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Etiopathogenic aspects of virus-induced exacerbatiuon of bronchial asthma treatment

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A characteristic feature of bronchial asthma (BA) is the variability of the disease with periodic exacerbation development – episodes of progressive increase of breathlessness, cough, wheezing and appearance of shortness of breath, chest compression or various combinations of these symptoms, which often appear to be life-threatening and as a result is significant Pulmonology problem [3, 9, 14, 15].

Among the many internal and external factors that contribute to the development of asthma and cause its eexacerbation recently a special importance is given to respiratory infections especially to viral, which is considered to be the one of the major triggers of asthma. Relationship between acute respiratory viral infection (ARVI) and exacerbation of asthma was determined by results of many epidemiological studies. In particular a direct correlation between the seasonal rise in the incidence of ARVI and the frequency of acute asthma is determined [13, 17, 21].

In patients with asthma with symptoms of ARVI a more pronounced violations of ventilation lung function and signs of laboratory symptoms of inflammatory reaction (the number of eosinophils and white blood cells, the level of eosinophilic infiltration of the lungs, etc.) are observed [3, 13, 17] and bronchial hypersensitivity persists after undergoing ARVI for 5 to 11 weeks [20].

According to the results of modern researches bronchial obstruction can be caused by various viruses: respiratory syncytial virus (RS virus), rhinovirus flu viruses A and B, adenovirus, parainfluenza virus, coronavirus, metapnevmovirus and others, but most often (80 % of all virus-induced exacerbations of BA) in adults and older children bronchial obstruction is caused by different rhinovirus types [12, 13, 20].

Respiratory viruses, especially rhinovirus and RS virus, can cause or aggravate airways inflammation due to direct alteration of bronchial epithelium, and also through displacement by damaged cells and effector cells (eosinophils, lymphocytes) of a number of proinflammatory mediators – cytokines and chemokines (interleukins , leukotrienes, platelet activating factor, tumornecrotizing factor, histamine, neutrophil proteases, etc.), that leads to further violations of bronchial epithelium, increased inflammatory response and the development of pulmonary insufficiency [12, 20]. In addition, immune mechanisms are enrolled: respiratory viruses oppress general and local immunity and also contribute to the activation of T-helper cells, which increase hypersensitivity reactions of both delayed and also immediate type in response to allergenic stimulation, leading to increased production of specific IgE and top further enhancement of allergic inflammation process [1, 10–13]. In the pathogenesis of virus-induced asthma exacerbation great role is also played by violations of neuroregulatory mechanisms – increased activity of the parasympathetic nervous system and level of neuropeptides, reduced level of neutral endopeptidase and production of NO, which play an important role in the development of bronchoconstriction. One of the important factors of the pathogenic effects of ARVI is the deterioration of mucociliary clearance and also inhibition of phagocytal activity of alveolar macrophages. This creates conditions for additional bacterial infection and formation of viral-bacterial associations [12, 17, 20, 21]. Often with ARVI contamination is originated by *M. pneumoniae* and *C. pneumoniae*, which leads to a more severe progression of asthma exacerbation [3, 12, 13, 20].

Despite its proven high efficiency of modern methods of basic treatment of BA patients, which prevents progression of the disease and the development of its exacerbations, the questions related to the occurrence, treatment and prevention of BA exacerbations remain actual global medical problem due to significant investment to treatment, incapacitation and invalidity of patients [3, 9, 14].

The modern approach to treatment of patients with BA, exacerbation of which is induced by ARVI, should be determined

by the peculiarities of the impact of viral infection on the patient [10, 17, 20, 21]. On the one hand, this is the suppressive effect on the immune system that promotes the adherence of bacterial flora, on the other – reducing the resistance of the organism as a whole, as well as the appearance of allergic reactions and symptoms of bronchoconstriction. In this regard, it is recommended to use the antiviral drugs, immunomodulators and in case of presence of «mixed infection» – antibacterial agents for the combined therapy and also for reinforced pathogenetic (baseline) treatment of BA according to the degree of its severity (adequate doses of corticosteroids, bronchodilators, expectorants, etc.) [12, 13, 20, 21].

