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Microcirculation in patients with bronchial asthma combined with non-alcoholic steatohepatitis

Key words: *asthma, non-alcoholic steatohepatitis, microcirculation.*

Introduction

Increasing prevalence of bronchial asthma (BA), necessity of long – basic treatment [10], environmental degradation, frequent use of xenobiotics in the home, so the spread of the disease from a combination of diseases of the digestive system [9], in particular with non-alcoholic steatohepatitis (NASH) [1, 7, 13, 14].

The combination of BA and NASH promotes the growth of the severity of the basic disease, earlier formation of complications. The mutual encumbrance and progression of BA and NASH is based on a combination of several pathogenesis of both diseases [1, 6, 11]. During the exacerbation BA systemic inflammation, oxidative stress, impair microcirculatory processes that are formed at the expense of elasticity and deformability of red blood cells and the formation of sludge in capillaries and are enhanced by increasing the ability of platelets to aggregation by reducing the time aggregation, slow process of disaggregation [3, 4, 6, 13]. The changes reologic properties of blood in the direction development of a syndrome hypercoagulation leading to blockage of the capillaries. By functional disorders of microcirculation go organic, which promotes the development of complications [5, 8]. In patients with chronic broncho-obstructive diseases value aggregation of red blood cells amplifies at the formation of chronic pulmonary heart disease [2, 12, 17]. Major contribution to improving the ability of platelets aggregation make eicosanoids – thromboxanes, which in large quantities are produced in acute BA [4, 6, 15]. However, features state of the microcirculation and the factors that cause them, with a combination of BA and NASH remain poorly studied.

Purpose – to examine the state of the microcirculation, the content of thromboxane A_2 (TxA_2) for its stable metabolite thromboxane B_2 (TxB_2) in patients with exacerbation of BA, combined with NASH.

The study was carried out in accordance with the basic plan for scientific publishing house research «Lugansk State Medical University» and a piece of research, «Clinical and pathogenetic features combined for diseases of internal organs, their correction and prognosis» (№ of state registration 0109U002725).

Material and methods

Investigated 46 patients with a mean age ($32,4 \pm 3,1$) years with moderate BA exacerbation flow, treated in Allergic department of Lugansk Regional Hospital during 2010-2013. Among male patients was 20 (43.5%), women - 25 (56.5%). Among them with BA, combined with NASH was diagnosed in 22 individuals. Treatment of BA, combined with NASH, performed according to the recommendations the order Ministry of Health of Ukraine № 128 of 19.03.2007, for the treatment of NASH address the recommendations of order Ministry of Health of Ukraine № 271 of 2005 (sorbents and of essential phospholipids). Control group consisted of 32 practically healthy persons at the same age range and gender. Content TxA_2 for stable metabolite of TxB_2 in serum and urine of patients and the control group was determined by enzyme immunoassay with the help reagent ELISA kit (Enzo Life Sciences, USA. Research of spontaneous and of ADP-induced aggregation ability of blood platelets of these patients was carried out on a laser ahehometri NPF Biola 230-LA.

Condition of microcirculation was studied the method bulbar conjunctival biomicroscopy (BBC) by slit lamp SCHL-2M (ZOMZ, RF) of the definition of conjunctival indices (CI): CI_1 (vascular changes) CI_2 (intravascular changes) and CI_3 (perivaskulyarni changes). Total CI – CI_{gen} was calculated as the sum of three indices ($CI + CI_2 + CI_3$). Intravascular aggregation of blood was determined by examining the presence of sludge-phenomen of by N. N. Knisely [16]. Statistical analysis of the material was carried out using parametric and nonparametric methods using the licensed software “Microsoft Excel” and “Statistica”.

Results and discussion

Content TxB_2 in serum of patients with acute exacerbation of BA was equal ($1118,3 \pm 102,8$) pg/ml and higher than the value in healthy individuals 7.7 times ($p < 0,001$). In patients with BA, combined with NASH concentration was TxB_2 ($3454,0 \pm 221,3$) pg/ml, which was higher than in healthy ($145,3 \pm 17,6$) pg/ml almost 23.8 times ($p < 0,001$) and with that of patients without NASH 3 times ($p < 0,01$) (Figure).

