DETERMINATION OF MECHANISMS OF PERIODONTAL TISSUE DAMAGE IN DIFFERENT TYPES OF DIABETES

Abstract. According to the conclusions of specialists in Ukraine, there is a rapid increase in the number of dental diseases among children and adolescents. Diabetes mellitus of types I and II is considered to be one of the factors that has become quite common in relation to the occurrence of periodontal diseases.
In adolescence, diabetes mellitus has the most aggressive course and is characterized by negative changes in the body's immune system, a progressive inflammatory process with subsequent destruction of periodontal tissues and a significant deterioration of the hygienic condition of the oral cavity and persistent tolerance to treatment.

That is why the purpose of the study was to determine the state of oral hygiene, the nature of its influence on the formation of microbiota in adolescents with chronic catarrhal gingivitis (CCG) against the background of both types of diabetes. For its achievement, 44 adolescents were examined: 18 of them - with type I and II diabetes aged from 11 to 16 years with manifestations of chronic catarrhal gingivitis of mild and moderate severity with duration of diabetes from several months from the first day of application to 2 years; 16 adolescents had only mild and moderate CCG without diabetes and a control group of their 10 somatically healthy peers.

The indicators of the rate of salivation, the viscosity of oral fluid were studied, the state of oral hygiene, the degree of dysbiosis (DM), the activity of urease and lysozyme enzymes were determined. Parents of all subjects were informed about the study and signed an informed consent to participate in it, measures were taken to ensure patient anonymity.

It was found not only a decrease in the pH of the oral fluid, which affected the increase in the concentration of hydrogen ions, but also a significant slowdown in the rate of saliva secretion, which significantly worsened the hygienic condition of the oral cavity and accelerated the formation of dental plaque and contributed to the development of the inflammatory process in the periodontal tissues. It was also established that there is a regularity between the deterioration of all studied indicators of homeostasis of the oral cavity with the formation of an inflammatory process in the periodontium.

It was concluded that diabetes mellitus changes the body's reactivity, negatively affects its most important protective mechanisms, activates the course of inflammatory periodontal diseases together with a low level of oral hygiene. Periodontopathogenic microflora causes further damage to periodontal tissues in adolescents with diabetes of both types. Therefore, it is important to comprehensively study the pathogenetic mechanisms of the impact on the body of both diabetes mellitus and inflammatory diseases of periodontal tissues, search and development of new substantiated methods of treatment and prevention of chronic catarrhal gingivitis in adolescents with both types of diabetes mellitus.

Keywords: adolescents, chronic catarrhal gingivitis, periodontal tissues, diabetes mellitus.
ВИЗНАЧЕННЯ МЕХАНІЗМІВ УРАЖЕННЯ ТКАНИН ПАРОДОНТА ПРИ ЦУКРОВОМУ ДІАБЕТІ РІЗНИХ ТИПІВ

Анотація. Згідно з висновками фахівців в Україні спостерігається стрімке зростання кількості стоматологічних захворювань серед дітей та підлітків. Одним із чинників, який став досить поширеним, щодо виникнення хвороб пародонта вважають цукровий діабет (ЦД) I та II типів.

У підлітковому віці ЦД має найбільш агресивний перебіг і характеризується негативними змінами в імунній системі організму, прогресуючим запальним процесом з подальшою деструкцією тканин пародонту та значним погіршенням гігієнічного стану ротової порожнини й стійкою толерантністю до лікування.

Саме тому метою дослідження стало визначення стану гігієнічного порожнини рота, характер його впливу на формування мікробіоти в підлітків, хворих на хронічний катаральний гінгівіт (ХКГ) на тлі ЦД обох типів. За для її досягнення обстежено 44 підлітка: з них 18 - з цукровим діабетом I та II типів
у віці від 11 до 16 років з проявами хронічного катарального гінгівіту легкого та середнього ступеня тяжкості з тривалістю перебігу ЦД від декількох місяців з першого дня звертання до 2 років; 16 підлітків мали тільки ХКГ легкого та середнього ступеня тяжкості без ЦД і контрольна група з їх 10 соматично здорових однолітків.

