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Oxidative stress and components of antioxidant defense in the mechanisms of formation of bronchial asthma in children

Bronchial asthma (BA) is a chronic disease with a complex multicomponent mechanism of development and progression. A significant increase in its prevalence in the pediatric population necessitates the search for some new possibilities for prevention and treatment taking into account the peculiarities of the child's organism, including adaptive mechanisms, not only on the organism but also on the cellular and molecular levels. An important role in the pathogenesis of the vast majority of diseases of the respiratory tract, including bronchial asthma (BA), is oxidative stress (OS), the main cause of which is the imbalance in the system of "oxidants-antioxidants", which is expressed by the excessive formation of active forms of oxygen (AFO) and weakening the effectiveness of antioxidant protection (AOP). By now it was proved that in the state of oxidative stress, under the influence of AFO, not only lipids, but also proteins of plasma membranes are subjects of peroxidation. It is believed that the negative effect of oxidation modified proteins in cells is connected with the fact that oxidized proteins are the source of free radicals that deplete the stores of cellular antioxidants. Products of free radical oxidation of proteins lead to oxidative DNA damage. In this case, peroxide oxidation of proteins (POP) is not only a trigger mechanism for pathological processes in stress, but also the earliest marker of oxidative stress. The dynamics of changes of the POP products is a reflection of the degree of oxidative cell damage and of the reserve and adaptive capacity of the body. It is believed that the level of indicators of oxidative modification of proteins (OMP) compared with the level of LPO is more informative marker of the presence of oxidative stress in the body. **The aim:** to study the state of the prooxidant system and the system of antioxidant protection in children with varying degrees of control of BA. **Materials and methods:** The study involved107 children aged from 10 to 18 years old, with asthma under exacerbation. According to the results of the Asthma Control Test (GINA, 2014) regarding the level of control of BA, children were divided as follows: 34 (31.8%) – with controlled (CBA), 47 (43.9%) – with partially controlled (PCBA) and 26 (24.3%) with uncontrolled bronchial asthma (UCBA). The control group consisted of 10 practically healthy children of the same age. It was established that children with low level of control have a prooxidant activation, which is manifested by a significant increase in the level of oxidation modified proteins. **Results:** The index of oxidative modification of proteins (OMP) -356, amounting to (0,293 ± 0,006) RVU (relative value unit) was significantly higher in children with uncontrolled bronchial asthma (UCBA) compared with the patients in other groups ($p < 0.05$). The maximum value of OMP-370 was registered in a group of patients with UCBA. This figure was significantly higher than that of those with a higher level of disease control ($p < 0.05$). Another trend was noted due to OMP-430 content indicators. Thus, a probable increase in its level was observed only in children with UCBA ($pN < 0.05$). The content of OMP-530 in children with UCBA was practically the same with that of the control group, and in children with partially controlled (PCBA) and controlled bronchial asthma (CBA), there was a significant decrease in the rates compared to healthy ones ($pN < 0.05$). Thus, the obtained results demonstrate the systemic activation of the POP process in children with BA, which may be the result of a long inflammatory process. The amplification of POP processes is accompanied by a weakening of AOP, manifested by a decrease in the activity of SOD, which catalyzes the dismutation of superoxide anion radicals and the antioxidant barrier of the first line of defense – catalase and indicates a significant reduction in the protection of the respiratory tract in BA from the accumulation of active forms of oxygen. **Conclusions:** In children with CBA there is a development of oxidative stress, which manifests itself in a significant increase and accumulation of the content of POP products against the backdrop of increased tension of the adaptive mechanisms of contact-protective system AOP. BA in children is characterized by heterogeneity of mechanisms of peroxidation and enzymatic maintenance of the prooxidant system, which is determined by the severity of the course of the disease and can be a pathogenetic basis for predicting the severity of BA in children. At the same time, we can observe weaken of the antioxidant protection in these patients, which is evident by a significant decrease in the activity of superoxide dismutase enzymes and, in particular, catalase.

