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FEATURES OF CLINICAL AND FUNCTIONAL INDICATORS OF PATIENTS SUFFERING WITH REFLUX INDUCED ASTHMA LIVING IN HOT CLIMATES

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Annotation: The results of a study of 94 patients suffering from reflux-induced asthma living in a hot climate in an arid and favorable zone were published. The highest degree of manifestation of clinical symptoms, deviations from the norm of functional indicators and severe course of the disease were revealed in patients living in an unfavorable arid zone. When diagnosing and preventing this disease, it is necessary to take into account the above data.

Key words: reflux-induced bronchial asthma, hot climate, clinic, spirography, immunity.

Reflux-induced bronchial asthma (RIA) is a chronic disease of the bronchopulmonary system, manifested by bronchospasm attacks that are provoked by gastroesophageal reflux. The disease is observed in patients with erosive and non-erosive forms of GERD. Asthma is characterized by typical paroxysms of suffocation and painful cough, which are complemented by heartburn, belching, chest and epigastric pain (5,11,16). The heterogeneity of RIA manifests itself in various disease phenotypes, many of which can be identified in routine clinical practice (7,17).

Environmental factors are considered as trigger and inducer stimuli. The former can cause clinical manifestations in sick people, the latter can either induce or contribute to its manifestation. The effect of triggers is realized through nonspecific mechanisms, while the effect of inducers is realized through specific ones. The first includes parameters of the physical state of the atmosphere, the second usually includes specific allergens that can cause inflammation in the bronchi and, as a result, bronchospasm (1,2). The frequency of exacerbation of bronchial asthma (BA) increases with a rise in atmospheric pressure, an increase in the partial pressure of oxygen, a drop in temperature and a rise in humidity (10).

Opposite data were obtained in Leningrad; an increase in asthma exacerbations in the general population was caused by an increase in air temperature and a drop in relative humidity; no connection was found with atmospheric pressure (5). As with hay fever, heat makes asthma symptoms worse. This is mainly due to higher humidity and more frequent lack of wind, which increases pollen levels and contributes to the accumulation of summer smog. The mountain climate is especially good for asthmatics. The mountain climate is characterized by a low partial pressure of oxygen in the air, low atmospheric pressure, the presence of ozone, increased solar radiation and air ionization (7,16,18).

In the last decade, there has been an increase in the role of factors influencing the development and manifestations of RIA. Internal factors include genetic predisposition to atopy and bronchial hyperreactivity, gender (in childhood, asthma is more common in boys; in adolescence and adulthood, in women) and obesity. In RIA, the cause of the inflammatory process of the mucous membranes of the bronchial tree is gastroesophageal reflux in up to 50% of cases. Factors in the reflux genesis of the development of bronchospasm include citrus fruits, tomatoes, fatty foods, mints, carbonated drinks,

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smoked drinks and dietary disorders, taking a horizontal position after meals, taking xanthines, antispasmodics, non-steroidal and steroid hormones, decreased smooth muscle tone, physical inactivity etc. (9,14,16). In parallel to this, an increase in external factors is observed, such as the role of the environment, allergens: house dust mites, pet allergens, cockroach allergens, fungal allergens, plant pollen, infectious agents (mainly viral), occupational factors, aeropollutants: ozone, sulfur and nitrogen dioxides, diesel fuel combustion products, tobacco smoke (active and passive smoking), increased consumption of highly processed foods, increased intake of omega-6 polyunsaturated fatty acids and reduced intake of antioxidants (in the form of fruits and vegetables) and omega-3 polyunsaturated fatty acids (in fatty fish). More than 300 million patients worldwide suffer from asthma. In the Russian Federation, according to epidemiological data, the prevalence of asthma among the adult population is 6.9% (2), and among children and adolescents – about 10% (5). The effect of traditional therapy gives good results to a significant number of patients, achieving disease control. However, there are difficult-to-treat BA phenotypes (20–30%) of patients (severe atopic BA, obese BA, smoker's BA, late-onset BA, BA with fixed bronchial obstruction), and some difficulties arise in their treatment. This category of patients has the highest incidence of exacerbations and visits to emergency medical care (2). In industrialized countries, 12% of patients suffering from asthma with exacerbation of the disease are treated in emergency departments and emergency departments of hospitals, of which 20–30% require inpatient treatment in specialized departments, about 4–7% in intensive care units (ICU) (10,12,14). 5% of patients with severe exacerbation of asthma require tracheal intubation and artificial ventilation (ALV), mortality reaches up to 7% (15). The main goals of asthma therapy according to the GINA 2015 concept are symptom control, reduction of airway damage and drug side effects (6,9,12,13).