Виявлено не тільки зниження рН ротової рідини, яке вплинуло на підвищення концентрації іонів водню, а ще й суттєве сповільнення швидкості слиновиділення, що у значній мірі погіршило гігієнічний стан ротової порожнини та сприяло розвитку запального процесу в тканинах пародонту. Також встановлено існування закономірності між погіршенням усіх досліджуваних показників гомеостазу ротової порожнини з формуванням запального процесу в пародонті.

Зроблені висновки, що ЦД змінює реактивність організму, негативно впливає на його найважливіші захисні механізми, активує перебіг запальних хвороб пародонта разом з низьким рівнем гігієни порожнини рота. Пародонтопатогенна мікрофлора викликає у підлітків з діабетом обох типів подальше ушкодження тканин пародонту. Отже, важливим є всебічне вивчення патогенетичних механізмів впливу на організм як ЦД, так і запальних хвороб тканин пародонта, пошук і розробка нових обґрунтованих методів лікування й профілактики хронічного катарального гінгівіту в підлітків, хворих на ЦД обох типів.

Ключові слова: підлітки, хронічний катаральний гінгівіт, тканини пародонта, цукровий діабет.

**Formulation of the problem.** Periodontal diseases are considered the undisputed leaders among the most common dental diseases. Chronic catarrhal gingivitis always had priority and was the most common pathology among inflammatory diseases of periodontal tissues, especially in young people [13].

Most periodontal diseases arise and develop under the influence of completely different factors, both local and general, against the background of changes in the body's reactivity and resistance in systemic somatic diseases. One of the most important local factors is the influence of periodontopathogenic microorganisms combined with poor oral hygiene. Common factors include endocrine pathology, in particular type I and type II diabetes and other somatic diseases of the body [3, 5].

Among all diseases of the endocrine system in youth, diabetes is the most common. In adolescence, it has the most aggressive course and is characterized by
negative changes in the immune system of the body and in the specific and non-specific protection of the oral cavity, a progressive inflammatory process with subsequent destruction of periodontal tissues, as well as a significant deterioration of the hygienic condition of the oral cavity and persistent tolerance to treatment [1, 3, 10].

Early pathological changes in diabetes usually occur in the oral cavity of patients, so dentists are the first to diagnose damage to periodontal and mucous membrane tissues along with metabolic changes in their body. That’s mean, diabetes of types I and II is also a dental problem, as it negatively affects the condition of all organs of the oral cavity. And that is why the definition of relationships between diabetes of various types and pathology of oral cavity organs in adolescence is the subject of many modern scientific studies of the dental community [19, 21].

Analysis of recent research and publications. Numerous publications of recent years indicate that every year the number of young patients who have already appeared the first signs of inflammation of periodontal tissues is increasing, the most common among them is chronic catarrhal gingivitis (CCG) [13].

The frequency of periodontal tissue damage in the presence of comorbid pathology is directly related to the duration, course and degree of severity of the somatic disease [5, 14, 20]. According to published WHO data, 80% of examined youth aged 10 to 20 have already been diagnosed with certain pathological changes in periodontal tissues. The number of complicated course and the degree of severity of periodontal diseases are significantly higher in children and adolescents with somatic pathology, in particular with type I and II diabetes mellitus [3, 10, 13]. Inflammatory and inflammatory-destructive changes in the periodontium are directly dependent on the age of the patients, the severity of the endocrine disease, stable compensation of glycemia, high-quality pathogenetic therapy, etc. [21]. Combined pathology is characterized by a complex course of diseases due to common multi-link mechanisms between all organs and systems of the macroorganism [14, 19, 20].

According to Yarova S.P. and co-authors [6] the fact that the hygienic condition of the oral cavity is deteriorating has a significant effect on the biochemical composition of oral fluid, complicates and accelerates the course of inflammatory periodontal diseases. That is, the high level of morbidity of oral mucosa and periodontal tissues usually corresponds to a low level of oral hygiene and a decrease in local mucosal immunity [1, 4, 6, 7, 9].

Now the attention of scientists is maximally focused on the study of the properties of oral fluid and its significance for the diagnosis of diseases, including systemic somatic ones. Interest in the study of the composition and functions of oral fluid is due to the presence of factors in it that reveal its high regulatory and trophic potential and provide an opportunity to study important mechanisms of oral cavity protection against negative factors of influence [12, 16, 17, 18].