TxB_2 concentration in the urine of patients in both groups in exacerbation of BA does not differ significantly and equal to respectively ($343,2 \pm 21,4$) pg/ml and ($305,9 \pm 46,3$) pg/ml at values of of healthy persons ($114,8 \pm 10,5$) pg/ml.

Index of spontaneous aggregation (SA_{sp}) in patients with BA in the treatment beginning was ($1,1 \pm 0,4$) units, which was less than that of patients with BA and NASH ($6,5 \pm 2,1$) units. almost 6 times ($p < 0,001$) with that of healthy individuals ($1,2 \pm 0,6$) units. Value of the index of ADP-induced

aggregation (SA_{adf}) equal to ($48,9 \pm 5,5$) units and this was less than in BA, combined with NASH ($75,3 \pm 5,8$) units 1.5 times ($p < 0,05$) with proper values ($35,0 \pm 6,2$) units. The maximum slope of the curve spontaneous aggregation ($SAMS_{sp}$) in patients with BA was ($0,27 \pm 0,04$), was significantly lower than the in BA combined with NASH - ($1,8 \pm 0,6$) units/min on average, 6.7 times ($p < 0,001$) with a reference norm ($0,3 \pm 0,1$) units/min. The level of maximum slope of the curve range of ADP-induced aggregation ($SAMS_{adf}$) reached in patients with BA ($12,9 \pm 2,5$) units/min at a rate ($14,3 \pm 1,5$) units/min, but was lower than that of patients with BA and NASH ($26,6 \pm 3,4$) units/min. to 2.0 fold ($p < 0,05$). The value of maximum aggregation curve intermediate range (SA_i) in patients with BA were equal ($72,8 \pm 6,3$ c), which was significantly less than corresponding in BA and NASH ($87,1 \pm 7,5$ c) of 1.2 times with those of healthy individuals ($67,8 \pm 3,6$ c). The degree of disaggregation (SA_{da}) in patients with acute exacerbation BA was significantly reduced to ($32,8 \pm 2,4$), but higher than its value in BA, combined with NASH ($26,8 \pm 2,7$ %) 1.2 times ($p < 0,05$) with proper values ($38,4 \pm 2,3$ %).

Between the indexes content TxB_2 and SA_{da} values in patients with a combination of BA and NASH medium strength correlation ($r = -0,645$, $p < 0,05$) and weak – in people with BA - ($r = -0,411$, $p < 0,05$).

In patients with BA without NASH during its exacerbation by BBC was observed narrowing of arterioles and venules expansion, reducing the number of functioning capillaries form in some cases, avascular areas, uneven caliber, sinuosity

