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ВЫЯВЛЕНИЕ НОВЫХ ГЕНЕТИЧЕСКИХ И ИММУНОЛОГИЧЕСКИХ БИОМАРКЕРОВ ТЯЖЕЛОЙ БРОНХИАЛЬНОЙ АСТМЫ КАК АКТУАЛЬНАЯ ПРОБЛЕМА

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АННОТАЦИЯ

В мире насчитывается 300 миллионов больных астмой, а уровень смертности колеблется от 0% до 18%. Во всем мире бронхиальная астма (БА), распространенность которой составляет от 1 до 18 процентов, становится все более распространенной. Согласно обновленному (GINA-2017) определению, астма классифицируется как разнообразное заболевание дыхательных путей, которое обычно характеризуется стойким воспалением дыхательных путей. Он характеризуется наличием в анамнезе закупорки дыхательных путей и респираторными симптомами, такими как свистящее дыхание, одышка, заложенность грудной клетки и кашель, с переменным началом, частотой и интенсивностью. В последние годы достигнуты значительные и многочисленные успехи в лечении бронхиальной астмы. Эти результаты связаны со значительной эффективностью ингаляционных кортикостероидов в топической диагностике и патогенетической терапии бронхиальной астмы. Однако, несмотря на достигнутые результаты, борьба с этим заболеванием не вызывает нареканий. У больных с тяжелой бронхиальной астмой ингаляционные кортикостероиды более эффективны при применении в комбинации с β2-агонистами. Почти каждого второго больного астмой беспокоят ночные приступы. Более половины больных имели ограниченную физическую активность, а каждый третий утратил трудоспособность. Большинство пациентов вынуждены обращаться к врачу из-за обострения и прогрессирования заболевания.

Ключевые слова: бронхиальная астма, биомаркеры, иммунология

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IDENTIFICATION OF NEW GENETIC AND IMMUNOLOGICAL BIOMARKERS OF SEVERE BROCHIAL ASTHMA AS A CURRENT PROBLEM

ANNOTATION

There are 300 million asthma sufferers globally, and the mortality rate ranges from 0% to 18%. Worldwide, bronchial asthma (BA), which has a prevalence of 1 to 18 percent, is becoming more common. According to the updated (GINA-2017) definition, asthma is categorized as a diverse airway condition that is typically characterized by persistent airway inflammation. It is characterized by a history of airway blockage and respiratory symptoms such wheezing, shortness of breath, chest congestion, and cough, with variable onset, frequency, and intensity. In recent years, significant and numerous successes in the treatment of bronchial asthma have been achieved. These results are associated with the significant effectiveness of inhaled corticosteroids in the topical diagnosis and pathogenetic treatment of bronchial asthma. However, despite the results achieved, the fight against this disease is not satisfactory. In patients with severe bronchial asthma, inhaled corticosteroids are more effective when used in combination with β2-agonists. Almost every second patient with asthma is concerned about nocturnal attacks. More than half of the patients had limited physical activity, and one in three lost the ability to work. Most patients are forced to see a doctor because of the exacerbation and progression of the disease.

Key words: bronchial asthma, biomarkers, immunology

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OG‘IR BRONXIAL ASTMA KASALLIGINING YANGI GENETIK VA IMMUNOLOGIK BIOMARKERLARINI ANIQLASH BUGUNGU KUNNING DOLZARB MUAMMOSI SIFATIDA

ANNOTATSIYA

Dunyo bo’ylab 300 million astma bilan kasallanganlar mavjud va o’lim darajasi 0% dan 18% gacha. Butun dunyoda 1 dan 18 foizgacha tarqalgan bronxial astma (BA) keng tarqalgan. Yangilangan (GINA-2017) ta’rifiga ko’ra, astma odatda havo yo’llarining doimiy yallig’lanishi bilan tavsiflangan turli xil havo yo’llari holati sifatida tasniflanadi. Bu o’zgaruvchan boshlanishi, chastotasi va intensivligi bilan nafas olish yo’llari tiqilib qolishi va nafas olish belgilari, masalan, xirillash, nafas qisilishi, ko’krak qafasidagi tiqilishi va yo’tal bilan tavsiflanadi. So’nggi yillarda bronxial astmani davolashda sezilarli va ko’p yutuqlarga erishildi. Ushbu natijalar bronxial astmaning topikal diagnostikasi va patogenetik davolashda ingalyatsion kortikosteroidlarning sezilarli samaradorligi bilan bog’liq. Biroq erishilgan natijalarga qaramay, ushbu kasallikka qarshi kurash qoniqarli emas. Jiddiy bronxial astma bilan og’rigan bemorlarda ingalyatsion kortikosteroidlar b2-agonistlar bilan birgalikda qo’llanilganda samaraliroq bo’ladi. Astma bilan og’rigan deyarli har ikkinchi bemor tungi xurujlar haqida qayg’uradi. Bemorlarning yarmidan ko’pi cheklangan jismoniy faoliyatga ega, har uchdan biri mehnat qobiliyatini yo’qotgan. Ko’pgina bemorlar kasallikning kuchayishi va rivojlanishi tufayli shifokorni ko’rishga majbur bo’lishadi.
Kalit so’zlar: bronxial astma, biomarkerlar, immunologiya

