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Выявляемость ЗНО шейки матки по Павлодарской области в 2021 году составила примерно 2%. Из 103 женщин, у которых была диагностирована дисплазия эпителиальных клеток шейки матки, у 2 обнаружен плоскоклеточный рак.

На основании этого можно сделать вывод, что своевременное прохождение профилактических осмотров позволяет предотвратить появление тяжелых заболеваний, в том числе рак шейки матки.

Заключение. Скрининг рака шейки матки в Павлодарской области за 2021 год охватил всю целевую группу населения, к которой относятся женщины в возрасте от 30 до 70 лет. Выявляемост.ь патологии составила 3% от целевой группы. Наличие злокачественного образования среди выявленных патологий составило 2%. Полученные данные свидетельствуют о том, что если женщины смогут своевременно проходить профилактический осмотр, то это значительно снизить риск возникновения ЗНО у женщин работоспособного возраста.

Обзор литературы показал, что за 13 лет проведения Национальной скрининговой программы заболеваемость раком шейки матки значительно снизилась. Среди выявленных патологий значительно уменьшилось количество онкологии. Это произошло по причине того, что скрининг позволяет выявить предопухолевое состояние и вовремя излечить его.

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SYSTEMIC CONTENT OF EICOSANOIDS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE CONCOMITANT WITH CORONARY HEART DISEASE

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Abstract

In paper we investigated the content of eicosanoids – leukotriene B4 and thromboxane A2 (by stable metabolite TxB2) in the blood serum and urine in patients with COPD, combined with CHD. We investigated 37 patients with exacerbation of COPD (clinical group B, GOLD II) associated with CHD – the main group, 27 patients with exacerbation of COPD (I^{st} comparison group) and 30 patients with coronary heart disease, stable angina pectoris (II^{nd} comparison group). Our research revealed the highest concentrations of LTB4 and TxB2 in the blood serum of patients with COPD associated with CHD, comparing to patients with COPD without CHD and with CHD

without COPD that was accompanied by increasing of their excretion with urine. The strength and direction of correlation links between concentrations of these eicosanoids in blood serum and indices of bronchial patency indicate their negative influence on bronchial patency of patients with a combination of COPD and CHD.

Keywords: leukotrienes, thromboxanes, Cronic Obstructive Pulmonary disease, Coronary Heart disease.

Introduction. Comorbidity is now a characteristic feature of modern internal medicine and pulmonology [1, 8]. An unfavorable ecological situation, bad habits, chronic stresses, irrational nutrition, aging of the population cause development of the co- or polymorbidity. The close anatomical and physiological relationship of the respiratory and cardiovascular systems in patients over the age of 40 years contributes to the frequent combination of chronic obstructive pulmonary disease (COPD) and coronary heart disease (CHD) [10]. The number of patients with COPD is steadily increasing. In persons over 40 years, the morbidity of COPD rises to 10.1%. Nowadays COPD has got the 4th place among all causes of death, accounting for 4% in their overall structure [7].

Coronary heart disease (CHD) and heart failure (HF) become among the leading, but not always timely diagnosed, causes of death in patients with COPD. According to large-scale population-based studies, the risk of death from cardiovascular disease in patients with COPD is increased by 2-3 times and accounts for about 50% of the total number of deaths [4]. In patients with COPD, the frequency of hospitalizations due to cardiovascular disease is higher than only because of COPD. At the same time, heart failure and CHD serve as the most frequent reasons for the need of patients in hospital care [1]. Deeper understanding of the subtle mechanisms of development of co-morbidity and complications in COPD, as well as the impact on them can improve the results of treatment and prognosis for the patient. The most formidable predictor of fatal complications in COPD associated with coronary heart disease is myocardial infarction as a consequence of thrombotic complications in the microcirculatory system. Aggregation of thrombocytes is stimulated by eicosanoids, which are the products of metabolism of arachidonic acid. Systemic chronic inflammation in COPD stimulates the production of a large number of inflammatory mediators [5], among which leukotrienes play an important role, in particular, leukotriene B_4 (LTB_4) (a product of neutrophilic leukocytes) and thromboxanes (Tx) (platelet aggregation stimulators). In patients with COPD [6], with CHD [2], as well as in cases of the combination of broncho-obstructive diseases with CHD [11], the negative role of increasing platelet aggregation capacity in the development of microhemocirculation disorders was shown, as well as the adverse effect of elevation of the leukotriene B_4 content to the bronchial patency [9]. The investigation of the role of eicosanoids - important mediators of the inflammatory cascade in the progression of COPD, combined with CHD, as well as the search for effective ways of influencing them, will increase the results of treatment and the quality of life of patients with comorbidity of COPD and CHD.

The purpose of the study was to investigate the content of eicosanoids - leukotriene B_4 and thromboxane A_2 (stable metabolite B_2) in the blood serum and urine of patients with COPD combined with CHD.