It is known that BA itself and especially its acute exacerbations oppresses immunological condition of the body, breaks metabolism and redox processes, impairs microcirculation, blood rheology, leads to mucociliary failure, hypoxemia, and as a consequence – the progression of respiratory failure. It is known that antioxidant system is the main factor limiting the pathological effects of active oxygen metabolites (AOM) in the human body. It is shown that in healthy people activity of antioxidant enzymes is increased depending on the production of AOM in substrate induction mechanism, and this is the reason why the adaptive alteration of cell metabolism occurs [16, 18, 19]. A number of researchers found that the use of corticosteroids in the treatment of BA exacerbations leads to disruption of oxidant-antioxidant defense system.

Because of this it should be rational for patients with acute exacerbation of BA in the background of enhanced baseline and antiviral therapy to assign additional pharmacological agent with antioxidant type of pharmacological effect [18].

The aim of this study – to improve treatment of patients with acute exacerbations of BA of viral etiology by optimizing treatment using in the mixed therapy the agent with antiviral activity – Vitaglutam and with antioxidant action – Quercetin.

Materials and methods

116 patients with exacerbations of BA: 60 (51,7 %) men and 56 (48,3 %) women aged 19–76 years (mean age – (40,2 ± 2,0) years) who were examined and treated in outpatient or inpatient care settings of State Institution «National Institute of Phthisiology and Pulmonology named after F.G. Yanovsky NAMS of Ukraine», Kyiv (NIPP NAMS of Ukraine) were included in this study.

Among the patients intermittent BA was diagnosed in 16,4 % of people, persistent – in 83,6 % (mild course – in 30,9 % of patients, moderate course – in 53,6 %, severe course – at 15,5 %). According to the data of AST-test prevailed group of patients had partly controlled (in 58,6 % of patients) or uncontrolled (in 21,6 %) course of the disease. Full control of BA was fixed only in 19,8 % of patients.

Disease duration of BA averaged (12,6 ± 2,5) years.

The average frequency of asthma exacerbations during the last year in examined patients was (2,5 ± 0,6) with a mean duration time of each – (12,6 ± 2,1) day. In 17,2 % of patients this BA exacerbation appeared for the third time during the year, in 5,2 % – for the fourth time.

According to the clinical and functional characteristics and severity of asthma exacerbation mild course of this exacerbation was diagnosed in 41,4 % of patients, moderate – in 53,5 %, severe – in 5,2 %.

Based on the data obtained about the role of viral aetiopathogens in the development of infectious exacerbation of BA and changes in the activity of antioxidant defense that are developed under its influence, the authors proposed to use for a drug therapy in patients with exacerbations of BA, which was carried out in accordance with the guidelines given in the order № 128 from 19.03.2007 of Ministry of Health of Ukraine [3], agents with etiotropic and pathogenetic action – an antiviral drug Vitaglutam drug and antioxidant agent – Quercetin.

Patients with severe decompensated or unstable somatic pathology that threatened the patient's life or worsened the disease prognosis; also who had complicated course of the underlying disease in a form of bacterial infection of the respiratory tract, which was determined clinically and / or laboratory; who received any antiviral (including preparations of interferon or interferon inducers) and/or antibiotics at the beginning of the observations; who had an allergic reaction to drugs studied and if from the moment of the first signs of virus-induced exacerbations of BA has been passed more than 2 days were excluded from a study of effectiveness of these agents in patients with exacerbations of BA [11].

Depending on the amount of therapeutic interventions patients were divided into three study groups.

