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Enteropathies and oxidative stress

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Background: Oxidative stress is related with digestive tract diseases – pancreatitis, duodenal ulcer, ulcerative colitis, glutenic enteropathy. Changes in the antioxidation system can be conditioned by malabsorbtion.

The aim of the work was to evaluate the alterations in peroxidation-antioxidation status indexes in cases of glutenic enteropathy associated with hypolactasia and with rheumatoid arthritis, to compare data received while examining patients and members of the control group.

Materials and methods: Peroxidative status was evaluated according to malondialdehyde (MDA) concentration in the blood serum in 64 subjects, among them 11 had glutenic enteropathy associated with hypolactasia, 23 – with rheumatoid arthritis, and 30 subjects (with digestive system diseases in remission phase) were from the control group. Antioxidation system status was analyzed by measuring catalase activity.

Results: It was established that in case of glutenic enteropathy associated with hypolactasia malondialdehyde concentration increased 1.5 times: 5.93 ± 0.31 versus 3.34 ± 0.12 ($p < 0.001$) in the control group; the concentration of diyenic conjugate increased 1.7 times 9.24 ± 0.74 versus the control group (5.6 ± 1.9, $p < 0.001$). Catalase activity decreased from 42.34 ± 2.2 in the control group to 28.71 ± 2.1 in glutenic enteropathy hypolactasia patients, i. e. 1.3 times ($p < 0.05$). For enteropathy glutenic patients with rheumatoid arthritis the following lipid peroxidation markers were established: concentration of malondialdehyde increased 1.5 times (5.67 ± 0.23) versus the control group (3.48 ± 0.11, $p < 0.001$); diyenic conjugates concentration increased 1.6 times (9.90 ± 0.66) versus 5.8 ± 1.9 ($p < 0.001$) in the control group. Catalase activity decreased from 42.96 ± 2.1 in the control group to 29.25 ± 1.8 in glutenic enteropathy patients with rheumatoid arthritis, i. e. 1.3 times ($p < 0.05$).

Our study proved that sampling and oxidative stress analysis of patients with digestive system and other autoimmune diseases is purposeful.

Key words: glutenic enteropathy, hypolactasia, rheumatoid arthritis, oxidative stress, lipid peroxidation

INTRODUCTION

Peroxidation of free radicals in lipids is a normal metabolism process of all tissues and organs in normal physiological status of the organism. Lipid peroxidation (LP) is strictly regulated by endogenic antioxidants. The main role is played by superoxide dismutase, catalase, glutathionperoxidase, glutathionreductase (1) The antioxidation system (AOS) is one of the adaptational systems of the organism. It regulates peroxidative processes of the lipids. It is diagnosed that regulation disorders of lipid peroxidation and exhaustion of the antioxidative system are closely related with many diseases (2).

Metabolic alterations in the organism start when the balance between LP and AOS is lost. Effects of LP and AOS first of all appear in the composition of lipids in cell membranes when formatting their structure and regulating membrane permeability. Despite the determinant causes, LP intensification influences the biological system and disbalances it (3).

Many diseases are associated with oxidative stress in the tissues. The latter is pertinent to age-related diseases such as heart diseases, diabetes, Alzheimer disease. (4)

Oxidative stress is also related with digestive diseases such as pancreatitis, peptic ulcer, ulcerative colitis, glutenic enteropathy (5,6). GE is a chronic small intestine disease. Gluten (specific cereal protein) is the main and characteristic factor in the pathogenesis of this disease. The disease cankers the mucous membrane and malabsorption. The main role in the pathogenesis is play-ed by such mechanisms as apoptosis, oxidative stress, seedbed metalloproteinases and disorders of proliferation and differentiation (7). Cereal proteins were found to affect the differentiation of the immune system, and gliadin-containing peptides are characteristic

of cytotoxic activity. It is related with oxidative imbalance which is characteristic of oxidative stress, oxidated-reduced glutathione proportion disbalance and loss of protein SH groups (8, 9).

In normal physiological conditions, lipid peroxidation is happening at a certain limited speed and is one of the links in cell metabolism. Reactive oxygen parts are involved in the processes of cell growth, segmentation and death. Their small concentration is useful for the organism, it takes part in the internal processes of cell signalization, protects them from microorganisms. High concentrations of free radicals play an important role in the pathogenesis of some diseases. Toxic oxygen combinations, peroxides, free radicals modify membrane permeability thus causing inflammation and disorder of separate organs.

In the recent years, the existing association between arthritis, gastrointestinal and glutenic enteropathy attracts attention (10, 11). It is believed that patients with celiac disease have immune complexes formed in the mucous membrane of the small intestine. These complexes accumulate in other organs and stimulate the origin and progress of autoimmune diseases (12).