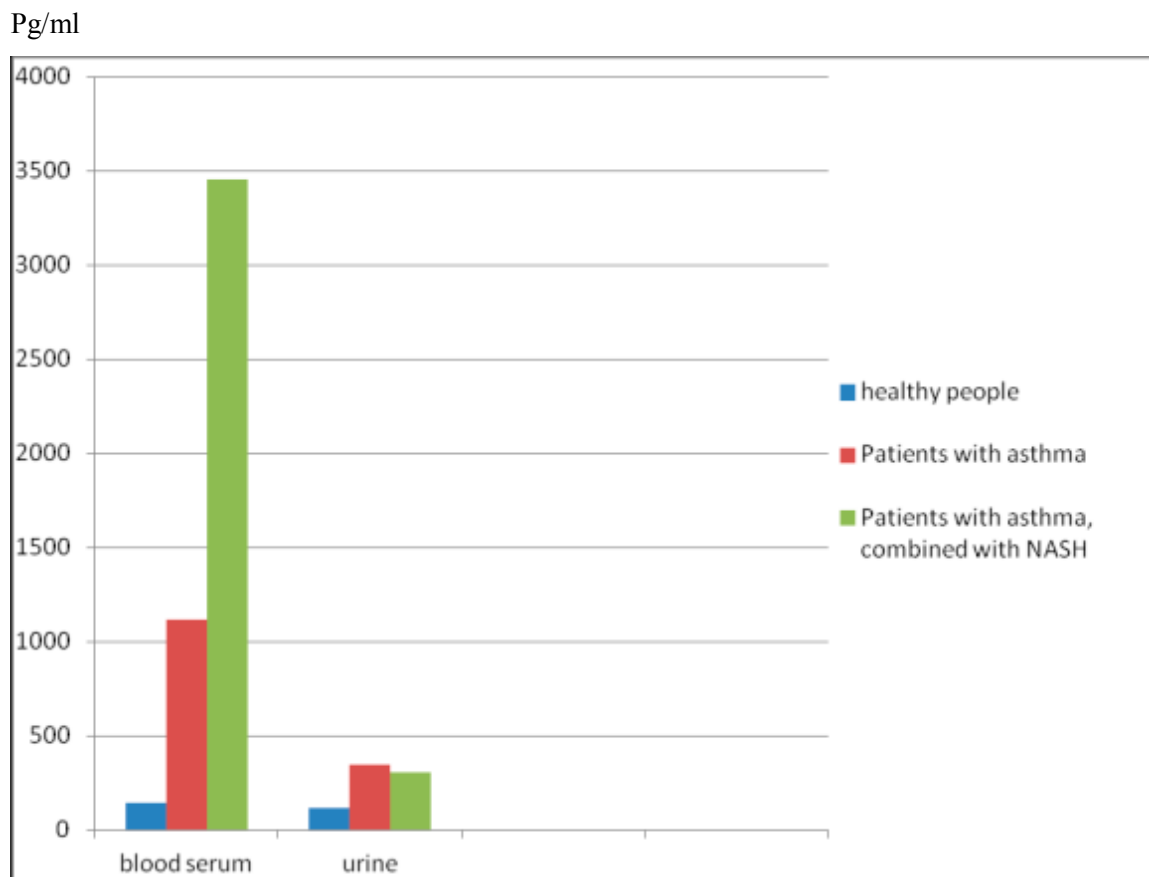


Figure. Content TxB_2 in serum and urine of investigated patients

and microvessel polymorphism, slow flow and sludge syndrome in 1.2 degree venules and arterioles, perivascular edema were found, indicating an increased permeability of the vascular wall. CI_1 higher than the same index in of healthy persons to 1.6 ($p < 0,05$), CI_2 – 2.9 times ($p < 0,01$), that testified to predominance of intravascular changes. All this led to an increase in CI_3 ($0,64 \pm 0,06$). So all CI in patients with acute exacerbation BA were higher than that effect and increase CI_{gen} that exceeded the the reference norm by 2.1 times ($p < 0,01$) (Table). All this underlines the presence microrheological disturbances in patients [11].

Table State of microcirculatory parameters in investigated patients (M ± m)			
Investigated indicators	Index healthy people	Patients with asthma (n=24)	Patients with asthma, combined with NASH (n=22)
CI_1	$2,72 \pm 0,21$	$4,26 \pm 0,21^*$	$4,53 \pm 0,26^*$
CI_2	$1,90 \pm 0,13$	$4,92 \pm 0,21^*$	$5,36 \pm 0,15^*$
CI_3	—	$0,64 \pm 0,06^*$	$0,75 \pm 0,08^*$
CI_{gen}	$4,62 \pm 0,16$	$9,82 \pm 0,43^*$	$10,88 \pm 0,52^*$

Note: * – $P < 0,05$ when compared to the indicators healthy people;
— $P < 0,05$ when comparing indicators between the groups pg/ml.