Key words: oxidative modification of proteins, bronchial asthma, children.

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Оксидативний стрес і компоненти антиоксидантного захисту в механізмах формування бронхіальної астми у дітей

Бронхіальна астма (БА) – це хронічне захворювання зі складним, багатокомпонентним механізмом розвитку та прогресування. Значне зростання її поширеності у дітей зумовлює необхідність пошуку нових можливостей профілактики та лікування з урахуванням особливостей дитячого організму в тому числі, адаптивних механізмів не тільки на клітинному, а й на молекулярному рівнях. В патогенезі переважної більшості захворювань респіраторного тракту, в тому числі і при БА важливу роль відіграє окисний стрес (ОС), основною причиною якого є дисбаланс у системі "оксиданти-антиоксиданти", що виражається надмірним утворенням активних форм кисню (АФК) і ослабленням ефективності антиоксидантного захисту. На сьогоднішній день доведено, що в стані окисного стресу під дією АФК перекисному окисненню підлягають не тільки ліпіди, а й білки плазматичних мембран. Вважається, що негативний ефект окисно-модифікованих білків у клітинах пов'язаний із тим, що окиснені білки є джерелом вільних радикалів, які виснажують запаси клітинних антиоксидантів. Продукти вільнорадикального окиснення білків призводять до окисного ураження ДНК. При цьому, перекисне окиснення білків (ПОБ) є не тільки пусковим механізмом патологічних процесів при стресі, а й найбільш раннім маркером окисного стресу. Динаміка змін продуктів ПОБ є відображенням ступеня окисного ураження клітин та резервно-адаптаційних можливостей організму. Вважається, що рівень показників окисної модифікації білків (ОМБ) порівняно із рівнем ПОЛ є інформативнішим маркером наявності окисного стресу в організмі. Мета: В статті викладено результати дослідження показників окисної модифікації білків та активності антиоксидантних ферментів у дітей із БА в залежності від ступеня контрольованості захворювання. Матеріали і методи: Обстежено 107 дітей віком від 10 до 18 років, хворих на БА в стадії загострення. За результатами застосування астма-тест контролю (GINA, 2014) щодо рівня контрольованості БА діти були розподілені наступним чином: 34 (31,8 %) – із контрольованою (КБА), 47 (43,9 %) – із частково контрольованою (ЧКБА) та 26 (24,3 %) – із неконтрольованою бронхіальною астмою (НКБА). Контрольну групу склали 10 практично здорових дітей аналогічного віку. В якості маркерів стану пероксидації визначали окисну модифікацію білків (ОМБ). ОМБ сироватки крові визначали на основі принципу взаємодії окиснених амінокислотних залишків білків з 2,4-динітрофенілгідразоном (2,4-ДФГ) з утворенням похідних 2,4-динітрофенілгідразону. Результати дослідження: Встановлено, що у дітей із низьким ступенем контролю має місце прооксидантна активація, що проявляється достовірним підвищенням рівня окисно-модифікованих білків. Так, показник окисної модифікації білків (ОМБ)-356, склавши (0,293±0,006) ум.од. був достовірно вищим у дітей із неконтрольованою бронхіальною астмою (НКБА) порівняно із пацієнтами інших груп ($p<0,05$). Максимальне значення показника ОМБ-370 зареєстроване в групі пацієнтів із НКБА. Цей показник вірогідно перевищував аналогічні у обстежених із вищим рівнем контролю над захворюванням ($p<0,05$). Іншу тенденцією відмічали щодо показників вмісту ОМБ-430. Так, вірогідне підвищення його рівня мало місце тільки у дітей із НКБА ($pN<0,05$). Вміст ОМБ-530 у дітей із НКБА практично не відрізнявся від показника групи контролю, а у дітей із частково контрольованою (ЧКБА) та контрольованою бронхіальною астмою (КБА) відмічалось вірогідне зниження показників у порівнянні із здоровими ($pN<0,05$). Водночас, у цих пацієнтів послаблюється антиоксидантний захист, про що засвідчує значне зниження активності ферментів супероксиддисмутази і, особливо, каталази. Висновки. У дітей з КБА має місце розвиток оксидативного стресу, який проявляється достовірним збільшенням та накопиченням вмісту продуктів ПОБ на тлі зростання напруженості адаптаційних механізмів контактно-захисної системи АОЗ. Бронхіальна астма характеризується гетерогенністю механізмів пероксидації та ферментативного забезпечення прооксидантної системи, що визначається тяжкістю перебігу недуги і може скласти патогенетичну основу прогнозування тяжкості перебігу бронхіальної астми у дітей.