Asthma affects 300 million people worldwide, and the mortality rate ranges from 0 to 18 percent. The prevalence of bronchial asthma (BA), which ranges from 1 to 18 percent, is increasing worldwide. Asthma is classified as a heterogeneous airway disease according to the revised (GINA-2017) definition, which is usually characterized by persistent inflammation of the airways. A history of respiratory symptoms such as wheezing, shortness of breath, chest congestion and cough, with varying onset, frequency and intensity, as well as airway obstruction, is what characterizes it.

Much earlier, scientists and medical professionals discussed the heterogeneity and “diversity” of bronchial asthma, which was reflected in the categorization of bronchial asthma and treatment methods based on the discovery of the pathogenetic mechanisms of the disease. Since Cook and Wander presented the results of an epidemiological study in 1916, the hereditary nature of AD has been known for over a century. There were 76 non- atopic probands (control group), 621 atopic probands and their family members. In 48.4% of probands with atopy and in 14.5% without it, a hereditary anamnesis aggravated by the condition was revealed [3]. In 2016, one hundred years later, Ulemar et al. found that AD was hereditary in 82 percent of cases in a study of 25,306 twins aged 9 to 12 years. According to the study, asthma is diagnosed more often in monozygotic twins than in dizygotic twins. Many authors claim that 60–80% of asthma cases have a genetic component. Numerous studies have shown that in patients with asthma, genetic factors significantly increase the impact of environmental factors. Recent studies of genomic associations have been published covering more than 500,000 genetic variants to determine association with asthma [4]. The earliest studies of the role of genetics in the pathogenesis of asthma in children relied on biology or a specific location in the genome. Asthma genetics has made significant progress through sequencing . According to Hap Map , 1000 Genomes and the latest 100,000 Genomes projects , there are more than 60 million different polymorphisms of single nucleotides and their pairs in humans [39]. According to their functions, the genes associated with the development of AD are proposed to be divided into the following categories: those involved in the second type of lymphocytic response (Th-2 response): GATA 3, STAT 6, interleukin (IL) 4, IL-13, IL-4 RA, TBX21 , Il-12B; those associated with inflammation (IL-18, tumor necrosis factor a (TNFa)); associated with sensitivity to environmental factors, primary immune response; those associated with the respiratory tract.

A group of researchers led by Moffatt completed the first study of general genomic associations of asthma in 2007. They included 1243 people without asthma (control group) and 994 people with childhood onset asthma. This study demonstrated a strong correlation between 17q21 and the onset of asthma [40]. It has been established that in severe cases and severe exacerbations, bronchial asthma is associated with 17q21 in a number of ethnic groups when it first appears in childhood [6,18,19,41]. It should be emphasized that the identified causal genes in the pathogenesis of bronchial asthma are consistent with the theory that the condition occurs as a result of impaired primary or adaptive immune response and initial dysfunction of the epithelial barrier. 2q (near IL-1 cluster), 4q, 5q, 6p (near major histocompatibility complex - MHC), 7, 9, 11q (contain FcsRI -ß), 12q (strong linkage), 13q, 16, 17q (strong linkage), 19q, and 21q are close to IL-1 clusters. The DENND1B gene located on chromosome 1q31 encodes a protein that interacts with the tumor necrosis factor receptor and is expressed by dendritic cells and natural killer cells [12]. It has also been associated with the onset of asthma. There were no racial differences. However, different results have been obtained regarding the role of loci in the occurrence of certain manifestations [25].