According to the literature, GE also often coexists with neurological diseases such as Alzheimer and Parkinson diseases. (13) During them, an increase in lipid peroxidation was tested. Enzyme tissue transglutaminase is involved in the pathogenetic mechanism of these diseases (14, 15).

What is more, GE can show itself only through neurological symptoms when gastrointestinal symptoms are missing. In this way GE can be related with the diagnostics of neurological diseases. Oxidative stress is important in their pathogenesis (16).

Glutenic enteropathy – a chronic disease classified as gut enzymopathy – is related with alterations of oxydative stress indexes (8). The antioxidative system's alterations can be conditioned by malabsorbtion (17).

The aim of the present study was to evaluate the alterations of indexes of the peroxidation-antioxidation status in case of with hypolactasia and glutenic enteropathy associated with rheumatoid arthritis, to compare data obtained while examining patients and people from the control group.

MATERIALS AND METHODS

Peroxidative and antioxidation system status was examined in 64 subjects, among them 11 had glutenic enteropathy associated with hypolactasia, 23 had glutenic enteropathy associated with rheumatoid arthritis, and 30 patients (with digestive system diseases in remission phase) were from the control group.

The peroxidative status was evaluated according to malondialdehyde (MDA) concentration in the blood serum (18). In order to quantify lipid peroxides, their transformation into a colour combination with thiobarbituric acid was used. Malondialdehyde (MDA) is a final product of fatty acid peroxidation, it reacts with thiobarbituric acid, making a coloured complex which is characterized by absorption maximum when the length of the wave is 532 nm. Data are expressed in nmol/ml.

Antioxidation system status was analyzed by measuring catalase activity (19). The essence of this is that the decline of hydrogen peroxide is measured time-wise. Hydrogen peroxide makes a stable colour complex with ammonium molibdate when the length of the wave is 410 nm. Enzyme activity is measured in nmol/l/min.

RESULTS

Malondialdehyde, diyenic conjugates, and the antioxidative enzyme catalase changes of lipid peroxidation markers were investigated in 64 subjects, among them 11 had glutenic enteropathy associated with hypolactasia, 23 had glutenic enteropathy associated with rheumatoid arthritis, and 30 patients (with digestive system diseases in remission phase) were from the control group. It was established that in the case of glutenic enteropathy associated with hypolactasia, malondialdehyde concentration increased 1.5 times: 5.93 ± 0.31 versus 3.34 ± 0.12 ($p < 0.001$) in the control group; the concentration of diyenic conjugate increased 1.7 times (9.24 ± 0.74) versus the control group (5.6 ± 1.9, $p < 0.001$). Catalase activity decreased from 42.34 ± 2.2 in people from the control group to 28.71 ± 2.1 in glutenic enteropathy hypolactasia patients, i. e. 1.3 times ($p < 0.05$). The data are presented in Table 1. In patients with glutenic enteropathy associated with rheumatoid arthritis, the following lipid peroxidation markers were established: the concentration of malondialdehide increased 1.5 times (5.67 ± 0.23) versus the control group (3.48 ± 0.11, $p < 0.001$); diyenic conjugates' concentration increased 1.6 times (9.90 ± 0.66) versus 5.8 ± 1.9 ($p < 0.001$) in the control group. Catalase activity decreased from

Table 1. **Changes of oxidative stress of glutenic enteropathy associated with rheumatoid arthritis patients and in control group**

Indices	GE + hypolactasia	Control group N = 30	p
MDA	5.67 ± 0.23	3.48 ± 0.11	<0.001
Diyenic conjugate	9.90 ± 0.66	5.8 ± 1.9	<0.001
Catalase activity	29.25 ± 1.8	42.96 ± 2.1	<0.05

Table 2. **Changes of oxidative stress of glutenic enteropathy associated with rheumatoid arthritis patients and in control group**

Indices	GE + RA N = 23	Control group N = 30	p
MDA	5.67 ± 0.23	3.48 ± 0.11	<0.001
Diyenic conjugate	9.90 ± 0.66	5.8 ± 1.9	<0.001
Catalase activity	29.25 ± 1.8	42.96 ± 2.1	<0.05

42.96 ± 2.1 in the control group patients to 29.25 ± 1.8 in patients with glutenic enteropathy associated with rheumatoid arthritis, i. e. 1.3 times ($p < 0.05$). The data are presented in Table 2. A comparison of lipid peroxidation markers in patients with glutenic enteropathy associated with hypolactasia and in patients with glutenic enteropathy associated with rheumatoid arthritis revealed no statistically reliable difference.

DISCUSSION

A comparison of changes of oxidative stress markers in the serum of people with rheumatoid arthritis and of those from the control group as well as of patients with glutenic enteropathy associated with rheumatoid arthritis and from the control group that lipid peroxidation increases. Inflammatory cell activation and free radical hyperproduction, which have a huge impact on the circulating products of lipid peroxidation, takes place. This is in agreement with data of other authors (20, 21). An increase in serum levels of malondialdehyde and diyenic conjugates and a decrease in catalase activity show the importance of free radicals in the inflammatory processes. In case of rheumatoid arthritis, joints cankered by inflammation suffer from oxidation because there are many active phagocytes which produce superoxide radicals, the excess of which damages joint tissues affected by illness.