To the 1 group were included 55 patients who used anti-inflammatory medications (inhaled and systemic glucocorticosteroids) in combination with bronchodilators (β_2-agonists and anticholinergic drugs of short or long-action), mukoregulators and antihistamines as the base medical therapy. Volume of therapeutic interventions and administration ways of drugs were determined by the severity of exacerbation and response to the initial phase of therapy.

The structure of the 2 group included 41 patients who were additionally appointed antiviral drug of regular use Vitaglutam (Ingavirin) orally at a dosage of 90 mg 1 time per day. The total duration of antiviral therapy was 5 days, in all cases it was empirical (was appointed in case of presence of clinical manifestations of ARVI until the results of virological studies were obtained).

The structure of the 3 group included 21 patients, 11 patients in addition to a mixed treatment (basic enhanced, antiviral) drug Quercetin was administered at a dosage of 80 mg daily for 7 days, 10 patients from group 2 were taken for comparison.

For virological studies a sampling of biomaterial by taking a nasal swab or lavage was performed in all patients.

Nasal swabs were taken by dry sterile probes with cotton pellets. For polymerase chain reaction (PCR-study) after taking the material a pellet (the working part of the probe with a cotton pellet) was placed in a sterile disposable microtube with 500 ml of sterile transport medium. The tip of the probe was broken or cut to give the opportunity of tightly closing the tube. Tube with transport medium and part of the probe was closed and placed in a special tripod and transported to the laboratory [2–5, 8].

To prevent inactivation of viruses a nasal swab was placed in a test tube with 2,0–3,0 ml of a special viral transport medium (VTM) or saline. Material (nasal swab or lavage and serum) for study was transported in containers with refrigerant

at a temperature +4 °C to virology laboratory of the National Medical Academy of Postgraduate Education named after P. L. Shupik of Ministry of Health of Ukraine.

A complex of methodological approaches that included modern express methods of viruses indication and viral antigens in clinical material – simple/rapid tests based on immunochromatographic analysis (ICA) and PCR with results fixation or in real-time – real-time-PCR or with using agarose gel and staining of DNA samples with ethidium bromide were used in the study [1, 2, 4, 5].

For rapid diagnosis of influenza A and B, adenovirus and RS-virus simple/rapid tests «CITO TEST INFLUENZA A & B» (Pharmasco, Ukraine) and «CERTEST RSV-ADENO RESP BLISER TEST» (SerTest, Spain) were used. Mechanism of their action is based on the immunochromatographic analysis (ICA) method – specific interaction of antigens and antibodies on the membrane of chromatographic test after its wetting with fluid of studied sample from a patient. This interaction occurs due to the diffuse movement of the tracer immune component, which is stained with colloidal gold (CG) that was previously deposited on the membrane, and antigens of the sample after its applying to the membrane. For visual identification of a specific immune response in a particular area-band of chromatographic membrane necessary components that allow to concentrate the staining agent in the form of colored band are previously tightly sorbed [5, 8].

Using PCR method the presence of pathogens DNA/RNA markers: adenovirus, bocavirus, metapneumovirus, coronavirus, influenza A virus (subtypes H1, H3, H5), influenza B virus, RS virus A and B, rhinovirus were determined. The PCR method is based on cells lysis with a help of powerful chaotropic agent guanidine thiocyanate (GuSCN) and sorption of DNA samples to the media (diatomaceous earth). After the washing adsorbed on a carrier DNA left in the sample, from which it can be very easily removed by eluting solution [1].

