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THE ROLE OF ORAL FLUID IN THE DEVELOPMENT OF PERIODONTAL DISEASES IN CHILDREN WITH DIABETES MELLITUS

Saliva is the only biological fluid with a unique set of research possibilities, which provide for non-invasive, multiple and almost unlimited sampling of material. Unfortunately, the mechanism that regulates the maintenance of a certain composition of saliva is still unclear. The main attention of clinical specialists is attracted by new laboratory methods of saliva analysis in order to obtain various diagnostic information. In the next few years, achievements are predicted in the field of diagnosis of diseases of the maxillofacial area, taking into account the properties of saliva. Oral fluid consists of mixed saliva, that is, a mixture of secretions of three pairs of large and many small glands of the oral cavity and organic impurities. Mineral and organic components determine the properties and functions of oral fluid. Therefore, the detection of quantitative and qualitative changes in oral fluid, especially in children, allows us to determine their role in the formation of pathological processes.

In addition to the fact that the composition of the oral fluid can change in the presence of systemic diseases (especially those that affect the function of the salivary glands), the possibility of simple, safe and non-invasive collection of the researched material is important. Existing scientific works confirm that diabetes mellitus (DM) leads to dysfunction of the secretory capacity of the salivary glands, which later develops into an increased susceptibility of the body to pathogens of the oral cavity. Type 1 diabetes mellitus is also known to affect the homeostasis of the oral cavity.

The study of saliva according to many clinical and biochemical indicators has advantages in comparison with methods of laboratory blood diagnosis. Unlike blood, saliva is an easily accessible biological fluid, its protein composition is largely identical to blood serum, and it is physiologically related to homeostasis. Saliva collection is carried out without invasive interventions, and it can be widely used in hygienic, toxicological, and immunological studies.

Moreover, some indicators of saliva are sensitive indicators of serious systemic diseases and conditions of the body. Even short-term and minor chemical and metabolic disturbances in the body, which accompany general somatic pathological conditions, can change the rheological properties of saliva. Early detection of the disease plays an important role in the success of its treatment. If the disease is diagnosed earlier, the chances of its successful treatment will increase. If the disease cannot be cured, early diagnosis will still allow better control of the course of the disease.

The aim of the study *was to find out the influence of oral fluid on the development of periodontal diseases in children with type 1 diabetes mellitus.*

Materials and methods. *The analysis included generalization and systematization of literature data on this topic.*

Scientific novelty. *Generalization and analysis of literature data according to the role of oral fluid in the development of periodontal diseases in children with diabetes mellitus. Study of cause-and-effect relationships of endocrine and dental pathology. In the future, this will allow to improve treatment and prevention measures in pediatric dentistry and will lead to an improvement in the quality of life of such patients.*

Conclusions. *Adequate knowledge about saliva and its role in maintaining oral health is very important. Some indicators of saliva are sensitive indicators of serious systemic diseases and conditions of the body. Early detection of the disease plays an important role in the success of its treatment.*

Key words: *saliva, cytokines, diabetes, children, gingivitis.*

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РОЛЬ РОТОВОЇ РІДИНИ В РОЗВИТКУ ЗАХВОРЮВАНЬ ПАРОДОНТУ У ДІТЕЙ, ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ

Слина – єдина біологічна рідина з унікальним набором дослідницьких можливостей, які передбачають неінвазивний, багаторазовий і майже необмежений за обсягом забір матеріалу. У найближчі кілька років прогнозуються досягнення в області діагностики захворювань щелепно-лицевої ділянки з урахуванням властивостей слини. Ротова рідина складається зі змішаної слини, тобто суміші секретів трьох пар великих і безлічі дрібних залоз порожнини рота і органічних домішок. Мінеральні і органічні компоненти визначають властивості і функції ротової рідини. Тому виявлення кількісних і якісних змін ротової рідини, особливо у дітей, дозволяє визначити їх роль у формуванні патологічних процесів.

Більш того, деякі показники слини є чутливими індикаторами серйозних системних захворювань і станів організму. Навіть короткочасні і незначні хімічні та метаболічні порушення в організмі, які супроводжують загальносоматичні патологічні стани, здатні змінювати реологічні властивості слини. Раннє виявлення захворювання відіграє важливу роль в успішності його лікування. Якщо захворювання діагностувати раніше, то й шанси на його успішне лікування збільшаться.

Цукровий діабет I типу (ЦД) – це системне захворювання, здатне викликати різноманітні ускладнення. ЦД також, як відомо, впливає на гомеостаз порожнини рота. Експертна група з діагностики та класифікації ЦД визначила пародонтит як один із патологічних станів, що часто зустрічається в осіб із ЦД.

