EVALUATION OF THE BIOCHEMICAL INDICATORS OF BLOOD OF PATIENTS AFTER MYOCARDIAL INFARCTION WITH DEPRESSIVE SYNDROME

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EVALUATION OF THE BIOCHEMICAL INDICATORS OF BLOOD OF PATIENTS AFTER MYOCARDIAL INFARCTION WITH DEPRESSIVE SYNDROME

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Resume,

Examination of 58 patients with myocardial infarction (MI) who were admitted for treatment to a cardiological hospital. Based on the presence of anxiety-depressive symptoms, patients are divided into 2 groups. The first control group consisted of 14 patients who had MI without depressive disorders. The second group included 44 age-comparable patients who underwent MI with symptoms of anxiety and depression without comorbid cardiovascular pathology. The results obtained allowed us to establish that an increase in anxiety-depressive symptoms is preceded by a pronounced decrease in caspase activity indicators after 3.6 and 12 months after a more significant increase in its level by 30 days in the examined patients of the comparative control group.

The goal is to search for pathogenetic predictors of the development of anxiety-depressive disorders in MI, to develop ways to correct them and to reduce the frequency of complications of the post-infarction period.

Material and methods.

Clinical studies were based on the examination of 58 patients with MI (average 59.2 ± 4.7 years) who were admitted for treatment to a cardiological hospital, and observation data for them at the rehabilitation stage. Based on the presence of anxiety-depressive symptoms, patients are divided into 2 groups. The first control group consisted of 14 patients who had MI without depressive disorders. The second group included 44 age-comparable patients who underwent MI with symptoms of anxiety and depression without comorbid cardiovascular pathology. The diagnosis of myocardial infarction was based on the results of a clinical examination, ECG changes, laboratory parameters, and echocardiography data. Biochemical studies and assessment of mental status were carried out in patients on 30, 90, 180, and 360 days after myocardial infarction. All patients received standard treatment upon admission to the hospital, including therapy for concomitant diseases. In order to assess the mental status of the subjects, subjective methods were used: the hospital anxiety and depression scale (HADS), developed by A. Zigmond and R. Snauth (1983) for somatic patients and recommended to use in patients with a post-infarction period. Blood for examination in patients was taken in the first 72 hours after the destabilization of the clinical condition of MI once after obtaining the informed consent of each patient.

The determination of caspase-3 activity in blood plasma was defined by the colorimetric method according to cleavage of the synthetic substrate Ac-IETD-pNA (N-acetyl-IleGlu-Tre-Asp-nitroaniline, "Sigma") (M. M. Bradford, 1976). The supernatant (protein concentration 2 mg/ml) was incubated for 60 minutes at 37 °C in a reaction buffer containing 150 mM HEPES, pH 7.5, 15% sucrose, 15 mM dithiothreitol, 0.15% CHAPS, 1 mM Na ethylenediaminetetraacetate. The reaction was carried out in two parallel samples, one of which contained 25 μM N-acetyl-Asp-Glu-Val-Asp-7-amino-4-trifluoromethylcoumarin (fluorogenic substrate for caspase-3), and the other 25 μM N-acetyl-Asp-Glu-Val-Asp-7-amino-4-trifluoromethylcoumarin and 5 μM N-acetyl-Asp-Glu-Val-Asp-CHO (caspase-3 inhibitor) (Biomol, USA). The optical density was recorded every 10 min within 1 hour on an IFA analyzer at a wavelength of 405 nm. Caspase activity was calculated by the difference in substrate cleavage rates in samples without inhibitor and in the presence of an inhibitor, taking into account the calibration curve of the optical density of the pNA standard. Theriv Scientific TSQ 8000 EVO system was used to quantify the plasma 5-OIAK content.