Condition of free radical lipid peroxidation activity was studied in 21 patients with viral induced BA exacerbations (10 patients from 2 group 11 patients from 3 group) in comparison with 9 almost healthy individuals (donors) in the initial state and after 1 week of treatment (observation). To determine the activity of free-radical lipid peroxidation system (FRLP) registration of spontaneous (SCL) and Fe^{2+}-induced weakest light emission of patient's plasma (chemiluminescence) was used. The Fe^{2+}-initiated chemiluminogram (ICG) was recorded for 6 min. The following parameters were determined on it: amplitude of fast flash luminescence (h, imp/s), the maximum amplitude of the slow flash of the weakest luminescence (H, imp/s) and its amplitude on the sixth minute of ICG registration (I_6, imp/s), the value «$\angle\alpha$» of the slow ICG of biological substrate flash growth inclination, the latent period of reaction after CL initiation – time from introduction into the biological substrate of the standard dose of Fe^{2+} to the beginning of a slow ICG flash (t_1, s) and the time of entering of the ICG-curve on a plateau or maximum luminescence (t_2, s). According to the data of chemiluminometer the ICG light sum was received for the registration period of 6 minutes (S_1, imp/6 min) and lipid peroxidation of biological substrate resistance indicator (S_2, imp/6 min) was calculated [5]. The results of patients examination in the output state on the 7th day of treatment were compared with the same data that were obtained from 9 healthy donors (intralaboratory control). The study was carried out in the laboratory of biomedical criteria of professional effects of «Institute of Occupational Medicine of NAMS of Ukraine».

11 patients from the 3rd group were administered the Quercetin in the officinal allowable doses and regiments (daily 40 mg orally 2 times a day) to overcome the prooxidant effects of acute infection on the patient and to improve the body's antioxidant defense.

Quercetin – an pharmacological agent, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-OH-dihydrate, which is obtained from the rutin (registration № UA/0119/02/01 from 12.04.2011 to 27.11.2013), anhioprotektor. Flavonoid Quercetin is an aglycone of many vegetational flavonoid glycosides including rutin. Pharmacological properties of Quercetin are stipulated by a pronounced antioxidant activity [6]. Due to capillarosctabilising properties which are associated with antioxidant, membrane-stabilizing action, the agent reduces capillary permeability. Quercetin has anti-inflammatory effect due to blockade of lipooxygenase pathway of arachidonic acid metabolism, decrease of synthesis of leukotrienes, serotonin and other inflammatory mediators. Quercetin has gastroprotective effect and also shows radioprotective activity. Cardioprotective properties of the drug are stipulated by the growth of the cardiomyocytes energy supplying through antioxidant action and improvement of blood flow. Reparative properties of Quercetin are concluded in accelerated wound healing. The drug can affect the bone remodeling process and shows a stable immunomodulatory activity. A diuretic, spasmolytic and anti-sclerotic properties of this agent also were experimentally determined. It is able to normalize blood pressure and stimulate the release of insulin, inhibit the synthesis of thromboxane, slow platelet aggregation. Due to its estrogen-like properties (impact on prolil-hydroxylase, inhibition of tumor necrosis factor and interleukins synthesis) this agent has proosteoclastic action [6].

Clinical efficacy of therapy was determined by the analysis of complex of functional and clinical laboratory parameters, taking into account the criteria listed in the European guide for clinical evaluation of antimicrobial drugs [17]. The treatment was considered to be clinically effective if after completion of the study symptoms had completely disappeared (recovery) or the severity of symptoms (salvage) and functional signs of disease exacerbation were significantly reduced. To evaluate the clinical efficacy of studied agents the results of treatment of patients who have completed a course of experimental drug treatment research as well as those who stopped intaking the experimental agents because of their inefficiency and/or development of serious adverse events were used.

Safety of treatment was assessed by quantity of incidence of adverse events, their severity and the onset of clinically significant changes of indicators in laboratory studies. Any adverse event (including clinically significant deviation in results of laboratory studies), which had originated in the patient during the clinical study regardless of whether it is associated with intaking this drug or not was considered as undesirable. For each adverse event according to specific definitive stated criteria the relationship with the experimental drug (doubtful, possible, probable, it is

impossible to estimate, missing) and severity (mild, medium, hard) was evaluated. To analyze the safety and tolerability of experimental antibiotics test results of all randomized patients who received at least one dose of experimental agent regardless of whether they completed the study or not were used.