Ключові слова: оксидантно-антиоксидантна система, окисна модифікація білків, бронхіальна астма, діти.

Bronchial asthma (BA) is a chronic disease with a complex multicomponent mechanism of development and progression. A significant increase in its prevalence in the pediatric population (according to the WHO data for the last 10 years, about 18%) necessitates the search for some new possibilities for prevention and treatment taking into account the peculiarities of the child's organism, including adaptive mechanisms, not only on the organism but also on the cellular and molecular levels [1].

In the pathogenesis of asthma intertwine the results of the influence of genetic factors and harmful environmental conditions on the patient's body. Maladaptation always has a multifaceted nature and simultaneously affects a large number of unbalanced parts of the adaptive response. At the baseline of the maladaptive pathogenetic mechanisms in the BA, there is a violation of the state and functions of the biomembranes, the immune system, the enzyme and non-enzymatic elements of the antioxidant system (AOS), the functioning of the detoxification systems, macro and microelement status, etc.

An important role in the pathogenesis of the vast majority of diseases of the respiratory tract, including bronchial asthma (BA), is oxidative stress (OS), the main cause of which is the imbalance in the system of "oxidants-antioxidants", which is expressed by the excessive formation of active forms of oxygen (AFO) and weakening the effectiveness of antioxidant protection (AOP) [2]. Such feature of the respiratory pathology is caused by the fact that the respiratory tract (RT) is exposed to the direct and instant influence of exogenous oxidants that are in the air (xenobiotics); unsaturated fatty acids of the pulmonary tissue serve as a substrate for the reaction of lipid peroxidation (LPO); pollutants and microorganisms cause the activation of phagocytes, which produce a significant amount of AFO.

It is proved that the main part of the AOP of the lungs is concentrated in the fluid that lays the epithelium of the RT. The functioning disorder of AOP leads to the formation of a large number of AFO. With its high reactivity, AFO can irreversibly damage the biologically important

molecules, causing inflammation as a result of activation of phagocytes accumulated in the lower sections of the RT and, consequently, results in oxidative stress.

By now it was proved that in the state of oxidative stress, under the influence of AFO, not only lipids, but also proteins of plasma membranes are subjects of peroxidation [2, 3]. It is believed that the negative effect of oxidation modified proteins in cells is connected with the fact that oxidized proteins are the source of free radicals that deplete the stores of cellular antioxidants. Products of free radical oxidation of proteins lead to oxidative DNA damage. In this case, peroxide oxidation of proteins (POP) is not only a trigger mechanism for pathological processes in stress, but also the earliest marker of oxidative stress. The dynamics of changes of the POP products is a reflection of the degree of oxidative cell damage and of the reserve and adaptive capacity of the body. It is believed that the level of indicators of oxidative modification of proteins (OMP) compared with the level of LPO is more informative marker of the presence of oxidative stress in the body [2, 3].

Mechanisms of free radical oxidation of macromolecules in the course of BA remain to be not well-studied and not fully disclosed. Currently, only a few publications on the state of processes of peroxidation of proteins in children with asthma are available, which led to the choice of research direction.

Purpose: to study the state of the prooxidant system and the system of antioxidant protection in children with varying degrees of control of BA.