Some literature sources indicate that in patients with rheumatoid arthritis malondialdehyde concentration and superoxide dismutase activity decrease, while catalyze activity remains unaltered (22). Our researches showed that in case of rheumatoid arthritis as well as glutenic enteropathy associated with rheumatoid arthritis, catalases activity decreases 1.4 times, malondialdehyde concentration increases 1.7 times in cases of glutenic enteropathy associated with rheumatoid arthritis, and 1.5 times in cases with rheumatoid arthritis only.

Recent studies have shown the importance of intracellurar antioxidant level in cell immunity protection (23). The data received when analyzing the antioxidative system in cases of rheumatoid arthritis are contradictory; even when malondialdehyde concentration increases, catalase activity is fixed (24, 25). Some authors state that oxidative stress has no significant influence in cases of inflammable joint illnesses (23). A comparison of oxidative stress markers in patients with glutenic enteropathy associated with rheumatoid arthritis and in patients with rheumatoid arthritis only revealed no significant disparity.

It is indicated in literature that in cases of glutenic enteropathy, malondialdehyde concentration the marker of lipid peroxidation, significantly increases compared with the healthy ones, and the level of the antioxidant alfatocoferol decreases (17).

We have not found data in the literature on the dynamics of lipid peroxidation markers in patients with glutenic enteropathy associates with hypolactasia and glutenic enteropathy associated with rheumatoid arthritis.

Summing up our results, we can state that glutenic enteropathy is not a very rare disease and its clinical expression has changed. Its symptoms became less evident and often can be detected only after compiling a comprehensive anamnesis. Absence of classic symptoms does not exclude the possibility of enteropathy. Our study proves that sampling and oxidative stress analysis in patients with digestive system and other autoimmune diseases is purposeful.

CONCLUSIONS

In patients with glutenic enteropathy associated with hypolactasia and in patients with glutenic enteropathy associated with rheumatoid arthritis, the concentration of MDA and DC was significantly increased and catalase activity was significantly decreased versus the control group.

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ENTEROPATIJOS IR OKSIDACINIS STRESAS

S a n t r a u k a

Oksidacinis stresas yra susijęs su virškinimo organų ligomis – pankreatitu, skrandžio, dvylikapirštės žarnos opalige, opiniu kolitu, gliutenine enteropatija. Antioksidacinės sistemos pokyčius gali lemti malabsorbcija. Mūsų tyrimais įvertinti organizmo peroksidacinės-antioksidacinės būklės rodiklių pakitimai sergančiųjų gliutenine enteropatija su hipolaktazija ir gliutenine enteropatija su reumatoidiniu artritu. Nustatyta, kad, sergant gliutenine enteropatija su hipolaktazija, malondialdehido koncentracija padidėja 1,5 karto, $5,93 \pm 0,31$, lyginant su kontroline grupe, $3,34 \pm 0,12$ ($p < 0,001$); dijeninių konjugatų koncentracija padidėja 1,7 karto, $9,24 \pm 0,74$, lyginant su kontroline grupe, $5,6 \pm 1,9$ ($p < 0,001$). Katalazės aktyvumas sumažėja nuo $42,34 \pm 2,2$ kontrolinės grupės tirtųjų iki $28,71 \pm 2,1$ sergančiųjų gliutenine enteropatija su hipolaktazija, tai yra 1,3 karto ($p < 0,05$). Nustatyti tokie sergančiųjų gliutenine enteropatija su reumatoidiniu artritu lipidų peroksidacijos žymenys: malondialdehido koncentracija išaugo 1,4 karto, $5,67 \pm 0,23$, lyginant su kontroline grupe – $3,48 \pm 0,11$ ($p < 0,001$); dijeninių konjugatų koncentracija padidėja 1,6 karto, $9,90 \pm 0,66$, lyginant su kontroline grupe – $5,8 \pm 1,9$, ($p < 0,001$). Katalazės aktyvumas sumažėja nuo $42,96 \pm 2,1$ kontrolinės grupės asmenų iki $29,25 \pm 1,8$ sergančiųjų gliutenine enteropatija su reumatoidiniu artritu, tai yra 1,3 karto ($p < 0,05$). Mūsų tyrimas patvirtina sergančiųjų virškinimo sistemos ir kitomis autoimuninėmis ligomis oksidacinio streso rodiklių tyrimo tikslingumą.

Raktažodžiai: gliuteninė enteropatija, hipolaktazija, reumatoidinis artritas, oksidacinis stresas, lipidų peroksidacija