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L. L. Reshetnyk
ORCID https://orcid.org/0000-0001-9295-7800
O. V. Bida
ORCID https://orcid.org/0000-0002-6038-6545

Bogomolets National Medical University

DENTAL COMPONENTS OF ENDOGENOUS INTOXICATION IN THE PATHOGENESIS AND TREATMENT OF GENERALIZED PARODONTAL DISEASES IN PATIENTS WITH EATING DISORDERS

Л. Л. Решетник, О. В. Біда

Національний медичний університет імені О. О. Богомольця

СТОМАТОЛОГІЧНІ КОМПОНЕНТИ ЕНДОГЕННОЇ ІНТОКСИКАЦІЇ В ПАТОГЕНЕЗІ ТА ЛІКУВАННІ ГЕНЕРАЛІЗОВАНИХ ЗАХВОРЮВАНЬ ПАРОДОНТА У ПАЦІЄНТІВ З РОЗЛАДАМИ ХАРЧОВОЇ ПОВЕДІНКИ

INFORMATION

Email address
for correspondence:
reshetnik.lujdmila@gmail.com

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ABSTRACT

Violation of the structural organization of cell membranes, in particular under the influence of free radical oxidation processes, determines the main pathophysiological and clinical manifestations and decompensation of the pathological process in the periodontium. Prognostic for the assessment of endotoxicosis is clinical and biochemical monitoring of antioxidant system (AOS) parameters, in particular medium-weight peptides in patients with eating disorders.

Aim: to determine some dental markers of endogenous intoxication in patients with generalized parodontal diseases with eating disorders.

Materials and Methods. The main group was 60 patients (aged 19–44 years) with GPD (generalized parodontitis (GP), initial-II stage, chronic course) with ED. The comparison group included 45 patients of similar age, equal in gender, with GPP without eating disorders and 35 people with ED without GPD, as well as 30 practically healthy people with clinically intact periodontium. Clinical-radiological, laboratory (determination of peptides of average mass), as well as statistical research methods were used.

Research Results. In patients of the main group the concentration of middle molecules weight determined in blood serum at a wavelength of 254 nm (MMW254) (corresponding chain amino acids), was equal to 0.067 ± 0.002 (opt. units) in contrast to the indicator in the comparative groups, which was set at the level of 0.060±0.001 (opt. units) and 0.076 ± 0.002 (opt. units) respectively. In the control group, this indicator was 0.053 ± 0.001 (opt. units). In patients of the main group, the MMW280 indicator was equal to 0.064 ± 0.001 (opt. units) in contrast to the indicator in the comparative groups, which was set at the level of 0.059 ± 0.001 (opt. units) and 0.082 ± 0.001 (opt. units) respectively. In the control group, this indicator was 0.049 ± 0.001 (opt. units).

Therefore, the maximum accumulation of middle molecules weight in the oral fluid in patients with combined pathology – GP and ED is evidence of parallel processes of potentiation of metabolic disorders characteristic of these pathological conditions.

Conclusions. The obtained data confirm the presence of a pronounced interdependence between the level of endogenous intoxication and the severity of generalized periodontitis in patients with eating disorders, which indicates the need to include in the complex treatment of detoxification agents – both systemic and local, in combination with professional and individual oral hygiene.

ІНФОРМАЦІЯ

Електронна адреса
для листування:
reshetnik.lujdmila@gmail.com

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Ключові слова: генералізовані захворювання пародонта, генералізований пародонтит, ендогенна інтоксикація, розлади харчової поведінки, середньомолекулярні пептиди, стоматологічна патологія, гігієна порожнини рота, пародонтальні індекси, антиоксидантна система.

АНОТАЦІЯ

Актуальність. Порушення структурної організації клітинних мембран, зокрема під впливом процесів вільнорадикального окислення, визначає основні патофізіологічні та клінічні прояви й декомпенсацію патологічного процесу в пародонті. Прогностичним для оцінки ендотоксикозу є клініко-біохімічний моніторинг параметрів антиоксидантної системи (АОС), зокрема пептидів середньої маси у пацієнтів із розладами харчової поведінки.

Мета – визначити деякі стоматологічні маркери ендогенної інтоксикації у пацієнтів із генералізованими захворюваннями пародонта з розладами харчової поведінки.