To diagnose and monitor asthma symptoms in adult patients, peak flowmetry (PEF monitoring) is recommended (10). According to the level of confidence of recommendations C (level of evidence, morning and evening PEF indicators are measured, daily PEF variability is observed. Pulmonary function testing is recommended to be carried out in patients with suspected asthma aged more than 5-6 years (10.16).

When identifying anamnestic data with asthma, it is recommended to identify the main factors of the onset of the disease, the presence and duration of clinical symptoms and the resolution of their signs, the presence of allergic reactions in the patient and his blood relatives, the cause-and-effect features of the occurrence of signs of the disease and its exacerbations (1,6,16). The main signs of asthma include the presence of more than one of the following symptoms - wheezing, shortness of breath, chest tightness and cough, especially in cases of: - symptoms worsening at night and early in the morning, symptoms arising during physical activity, exposure to allergens and cold air, the onset of symptoms after taking aspirin or beta blockers, a history of atopic diseases, the presence of asthma and/or atopic diseases, normal chest examination results in the presence of symptoms, change in voice, the occurrence of symptoms exclusively against the background of colds, a long history of smoking (more than 20 packs /years), widespread dry wheezing when listening (auscultating) the chest, low PEF or FEV1 (retrospectively or in a series of studies), unexplained by other reasons, peripheral blood eosinophilia, unexplained by other reasons. According to the ECRHS, a 10-year study in 10 EU countries found that chemical floor cleaners and cleaning aerosols contained substances that provoke asthma symptoms in adults; the use of such products is associated with about 18% of new cases (1,3, 6.16).

One of the urgent tasks of modern medicine is to study the influence of extreme climatic and weather factors on the development of various diseases, in particular inflammatory lung diseases (2,8,7).

There is a widespread belief that it is not individual meteorological factors and not a specific type of weather, but the change of different weathers that cause an increased load on a person's adaptive and regulatory capabilities. Contrasting climatic and weather factors, having a strong impact, not only lead

to a deterioration in well-being and a decrease in the performance of healthy individuals, but also significantly aggravate the clinical course of many diseases, including bronchial asthma (2,4,7).

The arid zone differs from other regions of the republic in its extreme climatic conditions, dry and hot summers, low air humidity, and minimal precipitation, which undoubtedly affect the health of the living population. In the last five years, due to global warming, the air temperature has been higher than previous values, in the Central Asian region especially from the beginning of June to the first half of August. According to the Uzhydrometcenter, during the last year of the summer season the air temperature has increased by 4-5 degrees when compared with previous decades. Due to the drying out of the Aral Sea and the reduction of its area, the process is further aggravated dozens of times. As a result of this, emerging environmental factors such as dry, dusty, hot air saturated with particles of various toxic substances entering the mucous membranes of the respiratory tract of the population living in the Aral Sea region have adverse effects (7,8). Based on this, there is a need to study the role of the above factors on clinical indicators of the respiratory system.

The goal is to study the features of the clinical course of reflux-induced asthma in the hot climate of the arid zone.