Research was carried out at the expense of state budget.

Results and Discussion

The screening virological examination of all patients included in the study has been conducted to establish the frequency of viral etiology BA exacerbations and detect spectrum of major viral etiological agents of viral-induced exacerbations of BA. According to laboratory examination of 80 patients – viral aetiopathogens have been identified in 46 (57,5 ± 5,5) %

46 virus strains were identified by means of multiplexed PCR method and 6 strains by means of ICA method (rapid tests «CITO TEST INFLUENZA A + B», «RS-virus + Adenovirus»). The greatest etiological importance among viral pathogens had rhinovirus – in the (52,2 ± 7,4) % of cases. Bocavirus has been determined more rare – in (13,0 ± 4,9) % of cases; metapnevmovirus – in (8,7 % ± 4,2) %; respiratory syncytial virus – in (6,5 % ± 3,6) %, coronavirus , adenovirus, parainfluenza virus, influenza A and B – in (4,4 ± 3,0) % of cases each.

In the beginning of treatment comparison groups for the main clinical and functional features of viral-induced exacerbation of BA did not differ significantly.

In the treatment process in most patients from all comparison groups a positive dynamics of indicators characterizing inflammation severity and presence of bronchial obstruction syndrome have been observed. On visits 2–3 the attention was attracted by faster (in average on 1–2 days) positive dynamics of disappearance of clinical presentations of intoxication and catarrhal symptoms of ARVI in patients from the 2nd and 3rd groups – significant ($p < 0,05$) decrease in number of patients with fever, weakness, head and muscle pain, mucosal hyperemia and conjunctival congestion, complicated nasal breathing, coughing, etc. In these patients on the 2–3rd day of observation a faster ($p < 0,05$) disappearance or reduction of nocturnal and daytime BA symptoms compared with patients from the 1 group was also fixed. However, the significant reduction in perforce usage of bronchodilators and clinical manifestations of bronchial obstruction at a next follow-up of patients in all groups were not recorded.

Analysis of clinical and functional parameters at the end of follow-up (visit 4) shows that the performed therapy helped to achieve a positive result in all comparison groups: all patients achieved improvement of the general condition, reduction of clinical signs of bronchial obstruction, frequency of daytime and nocturnal symptoms, requirement of emergency agents.

Results of treatment: complete elimination of exacerbation (return to original state) was established in (80,0 ± 5,4) % patients of 1 group, improvement – in (20,0 ± 5,4) %, in patients of 2 group – in (85,4 ± 5,5) % and (14,6 ± 5,5) %, respectively, in patients of 3 group – in (90,0 ± 6,7) % and (10,0 ± 6 7) %, respectively. It should be noted that the mixed usage of antiviral and antioxidant agents in the base treatment of viral-induced exacerbations of asthma secured the reduction of exacerbation duration in general due to more rapid disappearance of clinical manifestations of infectious inflammation.

In 11 (20,0 ± 5,4) % patients of 1 group and 2 (4,9 ± 3,4) % of patients in 2 group according to clinical and laboratory data bacterial complications (appearance of purulent sputum and increasing of its volume) has developed. This fact leads to the necessity of appointment of antimicrobials and extension of treatment period. Among the patients of 3 group there were fixed no cases of premature treatment discontinuation due to bad compliance, development of infectious complications or adverse reactions, including toxic-allergic.

Dynamics of clinical and functional parameters of viral-induced BA exacerbation completely coincided with the results of laboratory determination of free-radical lipid peroxidation state, which was performed in 21 patients with BA exacerbation of viral etiology (10 patients from 2 group and 11 – from 3 group) compared with 9 almost healthy individuals (donors).