Materials and methods of research. The study involved 107 children aged 10 to 18 years old, patients with asthma at the stage of exacerbation who were on inpatient treatment in the RCCHin Ivano-Frankivsk. Diagnosis of BA was established in accordance with the Protocol of diagnosis and treatment of BA in children of the Ministry of Health of Ukraine No. 868 dated 08.10.2013. According to the results of the Asthma Control Test (GINA, 2014) regarding the level of control of BA, children were divided as follows: 34 (31.8%) – with controlled (CBA), 47 (43.9%) – with partially controlled (PCBA) and 26 (24.3%) with uncontrolled bronchial asthma (UCBA). The control group consisted of 10 practically healthy children of the same age.

All patients were examined after getting the informative consent from the child and their parents according to the GCP IHC requirements.

As markers of the state of peroxidation, oxidative modification of proteins (OMP) was determined. OMP blood serum was determined by the principle of interaction of oxidized amino acid residues of proteins with 2,4-dinitrophenylhydrazone (2,4-DPH) to form derivatives of 2,4-dinitrophenylhydrazone [3].

For analysis, 0.05-0.1 ml of blood serum was used. The precipitation of serum proteins was carried out by using 20% trichloroaceticacid solution. To denatured proteins was added an equal volume of (1 ml) of 0.1 M 2,4-DFG dissolved in 2 M HCl. In the control sample, instead of 2,4-DPH, the volume of 2M HCL was added. Incubation was carried out at the room temperature for 1 hour. Then the samples were centrifuged at 3000 rpm for 15-20 min. The precipitate was washed 3 times with a solution of ethanol-ethyl acetate (1: 1) for lipid extraction and 2,4-DPH, which did not react with carbonyl groups of oxide proteins.

The resulting precipitate was dried to remove a solution of ethanol-ethyl acetate and then dissolved in 8 M solution of urea. Urea was added to a precipitate in a volume of 2.5 ml and was kept in a boiling bath for 5 minutes until complete dissolution. The optical density of the formed dinitrophenylhydrazines was recorded on a spectrophotometer SF-16. As a result of the oxidation of proteins there can be formed aldehyde and ketone groups of amino acid residues that can interact with 2,4-DFG.

For aliphatic ketone-dinitrophenyl hydrazones of neutral character, the absorption spectrum is 363-367 nm, the main character is 430-434 and 524-535 nm. The formed 2,4-dinitrophenylhydrazones were recorded at the following wavelengths: 356, 370, 430, and 530 nm [3].

The state of AOP was studied by determining the activity of superoxide dismutase (SOD) and catalase in blood according to the method proposed by N. Ravin (1956) in the modification of Babenko G. A. (1968). The principle of determining the level of catalase is based on the fact that a certain amount of hydrogen peroxide was added to a sample containing the enzyme and by titration with potassium permanganate was set the amount of undiluted peroxide. Reagents: peroxide of hydrogen – 1%, sulfuric acid – 10%, potassium permanganate – n / 10, distilled water.

Peripheral blood after the puncture with Frank's needle was collected in a quantity of 0.02 ml by micropipette and dissolved in 20 ml of water. 1 ml of diluted blood was transferred in a test tube containing 2 ml of a 1% solution of hydrogen peroxide and 7 ml of water, and left at room temperature for 30 min. At the same time, an experiment with diluted and boiled blood was conducted in order to establish the fissile action effect on hydrogen peroxide of other components that may be present in the blood. For this, 1 ml of boiled, diluted solution of blood was added in a test tube containing 2 ml of 1% solution of H2O2 and 7 ml of water.

After 30 minutes, 3 ml of 10% solution of sulfuric acid was added in both tubes from the burette. The resulting solution was titrated withn / 10 solution of potassium permanganate until a faint pink color appeared. There was determined the initial amount of hydrogen peroxide. In a test tube was added 2 ml of a 1% solution of hydrogen peroxide, 3 ml of 10% sulfuric acid and titrated with n-10 solution of potassium permanganate. The results were calculated: the difference was found between the amount of potassium permanganate that went into titration of 2 ml of a 1% solution of hydrogen peroxide and the amount of potassium permanganate spent on titration of the test sample.