It is known from literary sources that periodontal tissue diseases mainly occur with increased lipoperoxidation and autointoxication [22]. They are also characterized
by an increased number of immune complexes and pro-inflammatory cytokines in the oral fluid and blood serum, a gradual increase in the phagocytic activity of leukocytes, and an increased level of immunoglobulins. Also, the latest research results confidently prove that patients with comorbid pathology have certain changes in the immune status of the oral cavity and the body as a whole. Therefore, the presence of somatic diseases in the anamnesis usually suppresses specific and non-specific protective mechanisms of the body, which negatively affects the condition of periodontal tissues. A decrease in the humoral immunity of the oral cavity over time leads to sensitization of the body by its own microflora and its toxins, to the creation of foci of chronic autoinfection, and subsequently to the formation of significant structural changes in periodontal tissues [7, 8, 20, 22].

So far, convincing evidence of a violation in the humoral specific and non-specific protection systems of the oral cavity has been obtained, which affects the determination of the features of the course of inflammatory and inflammatory-destructive diseases of the periodontium. The results of modern research have confirmed that it is mucosal immunity that provides direct protection of the oral cavity against the pathogenic effects of some microorganisms and their toxins [11, 20]. The latest studies prove the formation of a vicious circle, which interconnects the negative impact of poor oral hygiene with a change in the biochemical composition of oral fluid. There is a deepening of pathogenetic changes in the oral cavity, which further complicates and significantly accelerates the course of inflammation in periodontal tissues [1, 6, 9, 10, 14].

That is why the goal of our study was to determine the relationship between the state of hygiene and the microbiota of the oral cavity, the intensity and degree of severity of the inflammatory process in the periodontal tissues in adolescents with CCG without endocrine pathology and in their peers with CCG, patients with type I and II diabetes mellitus.

Presenting main material. Material and methods. We examined 44 teenagers: 18 of them were type 1 and type 2 diabetes patients aged 11 to 16 years with mild to moderate chronic catarrhal gingivitis who were treated in the endocrinology department of the Poltava Regional Children's Clinical Hospital. (the duration of the course of diabetes on average ranged from several months from the first day of application to 2 years); 16 teenagers - with mild and moderate CCG without somatic pathology, who were registered at the municipal enterprise "City Children's Clinical Stomatological Polyclinic of the Poltava City Council". The control group consisted of 10 patients without CCG and any somatic pathology. All study groups were standardized according to the age and gender of the adolescents.

In the observation groups, we collected anamnesis, performed a clinical examination of the oral cavity, determined its state of hygiene with the help of indices: OHI-S (Green-Vermillion, 1964) and the hygienic index according to Yu.A. Fedorov and V.V. Volodkina (1971). Establishing the intensity, clinical
prevalence and degree of severity of the inflammatory process in the periodontal
tissues was evaluated using the PMA index in the Parma (1960) modification [4, 7].

Oral fluid was collected in test tubes in the morning on an empty stomach for
10 minutes. The pH of the oral fluid was determined by the color change of the
indicator paper strips, the diagnostic scale was from 5.7 to 7.4 [4]. The rate of
salivation was determined by the formula: Rs = V/T, where Rs is the rate of
salivation (in ml/min), V is the volume of saliva secreted (in ml), T is the time of
saliva sampling (in min) according to the method of T.L. Redinova and
A.R. Pozdeeva [7]. Oral fluid to determine the rate of salivation was collected on an
empty stomach in the morning for 5 minutes in measuring tubes, measured in
ml/min.

The research was carried out in accordance with the "Rules of Ethical
Principles of Conducting Scientific Medical Research with Human Participation",
approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EU
Directive No. 609 (from November 24, 1986), orders of the Ministry of Health of
03.08.2012 Parents of teenagers who were examined, informed and signed an
informed consent to participate in it.

The results of the research were statistically processed with the help of the
Microsoft Office license program - MS Excel 2007 using statistical methods [2].
Differences in indicators were considered probable at p <0.05.

Results and their discussion. It is known that the quantitative and qualitative
composition of saliva and oral fluid in patients with diabetes mellitus is changed,
and the secretory function of the salivary glands is reduced due to a slowdown in the
rate of saliva secretion and significant disturbances in the water-electrolyte balance
of the body, which was confirmed by the results of our research.