There are known genes responsible only for a person’s predisposition to develop asthma, and vice versa, there are known genes responsible only for the severity of the condition. For example, F.Assembled by Miriam et al . (2010) study showed that, with the exception of IL-13 and the HLA

region, loci controlling total serum IgE levels and those associated with asthma susceptibility have very little in common. The lack of correlation between sensitization and asthma in many populations suggests that elevated IgE levels may be an intermittent manifestation of asthma rather than its "basis". In contrast, the SERPINE1 gene controls the severity, progression, and response to long-term inhaled corticosteroids, despite the fact that it is not a gene associated with an increased risk of developing asthma. Higher serum IgE levels , more pronounced respiratory dysfunction and a more severe course of the disease are all characteristic of patients carrying the 5G allele . It has been established that a higher level of gene expression in the allele is associated with a better response to inhaled corticosteroids.

In the pathogenesis of bronchial asthma, it is important in the airways with mucus hypersecretion, swelling of the mucous membrane of the respiratory tract, bronchospasm , which leads to bronchial hops . Several blood cells, i.e. activated eosinophils, fat cells, macrophages, lymphocytes, and neutrophils, are involved in the development of continuous airway inflammation. These cells stimulate the release of biologically active substances that contribute to the appearance and persistence of inflammation. Chronic respiratory inflammation causes the development of bronchial wall remodeling with degeneration of its structures of connective tissue and muscles, smooth muscle hyperplasia, eosinophilic infiltration and lymphocytic mucosa, and transformation of goblet cells. Due to the impact of various irritants on the airways and on the lungs, the permeability of epithelial cells increases, the activity of the CIILATO epithelium decreases, which causes damage to the bronchial tree. An increase in the permeability of the respiratory mucosa leads to the penetration of various agents into the submucosal layer, where pollutants interact with smooth muscle cells, fibroblasts, mast cells, eosinophils, lymphocytes, and neutrophils.

The powerful oxidizing power of various inhaled pollutants is one of the mechanisms that lead to the development of BA [4.5]. Under the physiological conditions of life of the organism, the rate of formation of reactive oxygen species (AFC) is balanced by the activity of the antioxidant system (AOS). This balance is fluid, there is little transfer of this balance towards antioxidant protection, but when exposed to various factors, a natural increase in ROS formation is seen when the balance shifts to the left with an increase. with increase with increase with increase with increase with increase with increase with increase in lipid peroxidation processes (floor). With regard to the adequacy of the buffer capacity of the AOS, the balance deviation on the left is gradually determined whether the reserves of the AOS are exhausted [10]. This deviation from the balance in the biological system of oxidation in the overacidification of oxidation with the synchronous depletion of the antioxidant defense of the body was called oxidative or oxidative stress [7.8]. AFK is highly active and enters into an oxidative reaction with lipids, proteins, hydrocarbons, which leads to damage to body tissues. ROS are superoxide anionic radicals, hydroxyl radicals, perocal radicals, alcoholic radicals and ROS derivatives, include hydrogen peroxide, lipid peroxides . Hydrogen peroxide, which is a source of hydroxyl radicals, consists of the radical super oxidanan , released by inflammatory cells in the lungs. Superoxide dismutase (SOD) is involved in this process [9.5]. The complete restoration of oxygen in water requires a large energy consumption, and therefore, in AD patients, the restoration of ROS does not occur completely and leads to the formation of hydrogen peroxide and liporexisia . ROS are produced in significant amounts upon contact of various pollutants with phagocytes, and the phagocytic cells themselves have powerful mechanisms for the production of ROS. ROS generated inside phagolysosomes help phagocyte cells to use their ability for bactericidal activity. The cytotoxic effect of phagocytic cells manifests itself when ROS are released from the cell into the surrounding space [9]. SOD , catalase, glutathione peroxidase , glutathione transferase , glutamylcysteine synthase , glutaredoxins , thioredoxins , perosiredoxins , and other antioxidant enzymes have been found in the airways and lungs . [9,12,15,31]. Recent studies have shown that ROS modify the protein layer of cell membranes in addition to their lipid components [16, 17]. In addition, highly toxic ROS can contribute to the onset and maintenance of inflammation in AD [18]. The occurrence and progression of bronchospasm , as well as the chronicity of inflammatory changes in the respiratory organs, is influenced by excessive formation of ROS, which occurs during the development of oxidative stress [7,11,22]. Oxidative modification of proteins (OMP) is the first and most persistent sign of damage to body tissues caused by ROS [23,43]. It was found that a high level of myeloperoxidase in the extracellular space, combined with excessive destruction of leukocytes, contributes to the development of bronchospasm . Large protein aggregates or broken protein molecules are formed when proteins are exposed to ROS, which also causes disruption of the original protein structure. The hydroxyl radical affects protein aggregation, and the peroxide radical interacts with the superoxide anion, fragmenting proteins into low molecular weight fragments. Lipid radicals also contribute to protein fragmentation. At the same time, the presence of ROS negatively affects the native conformation of the protein domain, leading to an increase in the number of hydrophobic molecules on the surface of the globule and the formation of large protein fragments [23, 27]. Compared to lipid peroxidation (LPO) products such as malonic dialdehyde , diene conjugates , and Schiff bases , under oxidative stress, OMP products form faster and are less variable [23]. LPO and OMB processes are triggered by the onset and progression of AD [27,35]. Due to neutrophilic airway inflammation, which also causes activation of oxidative stress and persistence of inflammation, nonspecific airway hyperreactivity develops, which persists in AD [44]. Granulocytes acquire antigenic characteristics through PMB, and lipid peroxidation increases the production of thromboxane and leukotrienes , chemotactic protective factors that facilitate phagocyte migration [9]. The persistence of the inflammatory process and the development of an "inflammatory vicious circle" can be explained by the potential self-amplification of the activity of phagocytic cells in the focus of inflammation. Leukotrienes and thromboxane , which are biologically active substances, cause microcirculation disorders, imbalance of the -adrenergic system, swelling of the bronchial mucosa. These events cause the bronchi to become hypersensitive and reactive. It has been established that adenosine and purine nucleotides formed during its hydrolysis, such as adenosine monophosphate and adenosine diphosphate (AMP and ADP), play a significant role in the occurrence of bronchospastic syndrome and mediator inflammation in AD. There are not enough cholinergic receptors to isolate this pathogenetic variant of AD [32]. Purine nucleotides disrupt the ability of adenylcyclase to regulate the intracellular level of cAMP and the sensitivity of adrenergic and cholinergic receptors . AD Since