Results. Based on the data obtained, it can be argued that the biochemical manifestation of anxiety-depressive disorder in the development of MI is a more pronounced increase in serotonergic mediation in response to acute disturbance of coronary blood flow. The aggravation of affective symptoms was preceded by an increase in the level of 5-OIAK, which was manifested by an increase in 5-RT utilization on the 30th day of the study. A decrease in 5-RT utilization in patients who have undergone MI with the clinical manifestations of depression after 6 and 12 months allows us to predict
a decrease in the severity of symptoms of affective disorder. During these periods of the study, indicators of 5-HIAA in the blood tended to decrease relative to indicators on the 30th day of the study, on average by 41% and 49%, respectively.

Conclusions.

Thus, the obtained results of caspase activity in the course of this study made it possible to establish that an increase in anxiety-depressive symptoms is preceded by a pronounced decrease in caspase activity indicators after 3.6 and 12 months after a more significant increase in its level by 30 days in the examined patients of the comparative control group. A similar dynamics was noted regarding the content of 5-HIAA in the blood of the examined patients. Therefore, on the 30th day after MI, in patients with symptoms of anxiety and depression, there will be noted higher levels of endogenous intoxication, apoptosis processes and increased serotonergic mediation aggravate the course of the disease when compared with indicators of longer follow-up periods.

Key words: post-infarction depression, comorbidity, risk factors, pathogenetic predictors, caspase activity.

Relevance

A number of diseases are accompanied by the development of affective disorders, including depression, as a result of which the character of the patient’s sensations changes, his perception, and assessment of environmental events, which leads to disturbances in interpersonal relationships and a deterioration in the quality of life. It is known that depression is very often comorbid to others, somatic, diseases, and in such cases, diseases of two different areas - mental and somatic - exacerbate each other, sometimes leading to serious consequences. This is especially true for diseases of the cardiovascular system (1,2,3,4,5) Comorbid heart attack depression predetermines a three to four-fold increase in cardiovascular mortality, and also closely correlates with an aggravation of the clinical symptoms of MI and a worsening prognosis of this pathology. One of the factors determining the course and prognosis of myocardial infarction (MI) is the development of anxiety-depressive disorders (MAD). Manifestations of a major depressive episode occur in 15-20% of patients with this nosological form. In patients with a post-infarction period, depression is detected in 16-45% of cases. American scientists have shown that an increase in mortality after myocardial infarction is associated with even minimal symptoms of depression. Therefore, along with the ongoing diagnostic measures (instrumental and biochemical) in patients with myocardial infarction, it is necessary to pay attention to the psychological testing of patients to detect anxiety-depressive disorders. Although the number of studies on depression in post-infarction patients is relatively small, there is some evidence that without treatment, it becomes chronic within a year after a myocardial infarction (6,7,8,9). Thus, an analysis of the literature data showed that the development of the depressive disorder is associated with an aggravation of the pathophysiological changes characteristic of coronary heart disease and MI, in particular. However, the pathophysiological mechanisms of the relationship of depression and myocardial infarction, and most importantly, the mechanisms of development of depression in myocardial infarction, have not been completely studied.

In connection with the foregoing, it seems relevant to search for pathogenetic predictors of the development of anxiety-depressive disorders in myocardial infarction, which will allow us to develop ways to correct them, thereby reducing the frequency of complications of the post-infarction period, which was the purpose of our study. Based on the foregoing, it was of interest to us to study the dynamics of caspase activity of blood plasma and the content of 5-hydroxyindoleacetic acid (5-HIAA) in patients who had myocardial infarction with clinical manifestations of depressive syndrome, which constituted the main group and patients who had myocardial infarction without clinical manifestations of depressive syndrome (control group [10,11,12]. A set of biochemical studies was chosen because the change in caspase activity of blood plasma and the content of 5-hydroxyindoleacetic acid (5-HIAA) in patients who had myocardial infarction with clinical manifestations of depressive syndrome, which constituted the main group and patients who had myocardial infarction without clinical manifestations of depressive syndrome (control group [10,11,12]. A set of biochemical studies was chosen because the change in caspase activity of blood plasma and the content of 5-hydroxyindoleacetic acid (5-HIAA) in patients who had myocardial infarction with clinical manifestations of depressive syndrome, which constituted the main group and patients who had myocardial infarction without clinical manifestations of depressive syndrome (control group [10,11,12]. A set of biochemical studies was chosen because the change in caspase activity of blood plasma and the content of 5-hydroxyindoleacetic acid (5-HIAA) in patients who had myocardial infarction with clinical manifestations of depressive syndrome, which constituted the main group and patients who had myocardial infarction without clinical manifestations of depressive syndrome (control group [10,11,12].
patients with MI with depressive disorders are not well understood.

