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Effects of endogenous sex hormones on the periodontium

A graduation project is submitted to the dental Department in partial fulfillment of the requirements for the degree of Bachelor of dentistry

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بسم الله الرحمن الرحيم

(قَالُواْ سُبۡحَٰنَكَ لَا عِلۡمَ لَنَآ إِلَّا مَا عَلَّمۡتَنَآۖ إِنَّكَ أَنتَ ٱلۡعَلِيمُ ٱلۡحَكِيمُ)

صدق الله العلي العظيم

SUPERVISOR CERTIFICATION

I certify that the preparation of this project entitled

Graduation Document

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Was made under my supervision at dentistry college/maysan University in partial fulfillment of the Requirements for the Degree of Bachelor of dentistry.

Signature

Supervisor Name : Assistant Professor Dr. Khitam Jassim

Date: / /2024

Acknowledgement

With all meanings of pride and honor, I dedicate this humble research to all those who fell for the sake of this holy land and lit up with their blood a darkness that almost destroyed this country. To our martyrs, the flame of liberation and the beacon of the future.

Abstract

Hormones are specific regulatory molecules that have potent effects on the major determinants of the development and the integrity of the skeleton and oral cavity including periodontal tissues. It is clear that periodontal manifestations occur when an imbalance of these steroid hormones take place. This review focuses on the effects of endogenous sex hormones on the periodontium and the goal was to inform and update practitioners'knowledge about the impact of these hormones on periodontal status. In addition, this review will analyze how these hormones influence the periodontium at different life stages such as puberty, menstruation, pregnancy, menopause and postmenopause. It is clear that endogenous sex steroid hormones play significant roles in modulating the periodontal tissue responses. A better understanding of the periodontal changes to varying hormonal levels throughout life can help the dental practitioner in diagnosis and treatment.

Key words: Steroid hormones, periodontium, periodontal diseases, female, male

Introduction

Apart from the microbial etiology for periodontal diseases, a number of factors, namely, environmental and genetic factors, have been proposed, to modulate host microbial interactions, which ultimately decide the clinical picture of periodontal disease (50).

The periodontium involves complex multifactorial relationships, in which the endocrine system also plays an important role for the homeostasis (35) . Hormones are also known as specific regulatory molecules that modulate reproduction, growth, development and the maintenance of internal environments as well as energy production, utilization and storage(35).

As well as being the regulators of reproductive functions, 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 (36,28) .

Currently accepted periodontal disease classification recognizes the influence of endogenously produced sex hormones on the periodontium. Under the broad category of dental plaque induced gingival diseases that are modified by systemic factors, those associated with the endocrine system are classified as puberty, menstrual cycle and pregnancy associated gingivitis (36) .

Therefore, this review will focus on the effects of endogenous sex hormones on the periodontium .

Endogenous sex hormones

Androgens (testosterone)

Androgens are concerned with normal spermatogenesis and are responsible for the development of the Secondary sexual characteristics in male puberty (57). There are two types of androgens: gonadal androgen, Dihydrotesterone (DHT), and adrenal androgen, dehydroepiandrosterone. The former is the most active form. The adrenal androgen, androstenedione, is converted to testosterone and to estrogens in the circulation, and Represents an important source of estrogens in men and postmenopausal women (37).

Androgens may play a Significant role in the maintenance of bone mass and inhibit osteoclastic function, inhibit prostaglandin Synthesis and reduce interleukin-6 (IL-6) production during inflammation (38,58) . Further, testosterone stimulatesBone cell proliferation and differentiation and therefore has a positive effec on bone metabolism (25) .

Impacts: Effects of androgens on the periodontal tissues :

1- Enhance matrix synthesis by periodontal ligament fibroblasts and osteoblasts (26)

2 - Enhance osteoblast proliferation and differentiation (4,25)

3 - Inhibit prostaglandin secretion (7)

4 - Reduce IL-6 production during inflammation (51)

