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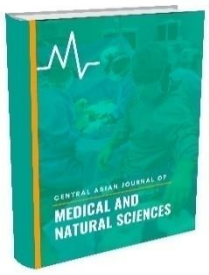

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On the Pathogenesis of Periodontal Disease in Mineral Metabolism Disorders

1. **Sunnatullo Gafforov**
2. **Ulugbek Nazarov**
3. **Gulomjan Khalimbetov**

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[1, 2, 3] Department "Dentistry, Pediatric Dentistry and Orthodontics", Centre for the Professional Development of Health Professionals under the Ministry of Health of the Republic of Uzbekistan

Abstract: The article presents a review of the literature on the pathogenesis, diagnosis and treatment of various forms of periodontal disease. Particular attention is paid to somatic diseases and their role in the pathogenesis and clinical course of periodontal disease. In conclusion, the author substantiates the prospects for further, more detailed study of the role of mineral and bone metabolism disorders in the emergence and development of aggressive forms of periodontitis, which, in the author's opinion, will enable to obtain new data on the state of system regulatory factors and their influence on local mechanisms of periodontal tissue damage, which will not only improve diagnosis of various forms, but also increase the effectiveness of treatment of this pathology.

Keywords: dentistry, somatic pathology, periodontal tissue, bone tissue, atrophy, osteoporosis, matrix metalloproteinase's.

Diagnosis and treatment of periodontal disease, we know, remains one of the pressing issues of our time. At the same time, the prevalence of this pathology is steadily increasing. According to the WHO, the prevalence of this pathology ranges from 40% to 70%, and trends of periodontal disease occurring as early as childhood have also been noted [11, 28]. This includes a combination of cardiovascular disease (CVD), rheumatism, diabetes mellitus, gastric ulcer, 12 duodenal ulcer, chronic renal failure and temporomandibular system pathologies with various periodontal pathologies in clinical trials. Also, the findings do not rule out the presence of a reverse, periodontal infection - the cause of systemic disease [1, 3, 9]. In addition, several authors argue that periodontitis is a precursor of diabetes mellitus, hypertension, atherosclerosis, associated with the cardiovascular, central nervous, endocrine, gastrointestinal systems, which results in a corresponding pathogenesis cause-effect relationship [12, 16]. For example, osteoporosis is a common systemic skeletal disease characterized by low bone mass and disorders of bone micro architecture, leading to increased bone fragility and fracture risk. For practitioners, the problem of choosing an adequate therapy for generalized periodontitis is quite acute with osteoporosis. Studies on the relationship between mineral metabolism and periodontal disease, although numerous, are quite contradictory, which necessitates additional research and detailed analysis using modern research methods [20].

Also, we know that the literature on the state of mineral metabolism in aggressive forms of generalised periodontitis is abundant, but quite contradictory, which determines the need for additional research, including genetic markers. However, there is increasing speculation about a significant genetic component in the development of various periodontal diseases. In recent years, new data on the status of mineral and bone metabolism in patients with generalised periodontitis and the identification of reliable genetic markers of predisposition to this pathology have been reported, helping to develop diagnostic criteria that can be used to more clearly determine the course and prognosis of the disease [12, 20].

