***DETERMINATION OF EARLY DIAGNOSIS MARKERS FOR DIGITAL TISSUE (ACE (I/D), TNF-α (308G/A), eNOS (894G/T), MMP20, KLK4, ENAM)ON BACKGROUND OF PERIODONTAL TISSUE DISEASES IN A YOUNG PEOPLE.***

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**The relevance of the problem.** The results of epidemiological studies of domestic and foreign scientists demonstrate significant differences in the prevalence of dental hypersthesia. According to the literature, 3 to 60% of the adult population suffers from increased sensitivity of hard tissues of teeth, reaching 85% in periodontal diseases, and this figure is growing steadily [10, 11, 16]. The age range of patients with dentin hypersthesia (HD) is very wide, but most patients are between the ages of 18 and 50 with a peak between 20 and 40 years. Women get sick more often and at a younger age [1, 2].

Most researchers agree that the onset and progression of cervical HD is often associated with periodontal disease. The main clinical sign of increased sensitivity of dental hard tissues is severe, short-term, acute pain that occurs under the influence of chemical, temperature and tactile stimuli. Such manifestations are often found with lesions of hard tissues of teeth, periodontal diseases, as well as without visible changes in the teeth. In this regard, it is proved that HD can act as an independent nosological form, and be a symptom of other diseases. In particular, HD is recorded in more than 90% of patients with pathological abrasion, wedge-shaped defects, enamel erosion [3, 4]. Visually, the dentin of teeth that have hypersensitivity does not differ from insensitive dentin, and the histopathological condition of the pulp in teeth with HD is still not precisely established.

As is known, the main structural elements of teeth are calcium and phosphorus (on average 57.67% of the mass of minerals of intact tooth enamel). Violation of the ratio of calcium and phosphorus in the periodontal bone and hard tissues of the teeth occurs in some systemic diseases and physiological conditions and is associated with changes in calcium-phosphorus homeostasis at the body level.

The urgency of the problem is confirmed by data obtained in recent years, which indicate a decrease in the total mineral saturation of compact bone (20-27%), trabecular bone (33-38%) in the population of Ukraine over the age of 20 years, an increase in the number of patients with systemic osteopenia and osteoporosis, as a result of adverse environmental conditions, unbalanced and deficient in relation to trace elements of the diet, low physical activity, etc. [5].

It is known that the content of trace elements in saliva has a great influence on the intensity of the processes of mineralization and demineralization of dental hard tissues, but the research results are far from straightforward. Resistance or susceptibility of a tooth to HD is also determined by the structure, chemical composition and genetic characteristics of its tissues.

**The purpose of the study** was to identify markers of early diagnosis of hyperesthesia against the background of periodontal tissue diseases in young people.

**Materials and research methods.** The study involved 170 patients with periodontal disease aged 18 to 45 years, 170 patients with periodontal disease. Of these, 37 people (aged 18-25 years) with hyperesthesia were selected, which were divided into 3 groups: group I (n = 16) included patients with hyperesthesia against the background of chronic catarrhal gingivitis; in group II (n = 12) - with hyperesthesia against the background of generalized periodontitis (PC <4 mm); Group III (n = 9) consisted of patients with hyperesthesia on the background of an intact periodontium. In all groups, 98 women dominated (57.6%). A dental examination of patients of all groups was performed.

In the work, a direct analysis of real samples of saliva of patients with dental hypersthesia was carried out to determine the content of a number of elements in them. Of particular interest to us was the determination of the concentration of Ca, P, K, Na, Mg in the oral fluid, since these elements play a leading role in the processes of mineralization, demineralization and remineralization of dental hard tissues, as well as the study of tumor necrosis factor (TNF, TNF). interleukins (IL) IL-4, IL-1β, nitric oxide (NO). For molecular genetic studies of the genes ACE (I / D), TNF-α (308G / A), eNOS (894G / T), MMP20, KLK4, ENAM allele-specific PCR and PCRP-PCR were used.

Comparative analysis between groups carried out using the test Mann-Whitney.

**Research results and discussion.** A survey of patients with hyperesthesia of the teeth showed that most of them (60%) had this problem for a long time (more than 3 years), and only 5% of patients noted that tooth hypersensitivity appeared in the last year. At the same time, the vast majority of patients (83%) noted that tooth hypersthesia gives them serious inconvenience. It is noteworthy that only 26% of persons with dental hyperesthesia were previously treated by a dentist, however, none of them were treated regularly, the rest of the patients very rarely visited a doctor about tooth sensitivity. In our opinion, this may be due to the fact that, from the patient’s point of view, HD is often considered to be too trivial to pay attention to it (mild hypersthesia, slight discomfort), or the patient considers this condition incurable as a result of the failed experience of the previous treatment. In some cases, patients successfully self-medicate. In general, the results of the study suggest that HD is a much more common pathology than previously thought. An analysis of the patient’s history revealed that periods of exacerbation are characteristic of HD and periodontal diseases with an increase in functional loads, a deterioration in general health, and an exacerbation of somatic diseases.