According to the data given in the table all the patients in the initial state before treatment compared with donors had the increased SCL level of plasma – (521 ± 24) imp/1 min vs (408 ± 16) imp/1 min ($p < 0,01$). In addition upon condition of initiation of FRLP process in the plasma of patients with Fe^{2+} ions the tendency to accelerate the flow of the process of lipid peroxidation (LP) in it – (32,4 ± 4,0) imp/s vs (22,4 ± 4,3) imp/s ($p < 0,1$) was determined and it was accompanied by a significant decrease of peroxidation products of free radical reactions – (10481 ± 566) imp/6 min against (12588 ± 694) imp/6 min ($p < 0,05$) and increase of resistance to lipid peroxidation – (7291 ± 688) imp/6 min ($p < 0,05$). The last thing testified the presence in patients of blood plasma lipid composition violations due to reduction of lipid fractions which are most easily oxidized. This indirectly indicates to the presence of a long activation of FRLP process in patients with bronchial asthma.

After 1 week in patients from 2 group the level of SCL in plasma was rapidly increased – (970 ± 8) imp/1 min vs (297 ± 33) imp/1 min ($p < 0,001$). During the registration of ICG the primary products of lipid peroxidation process – toxic lipid hydroperoxides were accumulated in it – (88,0 ± 2,7) imp/s vs (64,0 ± 8,5) imp/s ($p < 0,05$), the progress of the LP process has been accelerated – (48,0 ± 7,1) imp/s vs (19,3 ± 7,1) imp/s ($p < 0,02$) and (26,0 ± 2,7) imp/s against (12,7 ± 3,5) imp/s ($p < 0,01$) and also the rate of lipids oxidation – (15,3 ± 2,7) vs (7,0 ± 1,4) ($p < 0,02$), peroxide products of free-radical reactions were accumulated – (17929 ± 845) imp/6min vs (9353 ± 634) imp/6 min ($p < 0,01$); resistance to lipid peroxidation were decreased – (14122 ± 1804) imp/6 min against (10207 ± 362) imp/6 min ($p < 0,05$). In this case the duration of the latent period before the development of slow flash ICG and the output time of the weakest luminescence at plateau (or maximum) were respectively decreased on 29,8 % and 11,9 % indicating to the presence of an integrated antioxidant deficiency in the body of patients. Thus, the baseline therapy has clear and explicit prooxidant effect on patient's body.

Application in the treatment of patients with acute exacerbation of BA of viral etiology with mild course of Vitaglutam for 5 days and Quercetin for 1 week (third group) compared to 10 patients in 2 group who received in addition to mixed treatment only Vitaglutam for 5 days, has facilitated the significant reduction of

Table

The activity of free-radical lipid peroxidation system in plasma of patients (M ± m)

Checking group	SCL, imp/1min	Fe^{2+}-induced chemiluminescence							
		h, imp/s	H, imp/s	I_{6min}, imp/s	<a, o	t_1, s	t_2, s	S_1, imp/6min	S_2, imp/6min
1. Donors	408 ± 16	77,6 ± 9,4	22,4 ± 4,3	16,0 ± 5,2	7,4 ± 1,7	82,0 ± 4,3	328,0 ± 19,3	12588 ± 694	10250 ± 812
2. Patients (baseline therapy)	521 ± 24	70,5 ± 5,2	32,4 ±4,0	18,0 ± 6,5	8,6 ± 1,2	82,5 ± 16,2	312,0 ± 13,5	10481 ± 566	7291 ± 688
3. Donors	297 ± 33	64,0 ± 8,5	19,3 ± 7,1	12,7 ± 3,5	7,0 ± 1,4	78,3 ± 15,0	314,2 ± 12,1	9353 ± 634	10207 ± 362
4. Patients (baseline therapy + antiviral)	970 ± 8	88,0 ± 2,7	48,0 ± 7,1	26,0 ± 2,7	15,3 ± 2,7	55,0 ± 13,4	276,7 ± 14,6	17929 ± 845	14122 ± 1804
5. . Patients (baseline therapy + antiviral + Quercetin)	567 ± 66	87,3 ± 4,5	32,7 ± 7,8	26,7 ± 9,9	7,0 ± 0,9	78,3 ± 15,0	334,2 ± 17,4	13612 ± 989	10212 ± 419
P_{1-2}	< 0,01	> 0,5	< 0,1	> 0,5	> 0,5	> 0,5	> 0,5	< 0,05	< 0,05
P_{1-3}	< 0,02	< 0,5	> 0,5	> 0,5	> 0,5	> 0,5	> 0,5	< 0,01	> 0,5
P_{3-4}	< 0,001	< 0,05	< 0,02	< 0,01	< 0,02	> 0,5	> 0,5	< 0,01	< 0,05
P_{3-5}	< 0,01	< 0,05	< 0,5	< 0,5	> 0,5	> 0,5	> 0,5	< 0,01	> 0,5
P_{4-5}	< 0,001	> 0,5	< 0,2	> 0,5	< 0,02	> 0,5	> 0,5	< 0,01	< 0,05