Material and methods. The study involved 37 patients of the middle age (54,6 ± 3,3) years with exacerbation of COPD (clinical group B, GOLD II) associated with CHD - the main group who underwent inpatient treatment. 27 patients with COPD in the stage of exacerbation (Ist comparison group) and 30 patients with CHD, stable angina pectoris (IInd comparison group) made up the comparison groups. To develop the reference norm, 32 practically healthy volunteers were examined. The age and gender composition of the comparison groups, as well as healthy volunteers, corresponded to those in the main group. All patients underwent spirography examination with spirometer "Spirobank" (MIR, Italy), electrocardiographic examination. All patients, as well as healthy volunteers, were examined for serum and urine level of TxB_2 and LTB_4 in the blood serum and urine with the use of the Ukrainian-certified reagent TxB_2 ELISA kit (Enzo Life Sciences, USA) using the enzyme immunoassay (ELISA).

Statistical processing of the received data was carried out using licensed software products of Microsoft Office Professional 2003. To verify the correspondence between the distributions of the values of the series of measurements for the normal distribution the function NORMSAMP-1 in Microsoft Excel was used. On that bases the parametric (t-test of reliability of Student) or nonparametric (Wilcoxon test) statistical methods [3] with an estimation of reliability of the received results of researches at the set level of significance $p \leq 0.05$ were chorused.

Results and discussion. In all patients with COPD, included in the study, in admission to the inpatient department the exacerbation of disease was diagnosed. In patients with COPD, combined with CHD, the average range of the forced expiratory volume in the first sec. (FEV_1) was (67.7 ± 3.4) %, the post-dilatation FEV_1/FVC was equal to (69.3 ± 4.1)%. In the patients of Ist comparison group FEV_1 reached (69,4 ± 3,6)%, post-dilatation FEV_1/FVC - (70,9 ± 3,7)%. In the patients of IInd comparison group FEV1 was equal to (83.4 ± 4.1)%, post-dilatation FEV_1/FVC - (79.4 ± 3.3)%.

The concentration of TxB2 in the blood serum reached (3382.3 ± 290.8) pg/ml in the patients of the main group (see Table 1), exceeding the average level of healthy volunteers by 22.2 times ($p < 0.001$), the same parameter of patients with exacerbation of COPD without CHD by 2.2 times ($p < 0.01$) and by 1.4 times ($p < 0.05$) in patients with CHD.

Table 1

TxB_2 content in blood serum and urine of the examined individuals (M ± m)

Material for study	Healthy people (n=29)	Main group (n=32)	Comparison groups	
			I (n=25)	II (n=27)
Blood serum, pg/ml	152,4±19,2	3382,3±290,8*	1529,2±101,3*	2347,6±156,3*
Urine, pg/ml	131,5±12,7	183,6±13,2*	297,4±19,3*	328,4±21,6*

Note: * -p <0.05 when compared with healthy subjects.

The concentration of TxB_2 in the blood serum of patients from the I[st] comparison group was the lowest among all examined patients, however, it exceeded the reference norm by 10 times (p <0,001). In the same time, the average level of TxB_2 concentration was higher in 1.5 times in patients from the II[nd] comparison group (p <0.05). This difference in the TxB_2 concentrations between patients with COPD and CHD can be explained by the more significant production of this eicosanoid by activated blood cells and platelets because of their pronounced tendency to aggregation in the development of CHD [2, 6], while in case of COPD, the circulatory disorders could be influenced by sludge of thrombocytes. In patients from group II of comparison, the level of TxB_2 in the blood serum was reliably higher than in healthy volunteers in 15.4 times, equaling (2347.6 ± 156.3) pg/ml, however, it was less than that in the main group in 1,4 times (p <0.05). The concentration of TxB_2 in the urine of the patients from the main group (see Table 1) was 183.6 ± 13.2 pg/ml and in 1.4 times higher than in practically healthy individuals (p <0.05). Nevertheless, it was lower than the same parameter in patients of the 1[st] comparison group in 1.6 times (p <0.05), and reliably less than the value of this eicosanoid in the II comparison group by 2.5 times (p <0.01). In the urine of patients from the 1[st] comparison group, the concentration of TxB_2 exceeded the norm by 2.3 times (p <0.01) and was not reliably differ from that in the 2[nd] comparison group. In patients with coronary artery disease (group II of comparison), the values of TxB_2 in urine were reliably higher than in healthy individuals in 2.5 times, and were not reliably differ from those in group I of comparison.

The content of LTB_4 in the blood serum and urine of the examined persons is presented in Table 2.