For example, if the titration of the test sample took 7 ml of n-10 solution of potassium permanganate, and titration of 2 ml of a 1% solution of hydrogen peroxide – 11.3 ml of n-10 of potassium permanganate, then the amount of hydrogen peroxide destroyed by catalase and other substances of blood, is equal to: 11.3-7 = 4.3 ml n / 10 potassium permanganate. In order to determine how much of the n-10 solution of hydrogen peroxide was destroyed only by catalase, we must first calculate the correction for blood substances that affect the hydrogen peroxide cleavage reaction without an enzyme. To do this, it is necessary to subtract from the amount of potassium permanganate spent on titration

of 2 ml of 1% solution of hydrogen peroxide, the number of ml n / 10 of potassium permanganate solutionspent on titration of hydrogen peroxide in a sample with boiled blood. If the last figure is 11.2, then the correction for the substance is 11.3-11.2 = 0.1. After that, we found the amount of hydrogen peroxide, which was cleaved only by catalase: 4,3-0,1 = 4,2 ml of n-10 permanganate of potassium.

As 1 ml of n-10 solution of potassium permanganate is equivalent to 1,7 mg of hydrogen peroxide, the catalase number in this case will be: 4.2 * 1.7 = 7.4.

The catalase number of a healthy adult's blood fluctuates within 9,52-12,92 mg of hydrogen peroxide per 1 ml of blood (mgH2O2 / ml) [3].

The principle of determination of superorsyddysthymutase (SOD) is based on the iterating of nitrotetrazolium by superoxide radicals that are formed in the reaction between phenazinemethisulphate and the reduced form of nicotinamidenucleotide (NAD-H). The formation of nitroformase, a product of nitrotetrazolium iterating, is blocked by the presence of SOD in the sample. Thus, based on the amount of nitroformase, the activity of SOD can be estimated.

SOD isdetermined in 1 ml of hemolytase of blood (0.1 ml of blood + 0.9 ml of water). The effect of hemoglobin was eliminated by the addition of 0.5 ml of absolute alcohol, 0.25 ml of chloroform; and adding of 300mg of KH2PO4 we accelerated the separation of phases. The mixture was stirred vigorously and centrifuged for 30 min. at 4000-5000 rpm. SOD was determined by supernatant. We left it to stand at room temperature and measure the extinction of the blank and the test sample at 540 nm on a spectrophotometer. Extinction of a blank sample was about 0.680. The calculation was carried out according to the formula:

(E bl.samp- E t. samp.) / E bl. samp. * 100 = Percentage of the blockage of nitroformase formation.

E bl.samp. – Extinction of the blank sample (approximately equal to 0.680).

E t.samp. – Extinction of the tested sample [3, 4].

The results were analyzed using the computer software package STATISTICA licensed by StatSoft Inc. and Excel XP for Windows using parametric and non-parametric computing methods [5].

Results. Analysis of the results of determination of blood serum in patients with BA in the content of POP products suggests that they have oxidative stress, the severity of which is to some extent determined by the level of control of BA (Table 1).

Thus, the content of OMP-356 in the examined patients of all groups with BA probably exceeded the level of a similar indicator in healthy (pN<0.05). At the same time, the indicator OMP-356, which was (0,293 ± 0,006) RVU was significantly higher in children with UCBA compared to patients in other groups (p <0.05).

The study of the amount of OMP-370 in blood serum of children with different degrees of BA control allowed to establish that in all groups there was an increase in its level compared to healthy ones, and in children with CBA and UCBA this difference was significant (pN<0.05). In addition, the maximum value of OMP-370 is recorded in the group of patients with UCBA. This figure was significantly higher than that of those with a higher level of disease control (p <0.05).