In patients with BA, combined with NASH, microhemodynamics indicators were more pronounced. CI_1 was significantly higher than that of healthy subjects by 1.7 times and 6.3 % for patients with BA CI_2 without NASH. Most striking changes were CI_2 that patients with BA and NASH by 2.8 times ($p < 0.01$) was higher than the reference norm and 8.9 % higher than the index of CI_2 in researches with BA. CI_3 in patients with BA and 17.2 % of NASH exaggerated CI_3 in investigated on BA without NASH. Changes in all CI_{gen} researches with BA and NASH, reflected in increasing CI_{gen} which 10.8 % was higher than that of patients with BA without NASH.

Thus, in patients with a combination of BA and NASH was noted considerably more substantially increase in content TxB_2 , indices ADP_{sp} compared with patients with BA without NASH. Were characterized by violations of microvascular changes at all levels of the microcirculation most salient at the expense a vascular component. Such violations may microrheological promote the formation of mutual syndrome complication and need for a higher level of therapeutic effects.

Conclusion

1. In patients with acute exacerbation of BA, combined with NASH compared with patients with acute exacerbation of BA with a combination of content TxB_2 marked increase in serum 3 times along with increasing its secretion of urine.

2. Spontaneous and ADP-induced platelet aggregation in patients with BA in combination with NASH turns high when comparing with similar indicators of patients with BA without

NASH. Correlation between the content TxB_2 - SA_{da} and values in researches with BA and NASH is a strong negative than in BA without NASH.

3. Microvascular changes in patients with BA, combined with NASH, characterized by violations of at all levels of the microcirculation most salient at the expense a vascular component than in patients with BA without NASH.

Further research will focus on studying the effect of the basic means of treating patients with a combination of BA and NASH.

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**СОСТОЯНИЕ МИКРОЦИРКУЛЯЦИИ
У БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ,
СОЧЕТАННОЙ С НЕАЛКОГОЛЬНЫМ СТЕАТОГЕПАТИТОМ***Ю. Ю. Чумак*

Резюме. В статье рассматривается состояние микроциркуляции у пациентов с обострением бронхиальной астмы (БА) и БА, сочетанной с неалкогольным стеатогепатитом (НАСГ). Было отмечено, что микрососудистые изменения характеризуются нарушениями всех звеньев микроциркуляторного русла, наиболее выраженными за счет сосудистого компонента у пациентов с сочетанием БА и НАСГ. У больных с обострением БА, сочетанной с НАСГ, по сравнению с пациентами с обострением БА без такого сочетания, отмечается повышение содержания тромбоксана B_2 (TxB_2) в сыворотке крови в 3 раза, наряду с увеличением его секреции с мочой. Спонтанная и АДФ-индуцированная агрегация тромбоцитов у пациентов с БА в сочетании с НАСГ является повышенной при сравнении с аналогичными показателями у больных БА без НАСГ. Корреляционные связи между содержанием TxB_2 и значениями степени дезагрегации у исследованных с БА и НАСГ были более прочными негативными, чем при БА без НАСГ.

Ключевые слова: бронхиальная астма, неалкогольный стеатогепатит, микроциркуляция.

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**MICROCIRCULATION IN PATIENTS
WITH BRONCHIAL ASTHMA, COMBINED
WITH NON-ALCOHOLIC STEATOHEPATITIS***Y. Y. Chumak*

Abstract. This article discusses the state of the microcirculation in patients with acute exacerbation of bronchial asthma (BA) and BA combined with non-alcoholic steatohepatitis (NASH). It was noted that microvascular changes characterized by disturbances of all parts of the microvasculature, the most expressive due to the vascular component in patients with a combination of BA and NASH. In patients with acute exacerbation of asthma, combined with NASH, compared with patients with acute exacerbation of asthma without such a combination is marked elevation of thromboxane B_2 (TxB_2) in serum 3-fold, along with its increased urine secretion. Spontaneous and ADP-induced platelet aggregation in patients with BA in conjunction with NASH revealed elevated when compared with those in patients with asthma without NASH. Correlation between the content and values TxB_2 degree of disaggregation in BA and studied with NASH were stronger negative than in asthma without NASH.

Key words: asthma, non-alcoholic steatohepatitis, microcirculation.

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