Both local and general factors are important in the etiopathogenesis of periodontal disease. For example, it is generally accepted that the inflammatory process begins with the reaction of monocytes and macrophages, cells that initiate an acute-phase response (APR) to lipopolysaccharides (LPS) of the bacterial wall. The role of polymorphonuclear leukocytes, platelets, T-lymphocytes, endothelial cells, mast cells and fibroblasts in this mechanism is poorly understood, and macrophages also secrete many inflammatory mediators, such as free radicals and reactive oxygen species, prostaglandins and various regulatory cytokines. According to the authors, following the release of first-wave cytokines such as interleukin-1 and 3 (IL-1B), tumour necrosis factor alpha (TNFa) and interleukin-6 (IL-6), many changes occur as a result of inflammatory stress, including cytokine receptor expression. IL-1B, TNFaa and IL-6, in turn, initiate the second phase of reactions in the OPF to inflammation [20]. They also secrete macrophage inhibitory factor (MIF), which promotes the retention of monocytes and macrophages within the inflammatory focus and counteracts the anti-inflammatory and immunosuppressive effects of corticosteroids on cytokine production by macrophages and T cells, and, IL-1 and IL-6 also activate neuroendocrine secretion mechanisms [6, 23]. Studies have found that, like IL-1, IL-6 expression is increased in areas of periodontal inflammation. IL-6 has been identified in periodontal pocket fluid (PPF) collected from periodontal lesions, and a correlation between IL-6 concentration and clinical severity of disease has also been reported. IL-6 is secreted by human osteoblasts in response to exposure to bone resorbing agents including IL-ip, TNFaa, lipopolysaccharides and in vitro acts as a potent inducer of osteoclast formation [20].

Multiple enzymatic pathways for the degradation of the extracellular matrix of periodontal tissue have been identified [5]. They include matrix metalloproteinases (MMPs), a family of more than ten metal-containing enzymes [13]. MMPs are known to be part of all known extracellular matrix proteins, including intratissue collagen, and MMP activity is in turn regulated by specific inhibitors known as tissue inhibitors of metalloproteinase's (TIMPs). In response, activated stromal cells secrete tissue metalloproteinase inhibitor, which inhibits the metalloproteinase that causes matrix degradation during inflammation [3, 20]. Based on the above, it is clear that cytokines such as IL-1 and TNF, each with catabolic properties, are involved in the destructive process that characterises periodontitis, with the role of IL-6 not being fully clarified at present.

It is now known that bone is constantly self-renewing through the processes of resorption and formation. Bone, however, is not only a supporting organ, but also the most important participant in mineral metabolism with a significant reserve of inorganic phase. The systemic regulation of bone remodelling is carried out by a number of hormonal factors involved in calcium homeostasis. Systemic factors including parathyroid hormone (PTH), calcitonin (CAT), calcitriol, glucocorticoids, and gender hormones are directly involved in calcium homeostasis. Local factors such as cytokines and prostaglandins, growth and differentiation factors mediate the influence of systemic factors, some of which are produced by bone tissue cells when activated in a paracrine or autocrine manner. The study of these components of the complex mechanism of chronic periodontitis remains the most interesting and important unresolved task at present.

We know that calcium is one of the main components of mineralised tissue. More than 90% of the body's calcium is found in the bones, where it forms hydroxyapatite crystals together with phosphate. Most bone tissue can freely exchange calcium with extracellular fluid. In blood plasma, calcium is found in three forms: 1) in complex with organic and inorganic acids; 2) in protein-bound form; 3) in ionised form. Active ionised calcium (Ca2+) normally accounts for about 50% of the calcium excreted by the kidneys, where part of it is reabsorbed (3). Calcium is present in the serum in an amount of 2.2-2.75 mmol/l. Extracellular ionised calcium is the metabolic active fraction. It is essential for vital processes, including enzymatic reactions, mitochondrial and cell membrane functioning, intercellular communication, neural transmission, myocardial contractility, blood clotting and much more. The endocrine system maintains serum ionised calcium concentrations within a very narrow physiological range. The level of ionised calcium depends on the interaction of processes that occur in the gut, kidneys and skeleton, and is controlled by parathyroid hormone, calcitriol and calcitonin. The most important among them is parathyroid hormone, which rapidly increases calcium levels through its effect on all three target organs[17].

A number of literatures state that calcitonin is a natural, potent and rapid inhibitor of osteoclastic activity. Calcitonin inhibits osteoclast activity and thus prevents the mobilisation of calcium from bone tissue and stimulates bone mineralisation. This contributes to a decrease in blood calcium concentration, and calcitonin also causes osteoclast compression and inhibits the formation of resorptive lacunae in bone and dentin layers. In this case, a decrease in calcitonin levels in patients of both genders in response to hypercalcaemia, and in an earlier paper the opposite data were given [3, 9, and 24]. Therefore, the role of this hormone in the regulation of calcium homeostasis has not yet been defined, moreover, it is denied by some authors, and the question of how great is its role in the maintenance of calcium homeostasis is still open.