Table 2

LTB_4 content in blood serum and urine of the examined individuals (M ± m)

Material for study	Healthy people (n=29)	Main group (n=32)	Comparison groups	
			I (n=25)	I (n=25)
Blood serum, pg/ml	329,4±31,6	6678,0±375,4*	5142,6±284,2*	1728,3±118,4*
Urine, pg/ml	59,7±5,1	208,5±12,9*	139,7±10,6*	89,5±7,2*

Note: * - p <0.05 when compared with the parameters of healthy people

In patients from the main group, the serum LTB_4 content was the highest among all examined patients, reaching (6678.0 ± 375.4) pg/ml and exceeding the norm by 20.3 times (p <0.001). Evidently, systemic inflammation in COPD, combined with inflammatory manifestations in CHD, provided maximum concentration of this eicosanoid in the blood serum [5]. Some studies of LTB_4 in bronchial obstructive diseases indicated the pro-inflammatory role of LTB_4, produced mainly by activated neutrophils, and the need to find ways of the rational correction of that [8]. In patients from the I[st] comparison group, the concentration of LTB_4 was in 15.6 times higher than the reference norm (p <0.001), but less than the same parameter in the main group in 1.3 times (p <0.05) and more than it in the II[nd] group of comparison in 3.9 times (p <0.01). In group II of comparison, the serum level of LTB_4 was the lowest, reaching (1728.3 ± 118.4) pg/ml, but was in 5.2 times higher than in healthy subjects (p <0.01). The concentration of LTB_4 in the urine of the patients from the main group was (208.5 ± 12.9) pg/ml, exceeding the reference norm by 3.5 times (p <0.01). The concentration of this eicosanoid in the urine of the patients from the I[st] comparison group was in 1.5 times (p <0.01) less than in healthy individuals, reaching (139.7 ± 10.6) pg ml and by 1.5 times reliably exceeding the same parameter in persons of II[nd] comparison group. At the same time, the content of LTB_4 in the urine of the patients from the II[nd] comparison group, although it was the lowest (89.5 ± 7.2) pg/ml, however, it was in 1.5 times higher the norm (p <0,05). The increased content of this eicosanoid in the urine as a way of excretion of products of the inflammatory reaction, can serve as a confirmation of the systemic inflammation activity in the body of patients with CHD.

When analyzing the correlation between the bronchial patency rates and the level of LTB_4, it was found that negative correlation of the mean force (r = - 0.543, p <0.05) presents between the FEV_1 and the serum level of LTB_4 in the patients from the main group. At the same time, in the I[st] comparison group, this correlation was somewhat weaker (r = - 0.389, p <0.05) and was absent in patients of the II[nd] group of comparison. Only weak negative correlation was found between the level of bronchial patency and the concentration of TxB_2 in the blood serum in the patients of the main group (r = - 0.347, p <0.05). At the same time, positive correlation of different degrees were noted between the serum concentrations of the investigated eicosanoids in patients of all groups. The strongest one (r = + 0.614, p <0.05) was observed in the patients of the main group, slightly weaker - in the patients of the I[st] comparison group (r = + 0.528, p <0.05) and weak - in the patients of the II[nd]

comparison group (r = + 0.356, p <0.05). In our opinion, the existence of these correlation links between serum concentrations of the investigated eicosanoids in patients, taking into account the directivity of their biological effects, confirms their interaction, which enhances systemic inflammation, and needs to find ways of correction.

Thus, in the blood serum of patients with COPD associated with CHD, the concentrations of LTB_4 and TxB_2 are highest, compared with patients with COPD without CHD and CHD without COPD, which is accompanied by the rising of their excretion with urine. The strength and direction of the correlation links between the concentrations of these eicosanoids in the blood serum and bronchial patency indices indicate their negative effect on the bronchial patency of patients with the comorbidity of COPD and CHD. Correlation between the concentrations of LTB_4 and TxB_2 in the blood serum in patients with combined pathology confirms the synergistic effect of these eicosanoids on systemic inflammation, taking into account the biological direction of the action.

Conclusions.

The reliably growth of the LTB_4 concentration in the blood serum was identified in patients with exacerbation of COPD associated with CHD, exceeding by 20.3 times the norm, by 1.3 times the same parameter in patients with COPD without CHD and by 3.9 times - than in the patients with CHD itself (p <0.05). The urine level of LTB_4 was also elevated in all examined patients with the highest values in the main group.

The TxB_2 content in the blood serum of the patients from the main group was the highest and in 22.2 times higher than the norm, in 2.2 times higher than the same one in patients with COPD and in 1.4 times – than in patients with coronary heart disease (p <0.05). The urine level of of TxB2 was also elevated in all examined patients in all examined patients.

The character of the correlation links between concentrations of these eicosanoids in the blood serum and FEV_1 indicates their adverse effect to the bronchial patency of patients with COPD, while the interrelationship of LTB_4 with TxB_2 shows the mutual potentiating effect of these mediators on the systemic inflammation.

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