Матеріали та методи. Основна група – 60 пацієнтів (віком 19–44 роки) з ГЗП (генералізований пародонтит (ГП), початковий – II ступінь, хронічний перебіг) з РПХ. До групи порівняння увійшли 45 пацієнтів аналогічного віку, рівних за статтю, з ГЗП без розладів харчової поведінки та 35 осіб з РПХ без ГЗП, а також 30 практично здорових осіб з клінічно інтактним пародонтом. Використовували клініко-рентгенологічні, лабораторні (визначення пептидів середньої маси), а також статистичні методи дослідження.

Результати дослідження. У пацієнтів основної групи концентрація середньо-молекулярних пептидів, визначена в сироватці крові на довжині хвилі 254 нм (відповідні амінокислоти ланцюга), дорівнювала 0,067 ± 0,002 (опт. од.) ,на відміну від показника в порівняльних групах, який був встановлений на рівні 0,060 ± 0,001 (опт. од.) та 0,076 ± 0,002 (опт. од.) відповідно. У контрольній групі цей показник становив 0,053 ± 0,001 (опт. од.). У пацієнтів основної групи показник MMW280 дорівнював 0,064 ± 0,001 (опт. од.), на відміну від показника в порівняльних групах, який був встановлений на рівні 0,059 ± 0,001 (опт. од.) та 0,082 ± 0,001 (опт. од.) відповідно. У контрольній групі цей показник становив 0,049 ± 0,001 (опт. одиниць).Отже, максимум накопичення СМП у ротовій рідині у хворих із поєднаною патологією – ГП та РХП – є свідченням паралельних процесів потенціювання метаболічних порушень, характерних для цих патологічних станів.

Висновки. Отримані дані підтверджують наявність вираженої взаємозалежності між рівнем ендогенної інтоксикації та ступенем тяжкості перебігу генералізованого пародонтиту в пацієнтів із розладами харчової поведінки, що свідчить про необхідність додавання до комплексного лікування засобів детоксикаційної дії – як загальносистемних, так і місцевих, у поєднанні з професійною та індивідуальною гігієною порожнини рота.

Introduction. Endogenous intoxication (EI) is a pathological process caused by the formation and accumulation of substances with toxic properties in the body. Endogenous intoxication is accompanied by a complex of metabolic disorders, among which the main place is occupied by the imbalance of the active antioxidant system and the level of free radical oxidation [1]. Free radical oxidation reactions are initiated by active oxygen species, which

lead to chemical modification and destruction of biomolecules. Due to the presence of complex enzyme complexes in the body, the process of oxygen reduction occurs according to a multi-stage mechanism, which minimizes the possibility of the formation of highly reactive oxygen intermediates [2]. Under conditions of oxidative stress or increased formation of active oxygen species, the functioning of the antioxidant system may be impaired [3]. The main markers of endogenous intoxication are middle molecules weight, (MMW) and the erythrocyte intoxication index (EII), which increase in the blood with the accumulation of toxic substances. These substances are formed as a result of pathological processes and disruption of normal metabolism, which leads to intoxication of the body [4].

The relevance of the problem of parodontal tissue disease is due to the significant prevalence that occurs in various links of homeostasis of the human body. Among them, special attention is paid to diseases of the endocrine, cardiovascular, nervous systems, pathology of the gastrointestinal tract and musculoskeletal system, seeing common reference points for GP and these diseases. This circumstance allowed declaring the concept of comorbidity, association and affiliation of a number of somatic diseases and GP, in particular eating disorders [5].

Eating disorders (EDs) are serious mental illnesses characterized by profound and persistent disturbances in eating habits, as well as excessive, sometimes obsessive, thoughts about food, weight and body shape [6]. These conditions are not just “diets” or “phases”; These are complex biological and psychological disorders that can lead to serious physical complications and even be fatal in the absence of necessary treatment [7].

The lack of clear ideas about the cause-and-effect relationships of the development of parodontal diseases significantly complicates the implementation of effective prevention and adequate treatment of these diseases, slows down the achievement of stable remission of the pathological process, complicates the selection of adequate and justified pharmacotherapy and other components of the complex treatment of parodontal diseases [7, 8].