Calcitonin also has a significant effect on phosphorus metabolism, promoting its incorporation into bone tissue and periosteal fluid, while reducing the release of calcium from bone into the blood plasma. Its anabolic effect has long been successfully used to treat postmenopausal osteoporosis in women. The use of Calcitonin in the treatment of ChGP has also been used in the national dental practice [3, 25].

Impaired calcium homeostasis has been found not only in adults, but also in children with multiple dental hard tissue lesions [9, 14, 18, 22]. Hypercalcaemia in periodontal disease is associated with increased orthoclastic desorption of the alveolar process. When the interalveolar septum structure is fine, urinary calcium excretion is increased and inorganic phosphorus excretion is decreased [19]. Disorders of calcium, phosphorus and magnesium homeostasis have also been found in youths with ChGP [7,9,21]. However, the clinical interpretation and specific pathogenesis of the shifts that occur have yet to be elucidated.

Despite the increased interest on the part of dentists to study the role of impaired phosphorus-calcium metabolism in the pathogenesis of diseases of the dento-alveolar system, we have encountered few studies devoted to the study of calcium-regulating hormones in patients with dental pathology, including periodontal disease [9, 12, 20, 25]. At present, dentists are particularly interested in studying the effects of metabolic osteopathy on jawbone health. Disorders of mineral and bone metabolism associated with hypogonadism in postmenopausal women are one of the most common causes of this pathology. Among other things, the problem of periodontal inflammation in the setting of systemic osteoporosis is, in itself, of particular interest.

Numerous epidemiological studies have established not only an age-related decrease in skeletal bone mineralisation, but also significant gender differences in bone mineral density (BMD). Men have a higher bone mineral density than women, which may be due to their larger bones and greater bone mass in general. There are also different levels of peak bone mass attainment, which is higher in men

than in women due to the late onset of puberty. However, a number of studies have reported that the risk of reduced bone mineral density in men after 50 years of age is significantly lower than in women [8, 9, 20].

A review of the literature suggests that the relationship between systemic osteoporosis and periodontal disease is poorly understood. The available evidence is contradictory and requires further research that will provide a clearer understanding of the mutual influence of these diseases, which may contribute to the diagnosis and prevention of both osteoporosis and periodontitis. At present, it can only be stated with certainty that decreased skeletal mineralisation exacerbates pathological changes in the periodontium, but there is sparse evidence in the literature about the nature of the relationship between the development of osteoporosis and inflammatory periodontal tissue lesions [22].

The X-ray picture of the changes that occur has been well studied. The mineral content of the lower jaw decreases with age, and this process is more active in women than in men. Many authors have paid much attention to the study of alveolar atrophy after tooth extraction, but cases of alveolar resorption of the jaws in persons who have teeth have also been described [7,4, 23]. For a long time, pathological processes in the alveolar bone were considered in isolation from the bone condition of the supporting skeleton. At the same time, it has been noted that systemic osteoporosis caused by estrogen deficiency in menopausal women extends to the maxillofacial system [12, 22].

Also, an increase in calcium and fluoride inclusion in the bone of the femur bone of the animals under conditions of experimentally reproduced periodontitis was noted, suggesting a close functional relationship between the skeletal bones and the alveolar component of the periodontium. Women with secondary amenorrhoea, after Oophorectomy, with natural menopause and a control - women with normal ovarian function - were examined. The changes in the periodontium were accompanied by marked atrophy of the alveolar bone. It was particularly noted that the severity of osteoporosis was greater in the alveolar bone, which is dominated by cancellous bone, than in the forearm bone, which is dominated by compact bone. It is emphasised that osteoporosis is often accompanied by atrophy of the alveolar processes of the jaw, which may serve as an additional diagnostic sign of low bone mineral density [8, 9, 22, 23]. However, the relationship between the development of systemic osteoporosis and the occurrence and development of periodontal disease has not been conclusively established. In addition, no association has been found between systemic bone loss, periodontal disease and adentia.