cholinergic receptors are converted by AMP and ADP, there is no need to distinguish between pathogenetic and clinical variants of AD due to adrenergic imbalance. In addition, it is impossible to distinguish between autoimmune clinical and pathogenetic variants of the disease due to the production of antibodies to purinergic components. Purine metabolism disorders in AD patients must be corrected metabolically in order to reduce the effect of the purinergic system and its mediators on cyclase and adrenergic structures [37]. Kurbanov, A.K. Amonova DdotE . Having shown a strong correlation between the content of uric acid and bronchial patency at various levels, (2012) established the presence of a metabolic mechanism for the development of endogenous BA. Hypopurine diet was proposed by the authors for the treatment of patients with AD. Airway extracellular nucleotides have been found to be a major contributor to mucociliary clearance [6]. Extracellular nucleotides play a role in the capture and expulsion of microorganisms from the respiratory tract and lungs. Respiratory nucleotides/nucleosides are involved in mucin secretion through stimulation of P2Y2 goblet cell receptors and increased mucin hydration through activation of A2B and P2Y2 receptors in ciliated epithelial cells [6,32]. ATP is converted to AMP in the extracellular environment by extracellular ectonucleotide diphosphorylase , or CD39, and then AMP is converted to adenosine by ecto-5'-nucleotidase, or CD73 [8]. The role of extracellular adenosine in the onset and progression of respiratory diseases has recently become the subject of active research. The inflammatory process in the lungs persists as adenosine triggers the release of pro-inflammatory cytokines. Low concentrations of adenosine cause a greater dilating effect than histamine due to its effect on various structures [38]. In AD, an imbalance occurs between the production and consumption of adenosine, which leads to the destruction of lymphocyte membranes and the accumulation of harmful substances such as uric acid, ammonia, hydrogen peroxide and superoxide anion. Neutrophil granulocytes play a protective role due to degranulation and production of ROS, which alleviate the course of allergic forms of the disease [2]. Additional potential biochemical markers of respiratory pathology are lung chemokines (chemokine ligand CCL20), surfactant A and D proteins, defensins , Clara cell protein, interleukin-19, etc. [39].