According to literature data, the molecular marker of endogenous intoxication is middle molecules weight (MMW), which constitute a class of compounds with a molecular weight from 300–500 to 5000 daltons. The main part of MMW is made up of catabolism products of peptides, proteins containing chain and aromatic amino acids. Numerous clinical and experimental studies have established that MMW inhibit the processes of protein biosynthesis, tissue respiration and oxidative phosphorylation, change membrane permeability and membrane transport, and reduce the functional activity of immunocompetent cells [1, 5].

Thus, determining the level of EI and its dynamics are of great importance in the treatment of patients with periodontal disease in patients with periodontal disease. However, this issue is given little attention in the literature. Violation of the structural organization of cell membranes, in particular under the influence of free radical oxidation processes, determines the main pathophysiological and clinical manifestations and decompensation of the pathological process in the periodontium. Considering all of the above, clinical and biochemical monitoring of antioxidant system (AOS) parameters, in particular medium-weight spetides, is prognostic for the assessment of endotoxicosis.

The aim of the study was to determine some dental markers of endogenous intoxication in patients with generalized parodontal diseases with eating disorders.

Materials and Methods. The study used clinical and radiological, laboratory (determination of middle molecules weight), as well as statistical research methods. The main group was 60 patients (aged 19–44 years) with GPD (generalized parodontitis (GP), initial-II degree, chronic course) with eating disorders (ED). The comparison group included 45 patients of similar age, equal in gender, with GPD without eating disorders and 35 people with ED without GPD, as well as 30 practically healthy people with clinically intact parodontium. GPD was diagnosed according to the classification of M. F. Danylevsky, 2004.

Inclusion criteria were: (a) diagnosis of GD and ED for at least 1 year; (b) age 19–44 years; (c) signed informed consent to participate in the study.

Exclusion criteria were: history of diseases known to affect eating behavior: diabetes mellitus, thyroid disease and loss of appetite associated with cachexia syndrome (e.g., cancer, AIDS, renal failure, progressive liver disease, multiple sclerosis), refusal to participate in the study.

For oral examination and saliva analysis, a control group of 30 patients without ED, matched by sex and age, was selected from standard patients at the Dental Medical Center and the Department of Dentistry of the Institute of Postgraduate Education of the Bogomolets National Medical University.

The content of middle molecules weight (MMW), was determined by a modified method based on the precipitation of blood serum proteins with a 10% solution of trichloroacetic acid and the quantitative determination of medium-molecular peptides in the supernatant obtained by centrifugation. The determination of MMW fractions was carried out using a spectrophotometer “SF-46” with wavelengths of 254 nm (for identification of chain amino acids) and 280 nm (for aromatic amino acids). The results

obtained were expressed in relative (conditional) units of optical density [9, 10].

An increase in the MMW level was regarded as a marker of activation of proteolysis processes, accumulation of toxic products of incomplete protein breakdown, and disruption of protein and antioxidant homeostasis. The obtained data allowed to assess the intensity of endogenous intoxication and indirectly judge the severity of inflammatory and destructive processes in periodontal tissues against the background of metabolic disorders caused by eating disorders [10].

The method of determining the erythrocyte intoxication index (EII) was based on the property of erythrocytes to perform the function of a biological adsorbent. This made it possible to assess the degree of intoxication of the organism by analyzing the sorption capacity of cells for methylene blue, a polar compound that practically does not penetrate the cell membrane [11].

Statistical analysis. The obtained results are presented in the form of arithmetic mean (M) and standard error (m), taking into account the quantitative sample (n). The normal distribution of continuous variables was checked using the Kolmogorov-Smirnov criterion. The data were processed using the Wilcoxon-Mann-Whitney U-criterion using the Statistica 6.1 program (SN AJAX909E615822FB). Differences were considered significant at $p < 0.05$.

The study of patients was carried out in accordance with the Council of Europe Convention on Human Rights and Biomedicine (dated 04.04.1997), the Declaration of Helsinki of the World Medical Association on the Ethical Principles of Conducting Scientific Medical Research Involving Human Subjects (1964–2013). The study was approved by the Biomedical Ethics Commission of the Bogomolets National Medical University, Kyiv, Ukraine (protocol No. 156 dated August, 28, 2024). Written, informed consent was obtained from all participants.

The study was conducted as part of the research work of the Department of Dentistry of the Bogomolets National Medical University on the topic: “Interdisciplinary approach to the prevention, treatment and rehabilitation of patients with periodontal diseases and functional occlusion disorders” (State registration No. 0123U105134).