***Метою дослідження** було з'ясувати вплив ротової рідини на розвиток захворювань тканин пародонту у дітей на фоні цукрового діабету 1 типу.*

***Методи дослідження.** Аналіз включав узагальнення та систематизацію літературних даних по даній тематиці.*

***Наукова новизна.** Узагальнення та аналіз літературних даних щодо ролі ротової рідини в розвитку захворювань пародонту у дітей, хворих на цукровий діабет. Вивчення причинно-наслідкових зв'язків ендокринної та стоматологічної патології. Це в подальшому дозволить удосконалити лікувально-профілактичні заходи в дитячій стоматології і призведе до поліпшення якості життя таких пацієнтів.*

***Висновки.** Адекватні знання про слину та її роль у забезпеченні здоров'я ротової порожнини дуже важливі. Деякі показники слини є чутливими індикаторами серйозних системних захворювань і станів організму. Раннє виявлення хвороби відіграє важливу роль в успіху її лікування.*

***Ключові слова:** слина, цитокіни, цукровий діабет, діти, гінгівіт.*

Formulation of the problem. Type 1 diabetes mellitus (T1DM) is a systemic disease that causes different complications. These complications make worse the quality of life in people who suffer from this disease. Gingivitis and periodontitis are local inflammatory diseases. The above-mentioned diseases can affect other organs and organ systems. The expert group on the diagnosis and classification of T1DM identified periodontitis as one of the pathological conditions that often occur in adults with DM. Much data is indicating a correlation between periodontitis and type 1 DM in children and adults. But the effect of the level of glycemic control on the periodontal condition is still not fully understood. In addition, quantitative indicators of immunological markers in saliva in these two diseases are unknown.

Type 1 diabetes mellitus mainly occurs in children and adolescents and accounts for 5-10% of the total number of patients with both types of diabetes. The pathological basis of type 1 diabetes mellitus is the autoimmune destruction of pancreatic cells. It leads to complete loss of insulin secretion, and after to hyperglycemia. Various types of β-cells autoimmune destruction molecular markers can be detected in 85-90% of patients with hyperglycemia. Some of them, such as autoantibodies against insulin, glutamic acid decarboxylase, and tyrosine phosphatase, is used for diagnosis and risk assessment of type 1 diabetes mellitus. In 1993, periodontitis was identified as one of the clinical complications of diabetes mellitus.

The aim of the study was to find out the influence of oral fluid on the development of periodontal diseases in children with type 1 diabetes mellitus.

Materials and methods. The analysis included generalization and systematization of literature data on this topic.

Results and their discussion. Periodontitis is a local infection of the periodontium (consisting of gums, periodontal ligament, root cementum, and alveolar bone). Gingivitis is an inflammation that affects only the gums, while periodontitis is an inflammation of deeper tissues. Both diseases are the result of the interaction between periodontal pathogenic microorganisms and the host tissue. Dental plaque is a colony of microorganisms that accumulate on all hard surfaces of the mouth, primarily on the teeth. Gingivitis is initiated by the presence of periodontal pathogens that cause disease, but the response of the organism to infection is critical to disease progression. A variety of systemic factors can influence this immune response. The clinical course of periodontitis does not differ concerning the type of periodontopathogens that

induce immune-mediated destructive processes. The gums become red and swollen and bleed easily after touching them with a probe if dental plaque is present. Further spread of the inflammatory process into the deeper tissues of the periodontium leads to a violation of the epithelial attachment of the gums, because of which a periodontal pocket appears. The last feature is a pathognomonic sign of periodontitis. If the process is not stopped by treatment, it will lead to resorption of the alveolar bone, which will ultimately cause tooth loss. Previously, it was believed that gingivitis, if not treated, develops into periodontitis. However, gingivitis and periodontitis are two distinct nosological entities, and although periodontitis is often preceded by gingivitis, not all cases of gingivitis progress to periodontitis. Thus, it is still not entirely clear why and how gingivitis progresses to periodontitis [1, 2, 3].

Various markers of inflammation can be detected in samples of gingival fluid and saliva depending on the level of the host's immune response during the development of periodontitis. Some of these molecular compounds can affect gene expression in individuals with genetic polymorphisms and the presence of a predisposition to the development of periodontitis. These molecular compounds can be used as diagnostic markers and tests and methods for assessing the risk of developing periodontitis by measuring their level, as well as for monitoring the effectiveness of the treatment of the pathological conditions [3, 4].

The duration of DM is an important risk factor for the development of periodontitis. In young patients with type 1 DM, periodontal tissue destruction begins relatively early, in the pre-pubertal and adolescent periods, depending on the duration of the underlying disease. Loss of epithelial attachment is more widespread in patients suffering from type 1 diabetes mellitus for more than 10 years. At the same time, the results of some scientists are important because they show that type 1 DM plays an important role in the development of periodontitis in early childhood [1, 5].