Estrogen and Progesterone

Women change physically through the production of sex hormones at puberty. This begins with the secretion Increases vascular dilatation, thus increases permeability Increases the production of prostaglandins by the Anterior pituitary of gonadotropin hormones (follicle-stimulating hormone and luteinizing hormone), which Causes the ovaries to begin cyclical production and secretion of female sex hormones (estrogen and Progesterone) (1) . Estradiol is the principal premenopausal estrogen and is produced by the female gonad, the Ovary. Estradiol is additionally secreted by the placenta and certain peripheral tissues(64) .Estrogens play a crucial Role in many vital activities, including the development and maintenance of secondary sex characteristics, Uterine growth, pulsatile release of luteinizing hormone from the anterior pituitary gland and the development of Peripheral and axial skeleton (39, 40 ,41).Another hormone critical for females is progesterone secreted by the corpus Luteum, placenta, and the adrenal cortex, and it is active in bone metabolism and has significant effect in the Coupling of bone resorption and bone formation by engaging osteoblast receptors directly (16,14). Estrogen and Progesterone have significant biological actions that can affect other organ systems including the oral Cavity (29,30) . Receptors for estrogen and progesterone have been demonstrated in the gingiva, in which the Gingiva can be thought of as a target organ for progesterone and estrogen (62,63). Estrogen receptors are also found On periosteal fibroblasts, scattered fibroblasts of the lamina propria, and also periodontal ligament fibroblasts And osteoblasts (8,27). The effects of estrogen and progesterone on periodontal tissues are summarized below.

Impacts: Effects of estrogen on the periodontal tissues :

1- Stimulates the proliferation of the gingival fibroblasts (2)

2 - Stimulates the synthesis and maturation of gingival connective tissues (2)

3 - Increases the amount of gingival inflammation with no increase of plaque (55)

4- Increases cellular proliferation in blood vessels (30,31)

5 - Decreases keratinization while increasing epithelial glycogen that results in the Diminution in the effectiveness of the epithelial barrier (42)

6 - Reduces T-cell mediated inflammation (24)

7 - Suppress leukocyte production from the bone marrow (24,4)

8 - Stimulates PMNL phagocytosis (18)

9 - Inhibits PMNL chemotaxis (23)

10 - Inhibits proinflammatory cytokins released by human marrow cells (15)

Impacts: Effects of progesterone on the periodontal tissues :

1- Inhibits collagen and noncollagen synthesis in PDL fibroblast (57,60)

2- Inhibits proliferation of human gingival fibroblast proliferation (44)

3- Alters rate and pattern of collagen production in gingiva resulting in reduced repair And maintenance potential (52,61)

4- Increases vascular dilatation, thus increases permeability (4)

5- Increases the production of prostaglandins (9)

6- Increases PMNL and prostaglandin E2 in the gingival crevicular fluid (GCF) (9,10)

7- Reduces glucocorticoid anti-inflammatory effect (5)

8 - Increases the metabolic breakdown of folate which is necessary for tissue Maintenance and repair (52)

Periodontal manifestations related to endogenous sex hormones

Gingival alterations during puberty, pregnancy, and menopause are associated with physiologic hormonal changes in the patient. The changes associated with each phase of the patient life cycle

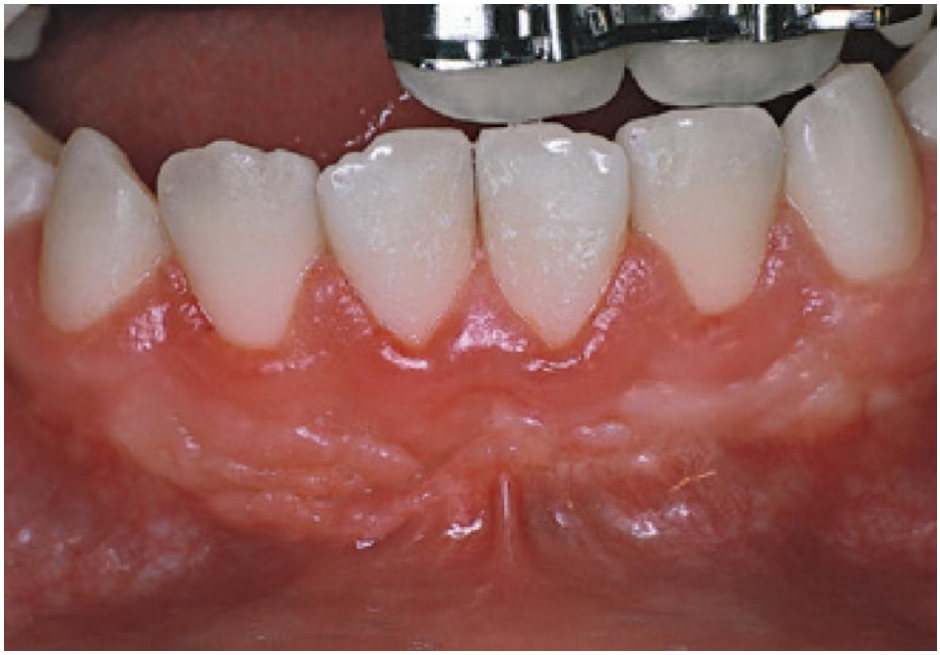
The puberty

Puberty marks the initiation of changes from maturation into adulthood (11). It is associated with amajor increase in the secretions of the sex steroidhormones: testosterone in males and estradiol infemales.

