopausal changes. Oral disturbances are not a common feature of the menopause. Gingiva and remaining oral mucosa are dry and shiny, vary in color from abnormal paleness to redness, and bleed easily. There is fissuring in the mucobuccal fold in some cases. The patient complains of a dry, burning sensation throughout the oral cavity associated with extreme sensitivity to thermal changes, abnormal taste sensations described as ‘salty’, peppery or sour and difficulty with removable partial prosthesis.

Clinical changes in the periodontal tissues during menopause and post menopause:
- Reduction in epithelial keratinization.
- Redness and abnormal paleness of the gingival tissues.
- Bleeding on probing and also during brushing.

Effect of osteoporosis upon Periodontium:
- Poor wound healing, less attachment formation
- Reduced bone mineral content in the jaws
- Increase of periodontosis and tooth loss.

Effects of oral contraceptives on periodontium\(^{19,20}\):
- Inflammation ranges from mild edema and erythema to severe inflammation with hemorrhagic or hyperplastic gingival tissues.
- A 50 per cent increase in gingival fluid volume.
- A 16-fold-increase in Bacteroides species effects of hormone replacement therapy on the periodontal tissues.
- A protection takes place against tooth loss
- Reduction in gingival bleeding

Women taking oral contraceptives demonstrate a significant increase in the number of Prevotella species in the gingival microflora. Increased female sex hormones substituting for the naphthoquinones required by certain Prevotella species most likely are responsible for this rise.

Influence of sex hormones on periodontal/implant wound healing:
At a molecular level, research has also shown that sex hormones have a regulatory effect on growth factors involved in the wound healing such as the keratinocyte growth factor which has been known to have wound healing regulatory effect including stimulation of proliferation, migration and morphogenesis of pluripotent

Conclusion:
Steroid hormones play an important role in influencing periodontal disease progression and wound healing. It is also clear that not all patients and their periodontium respond in the same way to similar amounts of circulating hormones. The influence of these hormones can be minimized with good plaque control as well as hormone replacement therapies. Further research is definitely needed in this area to delineate the effects of hormones on periodontal tissues and its management.
Fig 4 & 5: Clinical photographs of post-menopausal gingivitis.

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