Among the examined patients, in most cases a generalized form of hyperesthesia was observed. The data presented in table. 1, indicate that all patients to one degree or another responded to the stimulus. Half of the patients (50.0%) had moderate severity, and 23.5% had a severe degree, indicating a pronounced pain response to the irritant. Mild hypersthesia was diagnosed in 26.5% of patients.Studying the mechanisms of the occurrence of hypersthesia in periodontal disease, a decrease in Ca, P and Mg was found both in the gum and oral fluids and in the biopsy of hard tooth tissues, which is consistent with literature data, which indicate that the basis for changes in mineral metabolism in the oral fluid the patient’s hard tissues and bone tissue undergo metabolic acidosis, which is a common component of the pathogenesis of hypersthesia and periodontitis. Severe hypophosphatemia was observed, which was combined with a decrease in the content of inorganic phosphorus and calcium in the oral fluid, which is confirmed by data obtained by other authors [6].

The highest contents of Ca (> 3.0 mmol / L) and Mg (> 0.9 mmol / L) were revealed in the oral fluid of patients with hypersthesia against the background of generalized periodontitis (group II patients). An examination revealed a significant difference between the studied parameters in the groups: Ca (p = 0.004), NO (p = 0.001), TNF (p = 0.012); and also between I and III groups: Mg (p = 0.002), TNF (p = 0.031). Significant differences between groups I and III were found by the D / D genotype (p = 0.0019) for the ACE gene (rs 4646994). When conducting a comparative analysis of the obtained data in patients of groups I and II, it was found that the G/G genotype of KLK4 gene (rs2664152 T/G) was significantly more often (χ2 = 8.14, p = 0.004, OR = 12, 95% CI 2, 20–65.52) found among patients of group II, which indicates a 12-fold increase in the risk of dental HD on the background of periodontal disease. In addition, it was found that the risk of dental HD on the background of catarrhal gingivitis is increasing by almost 3 times in the presence of pathological C allele (χ2 = 3.99, p = 0.048, OR = 2.45 95CI%: 1.01-5.96) whereas in the presence of allele A of MMP20 gene, a significant decrease in the risk of dental HD was found (χ2 = 3.99, p = 0.048, OR = 0.41 95CI%: 0.17-0, 99). Genotypes A/A (ENAM) and G/G (KLK4) were met significantly more often (χ2 = 5.97, p = 0.015) among patients of group I, which indicates a decrease in the risk of dental HD in the presence of this combination, while genotypes A/G (ENAM) and A/A (KLK4) were significantly met more often (χ2 = 5.86, p = 0.016) among patients of group II, which led to an increased risk of dental HD.

**Conclusions:** In modern dentistry, the problem of tooth hypersensitivity is becoming more and more urgent, which is explained by the significant prevalence of this disease, its pathogenesis that has not been fully clarified, and complex and not always effective treatment. Hypersensitivity of teeth to temperature, chemical and mechanical irritants is a symptom that often accompanies periodontal disease, which aggravates the course of the underlying disease and complicates its treatment. A high level of manifestation of dental hypersthesia is due, first of all, to its multifactorial genesis.When assessing the prevalence and severity of CH, it turned out that among the examined patients in most cases a generalized form of hyperesthesia prevailed. At the same time, grade I hypertension was diagnosed in 26.5% of cases, degree II in 50.0%, and degree II in 23.5%. At the same time, the intensity and severity of tooth hypersensitivity were directly related to the characteristics of the periodontal tissue pathology.

 An individual approach with determination of the Ca and Mg contents in the oral fluid in combination with the D / D genotype of the ACE gene and MMP20, KLK4, ENAM genes is aimed at the early identification of risk groups for hyperesthesia against periodontal diseases in young people. Therefore, the justification and development of methods for early preclinical diagnosis of increased sensitivity of dental hard tissues based on the use of mineral metabolism markers taking into account genetic polymorphism is promising. Undetected and, accordingly, untreated, increased tooth sensitivity creates obstacles to the full completion of dental rehabilitation programs, since it is a factor that increases the risk of developing major dental diseases and reduces the quality of life of patients.

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