Currently, as a result of scientific research on the pathogenesis of the disease, six phenotypes of bronchial asthma have been identified: allergic asthma, non-allergic asthma, aspirin- induced asthma, late-onset asthma, asthma with fixed airway obstruction, and asthma in obese patients. However, the need to search for new severe AD phenotypes using various markers still exists [40,29]. It has been established that the imbalance of cytokines, the emergence of resistance to glucocorticosteroids (GCS), angiogenesis and remodeling of the bronchial wall, the determination of the immune response by the Th2 link are the most likely mechanisms for the development of a severe course of bronchial asthma. disease. The predominance of neutrophilic granulocytes in bronchoalveolar washings of patients with severe asthma treated with systemic corticosteroids was revealed . Eosinophilia was confirmed in patients not treated with systemic corticosteroids .

After absorption of various pollutants , neutrophils attached to the basement membrane or connective tissue fibers of the bronchial mucosa displace the contents of neutrophil granules through the still open phagocytic vacuole into the environment, completing incomplete phagocytosis. Neutrophil regurgitation is a condition that, in extreme cases, can lead to tissue damage. When neutrophils are stimulated, oxygen consumption increases dramatically (50 times), immunoglobulin G sticks together and more peroxides are produced. In addition, immunoglobulin aggregates can take on the characteristics of self-antigens . Self-maintenance of tissue damage occurs during prolonged attacks of AD due to neutrophilic granulocytes, which are activated during oxidative stress. Leukotriene B4 is the most active lipoxygenase and is especially interested in the activation of arachidonic acid derivatives [42]. The study of additional inflammatory profiles of the disease is relevant, given that about 55% of AD cases are caused by eosinophilic inflammation, and the other is associated with neutrophilic inflammation [43]. Allergy, delayed onset of asthma, and failure of inhaled corticosteroids are characteristics of eosinophilic inflammation in asthma.

Eosinophilic inflammation in AD is characterized by the Th2-endotype of the disease with a predominance of the Th2-lymphocyte response (allergic AD) or high activity of type II innate lymphoid cells, ILC2 cells, which are involved in the pathogenesis as non-allergic and allergic variants of AD. Interleukin 5 (IL5), which is crucial for the development of uncontrolled eosinophilic inflammation in the respiratory organs in patients with severe AD of the T2 endotype, is increased by Th2 and ILC2 cells. This leads to the maturation of eosinophil precursors in the bone marrow, the accumulation of eosinophils in the blood, the infiltration of eosinophils into the lung tissue, and the movement of eosinophils into the area of inflammation.

Neutrophil extracellular traps (neutrophilsextracellulartraps - NETs) are extracellular filamentous structures that are formed by neutrophil granulocytes to destroy pathogenic agents, according to recent studies [1]. Nuclear chromatin, decondensed and released into the extracellular environment, forms networks. The fact that most of the granules in NET are dissolved and that the nuclear membrane is highly fragmented is a characteristic of these cells. This provides a direct interaction between all parts - nuclear, granular and cytoplasmic - and the pathogen. Due to the use of the so-called oxygen-dependent cell death, bacteria and viruses that fall into this "trap" die [4,42]. Despite the protective role of networks, this phenomenon has some adverse consequences. As a result, NETs can worsen asthma by destroying the airway mucosa, causing neutrophil inflammation, and impairing the ability of alveolar macrophages to clear " neutrophil extracellular traps" from the body.

The severity of asthma can be determined by the amount of treatment that provides good control of the symptoms of the disease. GINA-2019 recommended step-by-step principles for asthma management.

The main goals of treatment:

Completely eliminate or significantly reduce the clinical symptoms of bronchial asthma, evaluate and prevent risk factors for adverse outcomes of bronchial asthma.

AD therapy is complex and includes:

Drug treatment: relief of asthma attacks, relief of asthma attacks, prevention of asthma attacks: supportive (basic) treatment, allergen-specific immunotherapy for allergic asthma.

Non-drug treatment: elimination (hypoallergenic) programs; diet therapy; speak; regular physical activity; acupuncture and climatotherapy.

Maintenance drugs reduce airway inflammation,

control clinical symptoms of asthma, and prevent exacerbations and the risk of worsening lung function (FL). They are designed for long-term daily use. These include: Inhaled corticosteroids; leukotriene receptor antagonists ;

long-acting β2-agonist and combined forms: ICS + short-acting β2-agonist, ICS + long-acting β2-agonist;

long-acting anticholinergic drugs and fixed combinations: short-acting anticholinergic drugs + β2-agonists;

inhaled forms of cromoglycic acid or nedocromilasodium ;

long-acting theophyllines; systemic GCS; biological drugs (anti- IgE , anti-interleukin-5, 13).