Results of the Study and Their Discussion. Impaired immunological reactivity of the organism with GPD in ED is accompanied by an increase in the level of medium-weight molecules and metabolic intoxication products, which causes damage to cellular structures and progression of the inflammatory process [7]. Endogenous intoxication is one of the key pathogenetic mechanisms that determine the development and progression of inflammatory processes in periodontal tissues [8]. It occurs as a result of metabolic disorders that accompany the development of generalized periodontal tissue diseases and leads to the accumulation of toxic metabolites in the systemic and local bloodstream. In particular, a significant increase in the level of medium-weight molecules plays a significant role in damage to cell membranes, causing their destabilization, impaired permeability and loss of functional activity [9]. The accumulation of such toxic compounds contributes to the development of oxidative stress, activation of lipid peroxidation and imbalance of the antioxidant system [10]. This increases the permeability of plasma and cytoplasmic membranes, which leads to damage to periodontal cells, microcirculation disorders and activation of a cascade of inflammatory reactions. A vicious circle arises when tissue degradation products and bacterial toxins additionally stimulate the immune response, which further exacerbates the inflammatory process and contributes to the destruction of the periodontal complex [11]. The level of endotoxicosis is determined by the concentration in the blood of both hydrophilic and hydrophobic metabolites, which accumulate due to metabolic disorders. Medium-weight molecules belong to the hydrophilic components of endogenous intoxication and are formed as a result of intensified proteolysis, which accompanies pathological conditions, in particular inflammatory processes in periodontal tissues [7, 8]. Due to their high biological activity, these molecules are able to interact with cell receptors, change membrane permeability and disrupt intercellular interactions, which ultimately contributes to the development of alterative changes in the body [8, 9]. Their ability to trigger a cascade of pathological reactions, in particular to enhance oxidative stress and the inflammatory response, makes them an important marker of the level of intoxication and the severity of inflammatory diseases [10, 11].

In the study groups – the main and comparison ((C_1)-GP-ED and (C_2)-ED) – significant changes in the level of middle molecules weight, (MMW) in the oral fluid of patients with GP associated with eating disorders were detected (Table 1).

So, as we can see from the table 1, in patients of the main group the concentration of middle molecules weight determined in blood serum at a wavelength of 254 nm (MMW_{254}) (corresponding chain amino acids), was equal to 0.067 ± 0.002 (opt. units) in contrast to the indicator in the comparative groups, which was set at the level of 0.060 ± 0.001 (opt. units) and 0.076 ± 0.002 (opt. units) respectively. In the control group, this indicator was 0.053 ± 0.001 (opt. units). In patients of the main group, the MMW_{280} indicator was equal to 0.064 ± 0.001 (opt. units) in contrast to the indicator in the comparative groups, which was set at the level of 0.059 ± 0.001 (opt. units) and 0.082 ± 0.001 (opt. units) respectively. In

Table 1

Indicators of the level of endogenous intoxication according to middle molecules weight, (MMW) in patients with GP with eating disorders, (M ± m)

	Survey groups			
	Control	**Basic**	**Comparative (C_1)**	**Comparative (C_2)**
Nosological form of the disease	Practically healthy	GP+ED	GP-ED	ED
Number of people surveyed	30	60	45	35
MMW_{254} (opt. units)	0,053 ± 0,001	0,067 ± 0,002 p < 0,01	0,060 ± 0,001	0,076 ± 0,002 p < 0,001
MMW_{280} (opt. units)	0,049 ± 0,001	0,064 ± 0,001 p < 0,001	0,059 ± 0,001	0,082 ± 0,001 p < 0,001

Note: the significance of the difference between groups is p ≤ 0.05.

the control group, this indicator was 0.049 ± 0.001 (opt. units).

The erythrocyte intoxication index (EII) is an important indicator of the state of cell membranes, which reflects a decrease in the sorption activity of erythrocytes in response to toxic effects [9]. Its increase indicates a violation of the structural integrity of the membranes and a change in their lipid composition, which, in turn, reduces the functional activity of erythrocytes. Under conditions of intoxication or an inflammatory process, erythrocytes can lose their ability to adsorb toxins and metabolites, which intensifies the manifestations of systemic intoxication and worsens the rheological properties of the blood [10]. Thus, changes in EII are an important marker of the depth of the pathological process and the degree of disorders in cell membranes.