The aim of the study was to examine patients with myocardial infarction admitted for treatment to a cardiological hospital, and their observation data at the rehabilitation stage.

Materials and methods

Clinical studies were based on the examination of 58 patients with MI (mean age 59.2 ± 4.7 years) who were admitted for treatment to a cardiological hospital, and observation data for them at the rehabilitation stage. Based on the presence of anxiety-depressive symptoms, patients are divided into 2 groups. The first control group consisted of 14 patients who had MI without depressive disorders. The second group included 44 age-comparable patients who underwent MI with symptoms of anxiety and depression without concomitant cardiovascular pathology. The diagnosis of myocardial infarction was based on the results of a clinical examination, ECG changes, laboratory parameters and echocardiography data. Biochemical studies and assessment of mental status were carried out in patients on 30,90,180 and 360 days after myocardial infarction. All patients received standard treatment upon admission to the hospital, including therapy for concomitant diseases. In order to assess the mental status of the patients, subjective methods were used: the hospital anxiety and depression scale (HADS), developed by A.Zigmond and R.Snaith (1983 (11)) for somatic patients and recommended to use in patients with a post-infarction period. Patients' blood was taken in the first 72 hours after destabilization of the clinical condition of MI once after obtaining the informed consent of each patient. The existence of caspase-3 activity in blood plasma was determined by colorimetric method by speed and cleavage of the synthetic substrate Ac_IETD_pNA (N-acetyl-IleGlu_Tre_Aspx nitroaniline, “Sigma”) (M. M. Bradford, 1976). The supernatant (protein concentration 2 mg/ml) was incubated for 60 minutes at 37 °C in a reaction buffer containing 150 mM HEPES, pH 7.5, 15% sucrose, 15 mM dithiothritol, 0.15% CHAPS, 1 mM methylenediaminetetraacetate Na. The reaction was carried out in two parallel samples, one of which contained 25 μM N-acetyl-Asp-Glu-Val-Asp-7-amino-4-trifluoromethylcoumarin and another 25 μM N-acetyl-Asp-Glu-Val-Asp-7-amino-4-trifluoromethylcoumarin and 5 μM N-acetyl-Asp-GIValyl-Asp-CHO (caspase-3 inhibitor) (Biomol, USA). The optical density was recorded every 10 min within 1 hour on an IFA analyzer at a wavelength of 405 nm. Caspase activity was calculated by the difference in substrate cleavage rates in samples without inhibitor and in the presence of an inhibitor, taking into account the calibration curve of the optical density of the pNA standard. Thermo Scientific TSQ 8000 EVO system was used to quantify the plasma 5-OIAK content. The concentration of 5-HIAAA was calculated by comparing the peak value in the sample with the peak value of the standard. Statistical processing of the obtained data was carried out using the software package Statistica 6.0 for Windows. The significance of differences between the average values was evaluated by Student. Differences were considered statistically significant at p < 0.05. Research results and discussion. When studying caspase activity in the blood plasma of patients after myocardial infarction with clinical manifestations of depressive syndrome (Table 1), we can note a peculiar dynamics of the activity of the studied enzyme relative to the group of patients who underwent MI without signs of depressive syndrome. So, in this group of patients, an increase in caspase activity in the blood 1 month after MI was noted by an average of 6.8 times. In our opinion, the observed dynamics of caspase activity is due to the fact that necrotic processes begin to prevail against the background of the prevalence of activity of catecholamine systems in the acute period of MI in patients with concomitant symptoms of anxiety and depression. This, possibly, leads to the formation of a relatively smaller volume of hibernating myocardium, for which the process of apoptotic death is characteristic. On the other hand, the activation of apoptosis in the early period after MI, which is more accentuated in patients with anxiety-depressive symptoms, leads to the fact that their cells die faster using this mechanism than in subsequent periods of the development of the disease. Thus, in patients who underwent MI with clinical signs of the depressive syndrome, higher levels of endogenous intoxication and apoptosis processes were observed within 30 days, exacerbating the course of the disease.