The analysis of the dependence of the oral hygiene condition of adolescents
with CCG and their peers with CCG and diabetes, on the indicators of oral fluid and
indicators of the state of periodontal tissues are shown in Table 1.

We determined the pH of oral fluid in adolescents with diabetes of both types,
which was 5.06±0.34, which is approximately 1.37 times lower than the indicator of
somatically healthy adolescents (6.94±0.28) and 1.2 times - for the pH indicator of
adolescents with CCG without diabetes (6.27 ± 0.05). The rate of salivation in the
same category of patients is also 1.63 times lower (0.27±0.11 ml/min) than the same
indicator in the control group (0.44±0.01 ml/min) and 1.22 times - than in peers with
CCG (0.36±0.22). Therefore, in all examined subjects, there is a direct relationship
between the rate of saliva secretion and the concentration of hydrogen ions in the
oral fluid.
Table 1. Indicators of oral fluid, hygiene and periodontal indexes in observation groups

<table>
<thead>
<tr>
<th>Observation groups</th>
<th>Hygienic index (F-V), points</th>
<th>Hygienic index (OHI-S), points</th>
<th>PMA, %</th>
<th>pH of oral fluid</th>
<th>Rate of salivation (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.51±0.08</td>
<td>0.63±0.11</td>
<td>—</td>
<td>6.94±0.28</td>
<td>0.44±0.01</td>
</tr>
<tr>
<td>Adolescents with CCG without somatic pathology</td>
<td>1.91±0.1*</td>
<td>1.68±0.07*</td>
<td>26.61±2.8</td>
<td>6.27 ± 0.05*</td>
<td>0.36±0.22*</td>
</tr>
<tr>
<td>Adolescents with diabetes mellitus and CCG</td>
<td>2.32±0.22**</td>
<td>1.89±0.08**</td>
<td>47.12±1.33*</td>
<td>5.05 ± 0.34**</td>
<td>0.27±0.11**</td>
</tr>
</tbody>
</table>

Note:
*– the probability of changes in adolescents with CCG without somatic pathology compared to controls (p<0.05)
**– the probability of changes in adolescents with diabetes mellitus with CCG, compared to controls (p<0.05)

Undoubtedly, adolescents with diabetes of both types have significant changes in the buffering capacity of oral fluid, which probably occur both due to a decrease in the functional activity of the salivary glands, and due to a significant shift in the pH of the oral fluid to the acidic side. And slowing the rate of saliva secretion contributes to an even greater decrease in the pH of the oral fluid. It is this that creates optimal conditions for the further reproduction of pathogenic microflora, the development of systemic changes in the biofilm and the formation of dysbiosis in the oral cavity of adolescents with diabetes mellitus. The microbial flora of the oral cavity additionally reduces the pH indicator with the products of its vital activity, that is, contributes to the formation of an acidic environment in the oral cavity.

According to Table 1, the hygienic indexes of adolescents with diabetes mellitus with CCG according to Fedorov-Volodkina and Green-Vermillion correspond to unsatisfactory oral hygiene and are 2.32±0.22 and 1.89±0.08 points, respectively. This is 1.54 and 3 times more than in healthy teenagers. In the examined teenagers with CCG, the hygienic index of Fedorov-Volodkina and Green-Vermillion indicate a satisfactory state of hygiene - 1.91±0.1 and 1.68±0.07, respectively. But even in the control group, the indicators are similar and on the border of good and satisfactory state of hygiene (1.51±0.08 and 0.63±0.11), respectively. The difference in the indicators of hygiene indices is most likely related to the low-quality implementation of the hygiene instructions of the doctor and parents, as well as to a significant reduction in the time spent brushing teeth and the lack of formed manual skills in the use of objects and hygiene products, and in adolescents with chronic obstructive pulmonary disease and diabetes also with increased gum bleeding due to hemostasis disorders and microvascular pathological changes in the periodontal tissues. This especially applies to the oral surface of the teeth.
Thanks to the determination of the hygienic condition of the oral cavity of patients with diabetes mellitus and CCG, it was established that the level of care for their oral cavity is insufficient and it must be strengthened [3, 5, 15]. Summarizing, it should be emphasized that adolescents with endocrine pathology have a worse state of oral hygiene than their healthy peers without accompanying comorbid pathology. Its level can be assessed as unsatisfactory, sometimes even it was on the border with poor hygiene according to various indices.