Several cross-sectional and longitudinal studies have demonstrated an increase in gingival inflammation without accompanying an increase in plaque levels during puberty of both sexes (43,19-58).

Increased gingival inflammation was positively correlated with an increase in serum estradioland progesterone (49) , so the women experience greater changes in gingival health than men as result of alterations in circulating plasma sexsteroid hormones, which continue into and past the menopause.(20)

Local causes that would typically cause a very modest gingival reaction instead cause noticeable inflammation, edoema, and gingival hypertrophy(eFig. 3.1)(48).



eFig. 3.1 Gingivitis during puberty, with edema, discoloration, and enlargement of the entire gingival margin and papillary areas around the mandibular incisors(48).

There is an increased prevalence of certain bacterial species such as Prevotella intermedia and Capnocytophaga species compared with healthy sulci in puberty(16).

Capnocytophaga species have also been noted to increase in number as well as proportion in the subgingival milieu during puberty, and have been shown to correlate with an increased bleeding tendency(16).

Menstruation

The reproductive or menstrual cycle is the cyclical pattern of increased synthesis and secretion of progesterone and oestrogen that coincides with puberty(57). The duration of normal reproductive cycle is 28 days(45), the monthly reproductive cycle has two phases (46,32). **The first phase** is the follicular or proliferative phase where the levels of follicle stimulating hormone and estrogen are elevated, and estrogen peaks approximately two days before ovulation(17). After ovulation the **secretory or luteal phase** begins at approximately day 14 of the cycle. This phase is characterized by the synthesis and release of estrogen and progesterone by the follicular cells (17).

During the menstrual period, the prevalence of gingivitis increases , Some patients may complain of bleeding gums or a bloated (48) .

The exudate from inflamed gingiva is increased during menstruation, which suggests that preexisting gingivitis is aggravated by menstruation; however, the crevicular fluid of normal, healthy gingiva is unaffected (21). Throughout the menstrual cycle, there is little change in the mobility of teeth (12) . When ovulation occurs, which can happen up to 14 days early, and during menstruation, the number of bacteria in the saliva increases (54).

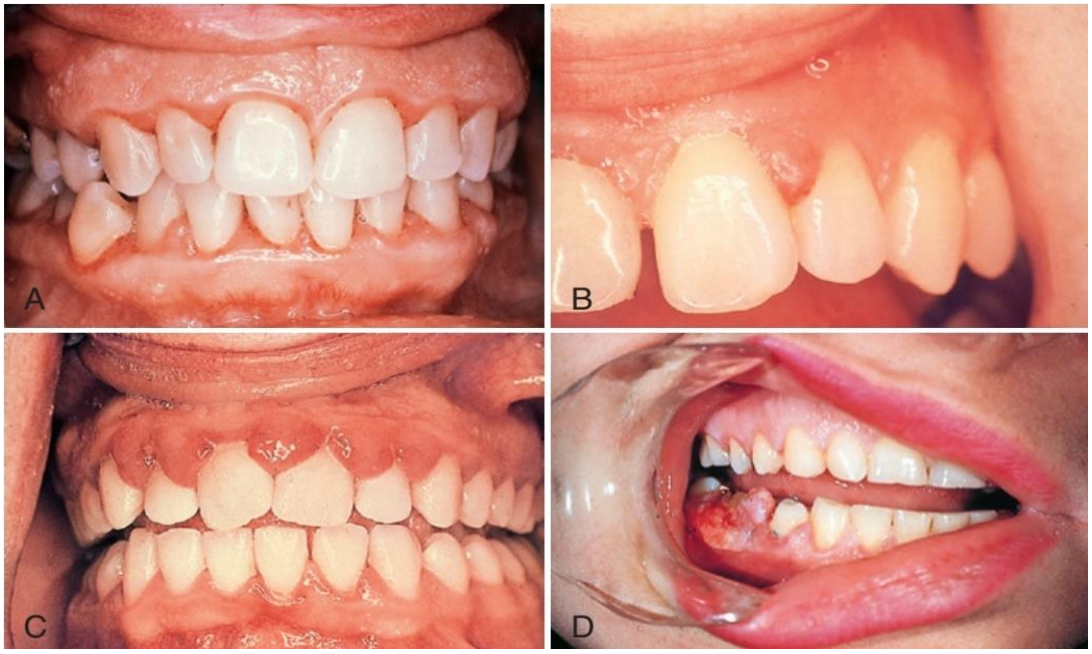
Women may also experience intraoral recurring aphthous ulcers (13), herpes labialis lesions, and candida infections during the luteal phase of the cycle, when progesterone is at its maximum level (56) .