Adequate knowledge about saliva and its role in ensuring the health of the oral cavity is necessary for dentists to timely identify and treat possible deviations from the norm. Despite the wide range of possibilities for saliva research, there are quite few data on the parameters of the oral fluid of children with type 1 diabetes mellitus in the available literature [6].

Saliva collection is carried out without invasive interventions, and it can be widely used in hygienic, toxicological, and immunological studies. The study of saliva according to many clinical and biochemical indicators has advantages in comparison with methods of laboratory blood analysis. Saliva is an easily accessible biological fluid, its protein composition is largely identical to blood serum, and it is physiologically related to homeostasis [5, 7, 8].

Moreover, some indicators of saliva are sensitive indicators of serious systemic diseases and conditions of the body. Even short-term and minor chemical and metabolic disturbances in the body, which accompany general somatic pathological conditions, can change the rheological properties of saliva. Early detection of the disease plays an important role in the success of its treatment. If the disease is diagnosed earlier, the chances of its successful treatment will increase. In the case when the disease cannot be cured, early diagnosis will still allow better control of the course of the disease [9, 10].

The development of molecular biology concerning insulin resistance and beta-cell dysfunction made it possible to reveal the increased role of inflammatory components, namely cytokines and elements of the innate immune system, in the pathogenesis of diabetes mellitus. Cytokine production because of oral infection can potentially affect insulin resistance in several ways. Children and adolescents with type 1 diabetes mellitus depend exclusively on exogenous insulin. This is the reason why the general condition of children and adolescents is disturbed in the following years, and therefore, the risk of developing severe forms of periodontitis is increased. Thus, similarly to adults, the same connection can be expected between a severe form of periodontitis and a significant increase in cytokine levels, which can negatively affect the quality of dental treatment of periodontal pathology [11, 12].

The pathological morphological characteristics of the capillaries of the gums and lips mucous membrane in patients with diabetes mellitus are more visualized compared to healthy individuals. Long-term leads to thinning of the basal membrane of the vessel walls, which leads to deterioration of tissue nutrition and leukocyte migration [13, 14].

There is evidence that periodontitis can stimulate or lead to a permanent increase in systemic chronic inflammation, which is expressed in increased levels of serum C-reactive pro-protein, interleukin-6 (IL-6), and fibrinogen, especially in those patients who have gram-negative periodontal pathogens in the oral cavity. Bacteremia and endotoxemia are the results of the systemic spread of periodontal pathogens or their products, causing a systemic inflammatory disorder with an increase in serum inflammatory markers. One of the studies showed that the level of endotoxin

in the blood of people with periodontitis was five times higher, compared to healthy individuals. The presence of periodontitis allows microorganisms of the oral cavity and their waste products to reach systemic circulation [15, 16].

Therefore, the scientific works available for study testify to the important role of immune mechanisms at the systemic and local levels in the pathogenesis of inflammatory periodontal diseases. Most data in the literature refers to the determination of the cytokine profile mostly in adults. The level of cytokines in the saliva of children with type 1 diabetes mellitus and periodontal diseases has not been sufficiently studied. Scientists registered an increase in the concentration of certain interleukins (IL-2, TNF-α, IL-6, IL-18) in the blood serum and the gingival fluid of patients with periodontitis, established their role in the processes of inflammation and even resorption of bone tissue [17, 18].

Saliva is the only biological fluid with a unique set of research possibilities, which provide for non-invasive, repeated, and almost unlimited sampling of material. Unfortunately, the mechanism that regulates the maintenance of a certain composition of saliva is still unclear. The main attention of clinical specialists is attracted by new laboratory methods of saliva analysis to obtain various diagnostic information. In the next few years, achievements in the field of diagnosis of diseases of the maxillofacial area are predicted, considering the properties of saliva [10, 19].

According to some authors, saliva has particular importance in the etiology of periodontal diseases and caries. Its composition, properties, and rate of secretion influence the accumulation of dental plaque, and its chemical composition and calcification play role in the development of the above-mentioned diseases. Some food substances are dissolved in saliva, and its enzymes can split a certain amount of carbohydrates and peptide bonds. A decrease in saliva secretion and the content of antibacterial factors in saliva leads to a change in the composition of the microflora of the oral cavity, which, accordingly, affects the condition of the teeth and periodontal tissues [16, 20].

The detection of quantitative and qualitative changes in oral fluid, especially in children, allows us to determine their role in the formation of pathological processes.