FRLP hyperactivity. In particular, the SCL level in blood plasma was significantly less frank – (567 ± 66) imp/1 min vs (970 ± 8) imp/1 min ($p < 0,001$). During the ICG registration concentration of primary products of lipid peroxidation process – toxic lipid hydroperoxides – was retained on it – (87,3 ± 4,5) imp/s vs (88,0 ± 2,7) imp/s ($p > 0,5$) and to a lesser extent – concentration of peroxidation products of free-radical reactions – (13612 ± 989) imp/6min against (17929 ± 845) imp/6 min ($p < 0,01$). However herewith a significant intensity decrease of the LP process was observed in plasma of patients from 3 group – (32,7 ± 7,8) imp/s vs (48,0 ± 7,1) imp/s ($p < 0,2$), and the rate of lipid oxidation – (7,0 ± 0,9) to (15,3 ± 2,7) ($p < 0,02$) and their resistance to peroxidation – (10212 ± 419) imp/6 min vs (14122 ± 1804) imp/6 min ($p < 0,05$) were normalized to control values – respectively (7,0 ± 1,4) and (10207 ± 362) imp 6 in donors. The duration of the latent period before the development of a weak ICG flash and the output time of the weakest luminescence at plateau (or maximum) did not differ from those in donors.

Therefore, usage of one of the modern antioxidant agents – Quercetin in treatment of patients with mild course BA exacerbation of viral etiology allows significantly to avoid the inevitable prooxidant effect of inflammatory process caused by exacerbation of the disease and carrying of baseline and antiviral therapy.

Thus, the results of the study indicate to a high clinical effectiveness of suggested treatment regimen of patients with BA exacerbation of viral etiology, which is to conduct basic treatment of acute asthma with the appointment of enhanced doses of corticosteroids and bronchodilators according to the severity of the exacerbation with additional empirical receiving of Vitaglutam in a dosage of 90 mg daily for 5 days and antioxidant Quercetin in pharmacopeia permissible doses and regiments (daily 40 mg orally 2 times a day) for 7 days, this allowed to significantly reduce: the duration of intoxication syndrome (mean for 1,5 days), the termination of apnea (mean for 1,5 days) and duration of exacerbation as a whole (for 3,8 days), as well as to reduce the number of bacterial complications by 15 % due to the antiviral action and improvement of performance of free-radical activity of lipid peroxidation (decrease in intensity of systemic activation of free-radical processes in the body of patients, induction of oxidative stress and lipid peroxidation process and avoidance of the inevitable prooxidant effect of the inflammatory process that occurs as a result of disease exacerbation).