A study of the effect of toxins on erythrocyte membranes in patients with GP with eating disorders revealed significant changes in the level of the erythrocyte intoxication index. In particular, in patients of the main group, the EII was 84.75 ± 0.47%, in contrast to the comparative groups, where this index was 65.29 ± 0.61% and 60.12 ± 0.33%, respectively. In patients of the control group, this indicator was 46.89 ± 0.31% (Table 2).

Thus, controlling the level of endogenous intoxication, correcting metabolic disorders, and normalizing antioxidant defense can be considered as promising approaches to the prevention and treatment of periodontitis, aimed at preserving the structural integrity of periodontal tissues and reducing the intensity of the inflammatory process.

The increase in the level of MMW in the oral fluid of patients with ED is due to the action of a complex of pathogenetic mechanisms, among which chronic hyperglycemia, oxidative stress and accumulation of advanced glycation end products (AGEs) play a leading role. Disturbance of carbohydrate metabolism is accompanied by mitochondrial dysfunction, activation of the polyol pathway, increased formation of free radicals and secondary toxic metabolites, which causes cell cytolysis, degradation of protein structures and accumulation of medium-weight peptides in the extracellular environment.

The results obtained provide grounds for including detoxification therapy methods in the complex treatment regimens of patients with ED – both general effects and direct effects on parodontal tissues against the background of professional and individual oral hygiene.

In patients with combined pathology – generalized parodontitis and eating disorders – these processes are intensified due to mutual potentiation of systemic and local inflammation, activation of the leukocyte-myeloperoxidase system, impaired

Table 2

Indicators of the erythrocyte intoxication index in patients with GP with eating disorders, (M ± m)

	Survey groups			
	Control	**Basic**	**Comparative (C_1)**	**Comparative (C_2)**
Nosological form of the disease	Practically healthy	GP+ED	GP-ED	ED
Number of people surveyed	30	60	45	35
Erythrocyte intoxication index, EII (%)	46,89 ± 0,31	84,75 ± 0,47 p < 0,001	65,29 ± 0,61 p < 0,001	60,12 ± 0,33 p < 0,001

Note: the significance of the difference between groups is p ≤ 0.05.

microcirculation and tissue hypoxia. This leads to a more intensive accumulation of products of incomplete protein metabolism, which is reflected in increased values of MMW in the oral fluid.

The results obtained by us indicate the violation of metabolic processes in patients with GPD at ED, which are manifested in different degrees of endogenous intoxication. It was established that in all patients of the main group in the blood serum there are significant changes in the indicators of middle molecules weight, (MMW) compared with the data of the control group. The dynamics of the concentration of both fractions of MMW indicates unidirectional changes in medium-molecular peptides.

Generalized parodontal diseases in eating disorders are accompanied by an increase in the level of endogenous intoxication, as evidenced by an increase in the content of both fractions middle molecules weight, (MMW) in the blood serum, and the degree of severity of endogenous intoxication depends on the duration of the action of the endogenous factor.

Conclusions: 1. One of the factors in the development of generalized parodontal diseases in patients with ED is endogenous intoxication. The data obtained confirm the presence of a pronounced interdependence between the level of endogenous intoxication and the severity of the course of generalized parodontitis in patients with eating disorders, which indicates the need to include in the complex treatment of detoxification agents – both systemic and local, in combination with professional and individual oral hygiene.

2. The results obtained confirm the pathogenetic feasibility of including vitamin and mineral correction in the complex treatment of patients with generalized parodontal diseases on the background of eating disorders, which allows to increase the effectiveness of dental rehabilitation and improve the quality of life of patients.

3. The obtained data emphasize the significance of individual differences in hypoxic tolerance in the formation of the oxidative component of periodontitis pathogenesis and can be taken into account when developing personalized approaches to its treatment and prevention.

Prospects for Further Research. Further research should be aimed at in-depth study of molecular mechanisms of periodontal tissue adaptation to hypoxic stress. It is promising to identify biomarkers of oxidative damage taking into account individual hypoxic resistance. This will allow developing personalized approaches to the diagnosis and antioxidant therapy of periodontitis in patients with eating disorders.

Conflict of interest. The authors deny any conflict of interest.

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