A slightly different trend was observed according to OMP-430 content indicators. Thus, a probable increase in its level was observed only in children with UCBA (pN<0.05). In other groups of examined patients with BA, the OMP-430 rates were close to those in healthy ones.

Regarding the content of OMP-530, its level in children with UCBA was practically the same as that of the control group, and children with PCBA and CBA showed a significant decrease in the rates compared to healthy ones (pN<0.05).

Thus, the analysis of POP status in children with BA showed a significant activation. However, qualitatively unidirectional changes were quantitatively uneven. The analysis of the dependence of the level of OMP on the severity of asthma has shown that a lower degree of control of the disease leads to a more vivid change in the state of biological membranes, which induces the depletion of protective mechanisms [6, 7].

Investigation of the content of enzymatic antioxidants in children with different degrees of BA has shown that in patients with UCBA and PCBA AO protection was characterized by a probable decrease in the activity of catalase and SOD (pN<0.05), which indicates the achievement of functional depletion of the enzymatic chain of AOP in this category of patients. At the same time, in the patients with CBA the AOP indicators were close to those in the healthy group (Table II).

Discussion. Thus, the obtained results demonstrate the systemic activation of the POP process in children with BA, which may be the result of a long inflammatory process. The amplification of POP processes is accompanied by a weakening of AOP, manifested by a decrease in the activity of SOD, which catalyzes the dismutation of superoxide

Table I

The state of peroxidation of proteins in healthy children and children with different degrees of control of BA

Indicator, RVU	UNBA 1 (n=26)	PCBA 2 (n=47)	CBA 3 (n=34)	Healthy 4 (n=10)
OMP-356	0,293 ± 0,006	0,281 ± 0,002 p1-2 <0.001	0.261 ± 0.010 p 2-3 <0.001	0.212 ± 0.011 p1-4 <0.001 p2-4 <0.05 p3-4 <0.05
OMP-370	0.374 ± 0.005	0.283 ± 0.004 p 1-2 <0.001	0,330 ± 0,009 p 1-3 <0.05 p2-3 <0.001	0.262 ± 0.010 p1-4 <0.001 p3-4 <0.001
OMP-430	0.181 ± 0.004	0.150 ± 0.002 p1-2 <0.001	0.158 ± 0.007 p 1-3 <0.001	0.143 ± 0.006 p1-4 <0.001
OMP-530	0,051 ± 0.001	0.038 ± 0.003 p1-2 <0.001	0.043 ± 0.002 p1-3 <0.001 p2-3 <0.001	0.050 ± 0.004 p2-4 <0.001 p3-4 <0.02

Notes: p – is the probability of the difference between the indicators relative to values in patients with UCBA (1), PCBA (2), CBA (3) and healthy (4)

Table II

Indicators of activity of catalase and superoxide dismutase in healthy children and children with different degrees of BA control

Indicator	UCB 1 (n = 26)	PCBA 2 (n = 47)	CBA 3 (n = 34)	Healthy 4 (n = 10)
SOD MO / mg	39.88 ± 2.14	40.63 ± 1.36	47.63 ± 2.30 p 1-3 <0.05	49.05 ± 2.51 p1-4 <0.001 p2-4> 0.05
Catalase RVU	4.57 ± 0.23	4.80 ± 0.27	5.30 ± 0.30 p 1-3 <0.001	6.61 ± 0.28 p1-4 <0.05 p2-4 <0.05

Notes: p – is the probability of the difference between the values for patients with UCBA (1), PCBA (2), CBA (3) and healthy (4)

anion radicals and the antioxidant barrier of the first line of defense – catalase and indicates a significant reduction in the protection of the respiratory tract in BA from the accumulation of active forms of oxygen.

In the early stages of BA with a high degree of disease control, the intensification of POP products is minor. Due to the BA progresses, activation of POP becomes more significant, which can partly be explained by the weakening of the functioning of AO mechanisms.