The pregnancy

The gingival changes of pregnancy were described as early as the late 1800s, before any knowledge about hormonal changes in pregnancy was available (3,53). Gingivitis is not brought on by pregnancy, as is the case with other systemic disorders. Just like in nonpregnant women, bacterial plaque is the cause of gingivitis during pregnancy(48). The hormonal changes of pregnancy accentuate the gingival response to plaque and modify the resultant clinical picture (eFig. 3.2)(48). No notable changes occur in the gingiva during pregnancy in the absence of local factors(48).

The reported incidence of gingivitis during pregnancy in well - conducted studies varies from 50% to 100% (33,47) . Pregnancy affects the severity of previously inflamed areas, but it does not alter healthy gingiva. Impressions of increased incidence may be created by the aggravation of previously inflamed but unnoticed areas (48) . Tooth mobility, pocket depth, and gingival fluid are also increased during pregnancy (22,34,65) .

During pregnancy, gingivitis becomes more severe starting in the second or third month. Patients who previously had moderate chronic gingivitis that received little care become conscious of their gingiva because previously inflamed areas grow, become edematous, and most noticeably, become discoloured. (see eFig.3.2A through C)(48).



eFig. 3.2 Periodontal condition during pregnancy. (A) Marginal erythema and easily bleeding gingiva in a woman who is 5 months pregnant. (B) Localized incipient gingival enlargement between the maxillary central and lateral incisors in a woman who is 4 months pregnant. (C) Generalized gingival enlargement of the interdental papilla and gingival margins on the facial surface of the maxillary incisors in a pregnant woman. (D) Extensive gingival enlargement localized on the buccal surface of the mandibular premolars in a pregnant woman. These lesions are often referred to as “pregnancy tumors” (48).

Partial reduction in the severity of gingivitis occurs by 2 months postpartum, and after 1 year, the condition of the gingiva is comparableto that of patients who have not been pregnant (6). Tooth mobility, pocket depth, and gingival fluid are also reduced after pregnancy.

The gingiva is inflamed and varies in color from bright red to bluish red (65). The marginal and interdental gingivae are edematous; they pit on pressure, appear smooth and shiny, are soft and pliable, and sometimes have a raspberry-like appearance. The extreme redness results from marked vascularity, and there is an increased tendency to bleed. The gingival changes are usually painless unless they are complicated by acute infection(48). In some cases, the inflamed gingiva forms discrete tumor-like masses, which are referred to as pregnancy tumors (see eFig. 3.2D)(48).

Conclusion

It is clear that endogenous sex steroid hormones play significant roles in modulating the periodontal tissue responses and may alter periodontal tissue responses to microbial plaque, and thus directly may contribute to periodontal disease. They can influence the periodontium at different life times such as puberty, menstruation, pregnancy, menopause and postmenopause. A better understanding of the periodontal changes to varying hormonal levels throughout life can help the dental practitioner in the diagnosis and treatment.

Here are some key considerations for dentists when managing periodontal health in patients affected by hormonal changes:

Specific Recommendations for Different Life Stages:

1. Puberty:

- Emphasize proper oral hygiene.

- Regular professional cleanings.

- Education on the importance of plaque control.

2. Menstrual Cycle:

- Schedule cleanings and treatments at times of the cycle when symptoms are minimal.

- Reinforce oral hygiene practices.

3. Pregnancy:

- More frequent dental check-ups and cleanings.

- Non-surgical periodontal therapy if needed.

- Avoid elective dental procedures during the first trimester and late third trimester.

General Recommendations:

1.Diet and Nutrition:

- Encourage a balanced diet rich in vitamins and minerals, particularly calcium and vitamin D, to support bone health.

2.Lifestyle:

- Advise smoking cessation as it can exacerbate periodontal disease.

3.Stress Management:

- Chronic stress can negatively impact the periodontium, so stress management techniques can be beneficial.

4.Education and Communication:

- Regularly update the patient's medical history, including hormonal therapies.

- Educate patients about the link between hormonal changes and periodontal health.

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