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ЭТИОПАТОГЕНЕТИЧЕСКИЕ АСПЕКТЫ ЛЕЧЕНИЯ ВИРУС-ИНДУЦИРОВАННОГО ОБОСТРЕНИЯ БРОНХИАЛЬНОЙ АСТМЫ

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Резюме

Объект исследования – *116 больных с инфекционным обострением бронхиальной астмы вирусной этиологии: 60 (51,7 %) мужчин и 56 (48,3 %) женщин в возрасте 19–76 лет (средний возраст – (40,2 ± 2,0) года).*

Цель работы – *повысить эффективность лечения больных с инфекционным обострением бронхиальной астмы вирусной этиологии путем оптимизации лечения с использованием в комплексной терапии препарата с антивирусной активностью – витаглутама и антиоксидантным действием – кверцетина.*

Материалы и методы исследования – *клинико-функциональные, вирусологические, биохимические, статистические.*

Результаты. *Проведенное исследование свидетельствует о высокой клинической эффективности предложенной схемы лечения больных с обострением бронхиальной астмы вирусной этиологии, которая заключается в проведении базисного лечения обострения бронхиальной астмы с назначением повышенных доз ГКС и брохолитиков соответственно степени тяжести обострения с дополнительным эмпирическим приемом витаглутама в дозе 90 мг сутки в течение 5 дней и антиоксидантного препарата кверцетин в фармакопейно допустимых дозах и режимах (ежедневно внутрь по 40 мг 2 раза в сутки в течение 7 дней), что позволило достоверно сократить: продолжительность интоксикационного синдрома (в среднем на 1,5 дня), длительность прекращение одышки (в среднем на 1,5 дня) и обострения в целом (на 3,8 дня), а также снизить количество бактериальных осложнений на 15,0 % за счет противовирусного действия и улучшения показателей активности свободнорадикального перекисного окисления липидов (уменьшение выраженности системной активации свободнорадикальных процессов в организме больных, индукции оксидативного стресса и процесса перекисного окисления липидов и избежание прооксидантного воздействия воспалительного процесса, который возникает в результате обострения болезни).*

Предложенную схему целесообразно использовать для лечения больных с инфекционным обострением бронхиальной астмы вирусной этиологии.

Ключевые слова: *бронхиальная астма, обострение, вирус, антиоксидантная система.*

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ETIOPATHOGENIC ASPECTS OF VIRUS-INDUCED EXACERBATIUON OF BRONCHIAL ASTHMA TREATMENT

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Summary

The object of study – *116 patients with infectious exacerbation of asthma of viral etiology: 60 (51,7 %) men and 56 (48,3 %) women aged 19–76 years (mean age – (40,2 ± 2,0) years).*

Purpose – *to improve the effectiveness of treatment of patients with infectious exacerbation of asthma of viral etiology by optimization of treatment with the usage for mixed therapy of agent with the antiviral activity – Vitaglutam and antioxidant activity – Quercetin.*

Methods of research – *clinical, functional, virological, biochemical, and statistical.*

Results. *The results of the study indicate a high clinical efficacy of the proposed treatment regimen of patients with bronchial asthma exacerbation of viral etiology that is to conduct basic treatment of exacerbation of bronchial asthma with the appointment of high doses of corticosteroids and bronchodilators respectively to exacerbation severity with additional empirical receiving of Vitaglutam in a dose of 90 mg daily for 5 days and the antioxidant agent Quercetin in Pharmacopeial permissible doses and regimens (daily inside of 40 mg 2 times a day for 7 days), this allowed to significantly reduce: the duration of intoxication syndrome (an average of 1,5 days), the termination of apnea (an average of 1,5 days), duration of exacerbation as a whole (by 3,8 days), as well as reduce the number of bacterial complications of 15,0 % due to the antiviral effect and improvement of performance of free-radical activity of lipid peroxidation (relief of systemic activation of free radical processes in the body of patients, induction of oxidative stress and lipid peroxidation process and avoidance of pro-oxidant effect of the inflammatory process that occurs as a result of disease exacerbation).*

The proposed scheme should be used for the treatment of patients with infectious exacerbation of asthma of viral etiology.

Key words: *bronchial asthma, exacerbation, virus, anti-oxidant system.*

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