The main goal of treating patients is to determine the control of asthma. This is based on the severity and characteristics of the disease process. More than 3-4 times). In order to prevent symptoms of BA and prevent its worsening, extensive methods should be followed: patient training: aims to reduce allergens in the environment with known exposure indicators and drugs with the elimination or reduction of inflammatory processes for preventive treatment: the monitor shows that the Monitor detects the monitor that reveals monitor that shows a monitor that shows a monitor that shows that the monitor shows that the monitor shows that the monitor shows that the monitor detects the elimination of inflammation or reduces inflammation: monitor. Deterioration of the patient's condition and the existence of a quick stop. Treatment depends on the appropriate behavior of the patient. His medical advice, doctors' understanding of the properties of the disease and drugs, to help the patient's treatment of the appropriate method.

The goal of treating an asthma attack is to quickly and minimize airflow obstruction and restore normal breathing function. According to WHO recommendations, outpatients should begin the treatment phase when symptoms worsen and peak expiratory flow (PEF) decreases, but patients under special supervision should be immediately transferred to a specialized hospital or, if necessary, to an intensive care unit. For exacerbations of mild to moderate severity, short-acting beta2-agonists are prescribed (if necessary, 2 doses from a metered dose inhaler every 20 minutes for 1 hour). The drugs of choice are β2-receptor agonists (albuterol , fenoterol, etc.) in metered dose inhalers, which can relax bronchial smooth muscle, increase mucociliary clearance, and reduce vascular permeability. They can quickly stop mild to moderate asthma attacks and are one of the most effective rescuers in this disease.

Bronchodilatory anticholinergic inhalants (ipratropium bromide, etc.) have a small and delayed effect (the maximum effect occurs 30-60 minutes after application), but their effect may be enhanced in combination with β2 receptor agonists, therefore, in more severe cases, a combination of these is recommended. drugs. Short-acting theophyllines, especially intravenously, remain in the arsenal of drugs for the treatment of acute asthma. They are less bronchodilatory than β2-agonists, but improve respiratory muscle activity and prolong or maintain the effects of β2-agonists.

Corticosteroids have anti-inflammatory effects, improve lung function, reduce bronchial hyperreactivity, and control asthma symptoms. BA control. In patients with severe disease, systemic corticosteroids are the first choice. When used early, these drugs can prevent long-term flare-ups and avoid hospitalization in many mild cases. The recommended starting dose is 30 mg oral prednisolone or equivalent for 5 to 10 days (depending on the severity of exacerbations) until clinical response is achieved and PEF has returned to optimal individual parameters, after which patients are gradually transferred to maintenance therapy. treatment with inhaled corticosteroids. For severe exacerbations, spacers or, better yet, specialty nebulizers are recommended . Systemic corticosteroids are prescribed (prednisolone at a dose of 0.5-1 mg / 1 kg of body weight) if the patient's condition does not improve or normalization of functional indicators (PSV> 80% of the best individual indicator) does not affect the patient's condition. body weight or other equivalent doses of corticosteroids). If good results are achieved, further treatment can be continued at home according to a plan drawn up by the doctor and the patient. The goal of treatment is to control asthma and prevent possible flare-ups.

Indications for hospitalization are: suspected or confirmed severe asthma exacerbation (PSV below 60% of the individual's best value), which can be life-threatening, therapy with beta2-agonists for 3 hours or corticosteroids for 2-6 hours. Treatment Despite adequate treatment, the patient's condition worsened. If the hospitalized patient did not receive outpatient treatment or was treated inadequately, beta2-agonists were initially administered via nebulizer every 20 minutes for 1 hour until arterial saturation exceeded 90%. As BA worsens, IGC will be taken because the bronchial spasm does not reach the affected area. In this case, systemic CC (30-60 mg or other GK drugs at an equivalent dose) was immediately started intravenously or Peros . Without complete response to treatment, choline degradation was added and choline assay was added (via nebulizer) and CCX therapy was continuously added continuously (if intravenous administration is required). If within 1 hour there is no reaction or degradation within 1 hour, the patient's pakrfira condition is reviewed and transferred to continuous monitoring of respiratory function in the intensive care unit. Necessary treatment is carried out and mechanical ventilation is based on indications. After branches, patients should regularly follow the lungs and allergies after 1-6 months of anti-cardiac treatment.