Despite the above data, there are conclusions that there is no correlation between the number of teeth in the mouth and periodontal tissue status, and changes in bone mineral density of the axial skeleton [2]. Moreover, this trend was found not only in women, but also in men with osteoporosis. Also, many common chronic diseases manifest secondary osteoporosis; a typical example is treatment with cytotoxic drugs, cytostatics, immunosuppressants, glucocorticoids (GC), which can lead to impaired bone cell function [26]. Rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and polymyalgia rheumatica, combined with local and systemic osteoporosis. Furthermore, immobilisation, nutritional deficiencies and especially GC therapy predispose to the development of osteoporosis in these patients, and it is noted that the incidence of osteoporotic fractures in patients with rheumatoid arthritis who have been treated with GC is significantly higher compared to age-matched controls. Another author, suggesting that the mechanisms of local inflammation in this pathology are identical, carried out a comparative assessment of the levels of MMP-8, MMP-13 and TIMR in the gingival fluid (GF) of patients with rheumatoid arthritis and periodontitis. The results of the study revealed a similar trend towards increased enzymes in GF in patients suffering from these diseases [27].

We know that aggressive periodontitis in a relatively short period of time (5-7 years) results in significant tooth loss due to rapid lysis of the alveolar bone and it is the most common form of

corrosion-progressive periodontitis (CPP), characterised by the absence of marked signs of inflammation. Recent scientific data state that among the possible reasons are both the growing interest of practising dentists in periodontics and the increased demands on the quality of life and health of the economically and socially mobile young population [22, 23]. It is generally accepted that the main etiological factor for all forms of periodontitis is microbial, the presence of periodontopathogenic flora, smoking and poor oral hygiene are also etiological and pathogenetic complexes, varying in number or combination of genes that control periodontal tissue development or are competent in cellular and humoral immunity, and may be a risk factor for disease. But on the other hand, the fact of uneven bone destruction throughout the same patient's dentition, on different jaws or even on different surfaces of the same tooth deserves attention. Clinical and radiological examination of children and adolescents suggest a different incidence of an aggressive form of periodontitis (AFP) - localised juvenile periodontitis and generalised juvenile periodontitis [9, 22, 23]. For example, 2.27% in the USA, 0.1% in Denmark, 0.1% in Finland, 0.8% in Nigeria, 0.3% in Brazil, 0.17% in England and 0.32% in Chile. Studies have shown that AFP is equally common in children and adolescents regardless of gender.

Currently, a new and very promising area of periodontology is the study of the role of juvenile skeletal bone changes on the development and course of periodontal disease. In the clinic, impaired bone mass formation peaks more frequently by the age of 30. Genetic, hormonal, nutritional and mechanical causes are responsible for the formation of low peak bone mass. The likelihood and rate of development of osteopenia or osteoporosis depend on the level of peak bone mass formation. Abnormalities in the formation of the supporting skeleton are more common in children with a low peak bone mass. When examining the relationship between low bone mineral density and the development of periodontal disease in young adults, a new aspect of this problem that has been actively discussed among dentists in recent years cannot be overlooked. Body mass is considered an important determinant of peak bone mass. A low body mass index (BMI less than 20 kg/m2) is an indicator of a low BMD. For example, a direct correlation between body mass index and the presence of periodontal pathology in various age groups of children has been established; also of interest are the data on the peculiarities of periodontal tissue condition in teenagers with dentoalveolar deformities, bite disturbances, crowding of teeth as well as in children with disorders of bone mass peak formation. [7,9, 22, 23].

This, analysis of the available literature has shown that the role of mineral and bone metabolic disorders in the emergence and development of aggressive forms of periodontitis has broad scientific promise. Obtaining new data on the status of systemic regulatory factors and their influence on local mechanisms of periodontal tissue damage will not only improve diagnosis of various forms, but will also increase the effectiveness of treatment of this pathology.

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