As a result of the development of cardiomyocytes, it dies from the formation of a connective tissue scar, which leads to a decrease in the contractility of the heart muscle and the development of apoptosis. In the subsequent periods of the study, downward trends and the
lowest numbers were revealed, which were observed for 3 months in patients who had MI with clinical manifestations of depressive syndrome when compared with a group without clinical manifestations of depression. After 6 months, caspase activity exceeded the initial level by 1.5 times, after 12 months - by 1.9 times when compared with the comparison indices of groups. Thus, in patients undergoing clinical manifestations, the highest caspase activity values are observed, which indicate endogenous intoxication and apoptosis processes that aggravate the course of diseases. Therefore, along with the ongoing diagnostic measures (instrumental and biochemical) in patients after MI, with clinical manifestations of depressive syndrome, it is necessary to pay attention to the research of apoptotic markers to detect anxiety-depressive disorders in the early stages after MI. An interesting dynamics is associated with serum 5-hydroxyindoleacetic acid, which is significantly increased within 1 month in patients who have undergone MI with clinical manifestations of depressive syndrome, which allows us to think about an increase in the use of serotonin (5-RT) in patients of this subgroup. Pay attention to the fact that the content of patients aged 3 to 32 months (p > 0.05) is lower than in the group of patients for 30 days. Consequently, an improvement in mental state (the progression of symptoms of depression) was preceded by an increase in the level of 5-HIAA and an increase in caspase activity after 1 month. This allows to conclude that patients of this group have a deficit in serotonergic mediation.

Table 1

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Patients with MI without Depression Control N=14</th>
<th>MI patients with depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caspase Activity pmol/min/ml</td>
<td>0,15+0,01</td>
<td>1,02+0,05</td>
</tr>
<tr>
<td>5-hydroxyindoleacetic acid content g/ml</td>
<td>14,6+0,91</td>
<td>48,02+5,05</td>
</tr>
</tbody>
</table>

Based on the obtained data, it can be argued that the biochemical manifestation of anxiety-depressive disorder in the development of MI is a more marked increase in serotonergic mediation in response to acute disturbance of coronary blood flow. The aggravation of affective symptoms was preceded by an increase in the level of 5-OIAK, which was manifested by an increase in 5-RT utilization on the 30th day of the study. A decrease in 5-RT utilization in patients who have undergone MI with the clinical manifestations of depression after 6 and 12 months allows us to predict a decrease in the severity of symptoms of affective disorder. During these periods of the study, indicators of 5-HIAA in the blood tended to decrease relative to indicators on the 30th day of the research, on average by 41% and 49%, respectively.

Conclusion

Thus, the obtained results of caspase activity in the course of this study made it possible to establish that an increase in anxiety-depressive symptoms is preceded by a pronounced decrease in caspase activity indicators after 3.6 and 12 months since a more significant increase in its level by the 30th day in the examined patients of the comparative control group. A similar dynamics was noted regarding the content of 5-HIAA in the blood of the examined patients. Therefore, on the 30th day after MI, in patients with symptoms of anxiety and depression, higher levels of endogenous intoxication, apoptosis processes, and increased serotonergic mediation aggravate the course of the disease when compared with indicators of long terms of observation.
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