Khatamov Kh.M. (2019) noted that, to date, there are no generally accepted recommendations regarding how much glucocorticoids should be administered depending on the stage of the disease. Many authors recommend different options based on their experience.

Example: In the first option, the authors recommend the use of hydrocortisone. Hydrocortisone is administered intramuscularly and intravenously in doses of 5-20 mg/kg every 3-4 days for asthmatics. hourly and hydrocortisone 7 mg/kg every 8 hours. The average daily dose is 20-24 mg/kg.

In the second variant, prednisone is prescribed in high doses. The initial dose is 250-350 mg intravenously, followed by continuous injections of 900-1000 mg every 2 or 6 hours, and if there is no effect, 250 mg every 3-4 hours. hour. The average daily dose is 2000-3500 mg.

In a third option, the authors recommend doubling the amount of intravenous and oral corticosteroids if the first dose of corticosteroids is ineffective. Example: prednisolone 60-90 mg IV, prednisolone 120-180 mg IV, if ineffective every 1.5-2 hours and prednisolone 20-30 mg orally or hydrocortisone 250 mg/sky. Daily doses can average up to 600-2000 mg.

In the fourth option: prescribe corticosteroids based on the status of bronchial asthma. If the first intravenous administration is ineffective, more GCS is added, increasing the dose upon repeated administration, and oral administration is

also prescribed. In stage I asthma, hydrocortisone 1 mg/kg/ hour (1500 mg/ day) or prednisolone 60 mg intravenously every 4 hours (10 mg/kg/ day), prednisolone 5 mg tablets 4 times a day. In stage II bronchial asthma, a single dose of corticosteroids is increased by 2-3 times, and prednisolone is administered at 90 mg intravenously every 1.- 1.5 hours or continuously every 1.5 hours. If the above methods of treatment are ineffective, the dose is increased to 150 mg over the next 2-3 hours, an additional 125 mg of hydrocortisone is administered every 4-6 hours.

Fifth protocol: The author recommends reducing the daily dose of corticosteroids by 25-50% after the patient recovers from asthma, and another protocol is to reduce the dose of corticosteroids by 25% every 48 hours.

Another group of researchers recommends completely abolishing prednisolone, starting with 40 mg/ day , others recommend using prednisolone at a dose of 120-180 mg/ day 3-4 times a day for 48 hours, with a decrease the next day. from 60-80 mg to 70% of the expiratory frequency or continue until the patient's condition improves clinically, reducing the dose of prednisolone to 40-60 mg after 3-10 days.

Doses of corticosteroids vary depending on the above treatments. However, a single standard of treatment has not yet been developed - the use of systemic corticosteroids for exacerbations of bronchial asthma.

According to Khatamov Kh.M. and others. (2019) In the peripheral blood of BA patients, the sensitivity of lymphocytes to seven corticosteroids used in medical practice was determined. Absolutely sensitive to betamethasone , nebufluxone , dexamethasone and triamcinolone and slightly sensitive to methylprednisolone , hydrocortisone, nebufluxone and prednisolone. With this approach, the use of corticosteroids was 1.8 times less in stage III and 1.78 times less in stage IV than standard treatment. As a result, lower doses of corticosteroids were used in a shorter time, the recovery of patients was accelerated, the time spent in the hospital was reduced, and the overall costs of treatment were several times reduced.

In the treatment of AD, it is important to take into account the patient's attitude towards treatment. In this regard, it is recommended to educate patients regardless of the duration of the disease ("asthma schools", conversations, written consultations, action plans for each situation, condition monitoring using structured questionnaires, etc.). The duty of doctors is to provide patients with all the necessary information about diseases, methods of prevention and treatment.

Patients should be informed about the characteristics of various pulmonary drug delivery systems, self-monitoring methods - maximum flow measurement, knowledge of measures to limit exposure to pathogens, important allergens and adverse environmental factors.

Although researchers have proposed different recommendations and approaches to the treatment of asthma, our review suggests that the development and standardization of the treatment of asthma with systemic exacerbations is still relevant . , which is based on the determination of the sensitivity of lymphocytes to corticosteroids in bronchial asthma. Further research will help develop new approaches to the treatment of bronchial asthma.

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