Existing scientific works confirm that DM leads to dysfunction of the secretory capacity of the salivary glands, which later develops into an increased susceptibility of the body to pathogens of the oral cavity. Type 1 diabetes mellitus is also known to affect the homeostasis of the oral cavity. Several studies have shown the prevalence of gingival inflammation in patients with DM. Hygienic indices, periodontal indices, and bleeding gums are the indicators that increase in groups of teenagers with type 1 diabetes mellitus. Foreign scientists studied changes in the protein composition of saliva in patients with type 1 DM. For example, with the help of enzymatic analyses, it was found that the concentration of aminotransferases and lactate dehydrogenase in saliva increases in patients with type 1 diabetes mellitus compared to healthy individuals. Similarly, the use of immunoenzymatic analysis made it possible to detect glutamic acid decarboxylase autoantibodies in the oral fluid of patients with type 1 diabetes mellitus [18, 21].

It is known that a violation of the acid-alkaline balance leads not only to the progression of the development of caries but also to the acceleration of the formation of hard dental plaque, especially in people suffering from inflammatory periodontal diseases. Thus, it can be concluded that the correction of the acid-alkaline balance is undeniably necessary both in individuals who are favorable for tooth decay and in persons with periodontal pathologies [3, 15].

Hyposalivation entails a decrease in the cleansing ability of saliva, a deterioration of its antimicrobial, buffering, and remineralizing functions, and, as a result, a decrease in its caries-protective properties. The less saliva is secreted, the smaller its buffer capacity and the longer the pH value of the biofilm remains in an acidic state after each meal. This significantly increases the risk of developing caries [16, 19].

The crystal-forming properties of saliva are largely determined by the somatic state of the human body. Several works of Ukrainian and foreign authors are devoted to the study of microcrystallization of saliva in various somatic pathologies. According to some authors, the main disease causes changes in the homeostasis of the oral cavity and contributes to the development of dental caries. Another important indicator of the mineralizing function of saliva is the value of its microcrystallization. Microcrystallization of saliva is a general indicator of the body's homeostasis. This research method can be used both to evaluate the effectiveness of preventive, therapeutic, and rehabilitation measures and for predicting the course of diseases. There are works devoted to the methods of diagnosing common diseases by analysing the mineral composition and properties of saliva in modern medical literature [20, 21].

Unfortunately, most often the diagnosis is established only after the development of the first symptoms of the disease. Therefore, to accelerate the speed of early diagnosis of diseases, modern

scientists are focusing on the detection of biomarkers that could indicate the presence of a certain disease in a person even before the appearance of clinical symptoms. For the diagnosis of the initial, hidden forms of the disease, various markers in saliva have recently been increasingly used as diagnostic tests for gingivitis and periodontitis [22].

Saliva is of interest to scientists because the liquid is a filtrate of blood plasma, it can be collected easily and non-invasively, this liquid is suitable for the study of many biochemical parameters, such as free oxygen radicals, products of lipid peroxidation, for example, malondialdehyde (MDA), cytokines [16, 18, 23].

The biological activity of cytokines directly affects the degree of periodontal destruction. Recent literature suggests that hyperglycemia can lead to increased production of inflammatory mediators, for example, poor metabolic control is associated with increased interleukin IL-1β levels in the gingival fluid. Periodontal monocytes, macrophages, fibroblasts, and endothelial cells react to microorganisms, lipopolysaccharides, and other plaque antigens and secrete numerous chemokines and inflammatory cytokines, mainly TNF, interleukins IL-1β and IL-6 in the systemic circulation. The end products of glycolysis, accumulated in monocytes due to hyperglycemia, increase oxidative stress in cells and activate the transcriptional nuclear factor kappa B, which affects the phenotype of macrophages and leads to an increase in the production of other inflammatory cytokines, such as IL-8 and TNF-α [17, 24].

Conclusion. Type 1 diabetes mellitus is an important etiopathological factor in the development of periodontal pathologies. This is confirmed by a statistically significant increase in morbidity (gingivitis and periodontitis) and a pro-inflammatory state of the body. Hyperglycemia can destroy periodontal tissues in several ways, first, due to a violation of the immune response mechanism, non-enzymatic glycosylation, and an increase in the level of oxidative stress. Clinical, microbiological, biochemical, and immunological markers of periodontal disease in patients with diabetes mellitus should be studied more. There is quite important and relevant to establish the etiological factors and pathogenetic mechanisms of caries and periodontal diseases in persons with DM to create new methods of prevention and treatment of these dental diseases. According to the above-mentioned facts, understanding the significant prevalence of periodontal diseases among children with type 1 diabetes mellitus and their potentially serious consequences in the future, other medical specialists (pediatricians, pediatric endocrinologists) should play an important role in encouraging patients to visit dentists regularly to control etiological factors, especially the occurrence of dental plaque.

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