Activation of the oxidative mechanisms in children with BA can stimulate the development of bronchoconstriction and vasoconstriction. In addition to direct toxicity (DNA degradation, the launch of the chain reaction of POP), oxidants indirectly affect a large number of other negative processes in the body: damage fibroblasts, reduce the activity of surfactant, stimulate the formation of thromboxane, increase the penetration of the epithelium and endothelium, enhance the secretion of mucus, lead to activation of obese cells, deterioration of β-adrenoceptor function, etc. The induced inhibition of the activity of membrane enzymes by the oxidative damageis extended by the changes in the physico-chemical qualities of the lipid bioassay. Such mechanism lies at the basis of oxidative stress processes and is one of the key components of the pathogenesis of BA [8, 9, 10, 11].

Conclusions

1. In children with CBA there is a development of oxidative stress, which manifests itself in a significant increase and accumulation of the content of POP products against the backdrop of increased tension of the adaptive mechanisms of contact-protective system AOP.

2. BA in children is characterized by heterogeneity of mechanisms of peroxidation and enzymatic maintenance of the prooxidant system, which is determined by the severity of the course of the disease and can be a pathogenetic basis for predicting the severity of BA in children.

Prospects for further research. Further study of POP and AOP parameters in children with different degrees of control can be used in the system of clinical diagnosis, prognostication and individualized correction of these disorders in children with BA.

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REFERENCES

1. Chernyuk N.V, Yacishyn R.I., Kaminsky V.Ya. Suchasni poglyady na rol genetichnykch ta epigenetychnykch faktopiv u formuvanni bronchialnoi asthmy [The modern only individual to the role of genetic and epigenetic factors in formation of the bronchial asthma]. The Clinic Immunology. Allergology. Infectology. 2019;2(115): 5-10. (in Ukrainian).
2. Umanets TR (2015) Novi pidkchody do basisnoi therapii bronkchialnoi astmy u ditey. [The new practice to basis therapy of bronchial asthma in children. The Health of Ukraine]. 2015; 4(12): 4-5. (in Ukrainian).
3. Karimov I.Z. Okysna modifikasiya I perekysne okysnennya lipidiv u rosvytku metabolichnoi intixicacii pry patologii [The oxidant modification of proteins and the peroxidation of the lipids during metabolic intoxication in pathology]. Laboratory diagnostics. 2005;1 (31):7-13. (in Ukrainian).
4. Saikat S., Chakraborty R. The Role of Antioxidants in Human Health. ACS Symposium Series. 2014; 3:23-34.
5. Lyakch M. Yu. Osnovy komputernoy biostatistiky : analis informacii v biologii, medicine I farmacii statisticheskim paketom MedStat [Anderlying of komputer's biostastistic: the analise of information in biology, medicine and pharmacii by the statistic programe MedStat] In Lyakch M. Yu, Guryanov V.G, Kchomenko V.N et al. Donetsk: 2006, 211 p. (in Russian).
6. Global Initiative for Asthma: Revised, 2016. www.ginaasthma.org
7. Order of the Ministry of Health of Ukraine No 868 dated 10/08/2013. Protocol for the diagnosis and treatment of bronchial asthma in children.
8. Sana MD, Galeotti NJ Central neuronal functions of histamine H4 receptors. Oncotarge. 2017; 8(8): 123-126.
9. Hashimoto M, Sato EE, Hashimoto K. Role of adrenocorticotropic hormome in the modulation of pollinosis induced by pollen antigens. Neuroimmunomodulation. 2015; 22(4): 256-262.
10. Mc Donald NJ, Bara AD (2013) Anticholinergic therapy for chronic asthma in children over two years of age. Cochrane Database. Syst. Revised 3: CD 003535.
11. Garcia-Aymerich j., Agusti A., Barbera J. et al. Phenotypic heterogeneity of chronic obstructive pulmonary disease. Arch. Bronconeumol. 2009; 45(93):133-142.