Studying the condition of the periodontal tissues according to the PMA index, 26.61±2% of adolescents with CCG without endocrine pathology and 47.12±1.33% with CCG and diabetes had a mild and moderate degree of severity of chronic catarrhal gingivitis, respectively, but the severity of gingivitis was determined closer to severe in patients with diabetes mellitus and CCG.

In our opinion, the average degree of severity of CCG in adolescents with diabetes is related only to the short-term course of the endocrine disease (from a few months from the first day of treatment to 2 years at most). In healthy adolescents without somatic pathology, gingivitis practically did not occur (the PMA index of the control group was 0%).

Usually, in healthy adolescents, the microbiota prevents colonization by pathogenic microorganisms of the oral cavity and forms a biofilm, which actually activates the immune response at all levels. Once in the oral cavity, carbohydrates begin to be broken down by salivary enzymes with the formation of organic acids, which then accelerate the formation of dental plaques, as well as activate the reproduction of periodontopathogenic microflora in the gingival sulcus, which causes the development of the inflammatory process in the periodontium. Therefore, dental plaque is formed due to the functioning of the microbiota of the oral cavity [9]. Violation of glycemic control in diabetes leads to a violation of the response of periodontal tissues to the action of pathogenic plaque microflora, creating a favorable environment for the occurrence and development of inflammation in it. And the presence of periodontopathogenic microorganisms in the gingival sulcus, most of which produce the urease enzyme, is also identified as one of the most important etiological factors of inflammatory and inflammatory-destructive periodontal diseases [4, 9, 19].

Without a doubt, there is a close relationship between the general state of health of the body and the biochemical and immunological parameters of the oral fluid. Some indicators of oral fluid are very sensitive indicators of systemic pathological changes in the body. Even short-term and insignificant metabolic changes in the body are accompanied by changes in the rheological properties of oral fluid [12].

sIgA, lysozyme and urease are important monitoring indicators that clearly characterize the state of the oral cavity. It is known that sIgA affects the increased lysis of pathogenic bacteria, prevents colonization and bacterial contamination of oral cavity tissues, neutralizes viruses and activates the phagocytic activity of
leukocytes [17, 18]. Lysozyme is one of the particularly important non-specific local mucosal factors of oral cavity resistance. Its action is not limited to antibacterial effects, it also promotes regenerative processes, activates the phagocytic activity of leukocytes and accelerates the healing of damaged areas of the oral mucosa. [11, 16, 18].

Thanks to recent studies, it was found that urease activity in adolescents with diabetes and CCG always increased compared to the control group. And the decrease in lysozyme activity mainly occurred simultaneously with a decrease in other factors of mucosal immunity. This is precisely evidence of increased bacterial contamination of the oral cavity by pathogenic microflora in adolescents with inflammation of the gingival margin, both with and without diabetes [5, 10, 21]. Consequently, when the microbial profile of the biofilm changes, the level of urease activity increases, the activity of lysozyme and mucosal immunity of the oral cavity decreases.

Thus, patients with comorbid pathology always have significant changes in their immune status. It is the violation of specific and non-specific protection that contributes to the formation of the inflammatory process and destructive changes in the tissues of the oral cavity and subsequently causes severe pathological changes in the body. And the presence in the anamnesis of somatic diseases significantly suppresses the activity of all the body's protective mechanisms, which negatively affects the condition of periodontal tissues and oral mucosa. [4, 20].

**Conclusions.** The obtained results showed a significant suppression of all indicators of homeostasis of the oral cavity and a significant deterioration of its hygienic condition, along with the formation and further strengthening of the inflammatory process in the periodontal tissues in adolescents with diabetes mellitus.

**Prospects for further research.** Our further research will be aimed at studying and analyzing the mechanisms of pathogenesis, formation and course of inflammatory and inflammatory-destructive periodontal diseases in children and adolescents with diabetes of both types, as well as early diagnosis, treatment and prevention of complications in the oral cavity of such patients.

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