Materials and methods of research. *94 patients with varying degrees of severity of RIA, aged from 20 to 60 years, were studied. Of those examined, 54 (I - main group) patients lived in the hot climate of the arid zone of the Bukhara region (residents of the Alat, Karakul and Peshkun districts). 40 (II-control group) - in the favorable zone (Bukhara, Vabkent and Romitan districts) of the region. The compared groups were representative by gender, age and duration of the disease. The patients underwent general clinical, radiological and functional examination methods. The intensity of clinical symptoms was assessed on a three-point scale: 1 point - weak manifestations, 2 points - moderate, 3 points - strong manifestations of symptoms. The study of external respiration function was carried out using a device from MEDICOR (Hungary), peak flowmetry - using an individual peak flow meter "Vitalograf" (Germany).* Serum immunoglobulins were studied using the radial immunodiffusion method (Mancini I., 1965). Local protection of the mucous membranes of the upper respiratory tract was studied using the "drug fingerprint" method (5).

The cytological characteristics of the inflammatory process in fingerprint preparations from the mucous membranes of the palatine tonsils and nasopharyngeal region were assessed according to S.T. Nadzhimitdinov. The morpho-functional characteristics of peripheral blood platelets were studied using a light microscope METZER BIOMEDICAL, Mumbai (Nadzhimitdinov S.T., Sadykova G.A., 2002). Statistical processing of the results was analyzed using the Student's test.

Research results and their analysis. Based on the results of the study, differences in the clinical course of RIA in patients living in different zones were established.

Table 1. Clinical indicators in patients with RIA living in hot climates, arid and favorable zones (scores).

Clinical symptoms	Main group n= 54	Control group n=40
Cough	3,1±0.2	2.8±0,1
Sputum discharge	1,5±0,1	2.9±0,2*
Expiratory dyspnea	3,2±0.1	1.9±0,1*
Heartburn	3,0±0.1	1.8 ±0,2*
Otrizhka	2.7±0.2	2.3±0,3
Sweating	3.1±0.3	2.3±0,4*
Dry wheezing	2,8±0.2	2,9±0,1

Note: * - p<0.01 when comparing clinical parameters between the main and control

groups.

Thus, an analysis of the intensity of clinical symptoms (Table 1) showed that in patients of group I, the intensity of sputum discharge was 1.5 points lower, and the severity of expiratory shortness of breath and symptoms of intoxication was 1.3 and 1.2 points higher than in patients control group ($p<0.001$). A decrease in the intensity of sputum discharge together with a pronounced intensity of shortness of breath, heartburn and intoxication syndrome in patients of group I indicate a violation of mucociliary clearance as a result of exposure to climatic factors of the arid zone. A significant difference between the compared groups also revealed the need for ß-agonists in a daily dose, which turned out to be 1.5-2 times higher in patients living in the hot climate of the arid zone, which also indicates the severity of the disease.

Along with an increase in the intensity of clinical indicators, significant decreases in peak flow measurements were revealed in all patients. The decrease in peak expiratory flow on average was 16% in patients in group I and 8.5% in group II ($p <0.005$), which indicates a decrease in bronchial patency under the influence of various aggressive factors in the arid zone.

Spirography indicators in patients with RIA living in hot climates, arid and favorable zones.

Indicators	Main group п= 54	Control group п=40	p
FVC	52.8±3,7	68,9±2,9	<0,01
FEV1	59.2±3.1	70,0±2,8	<0,01
POS	56.4±2.4	70.3±2,7	<0,01
MOS 75	60,3±3.1	67,3±2,4	>0,01
MOS 50	63.1±2.4	65,9±3,2	>0,01
M0C 25	62.8±4.2	68,4±3,4	>0,01

Note: spirography scores were compared between the study and control groups.

In parallel to the above peak flow metry indicators, a significant decrease in spirography indicators was observed in patients living in a hot climate in an arid zone. A comparison of the nature of ventilation disorders showed that patients in the main group had an obstructive type of disorders 1.5 times more often (82.4%) than patients in the control group (54.9%), $p <0.01$.

Disturbances of bronchial obstruction in the peripheral parts of the bronchi, characterized by a decrease in speed indicators at the level of small and medium bronchi, were moderate and were detected in the majority of patients in both groups (Table 2). Generalized obstructive disorders were observed 1.9 times more often in patients of the main group (38.2%) compared to the control group (20.1%) $p<0.01$.

Analysis of immune status indicators revealed that all patients living in the hot climate of the arid zone had decreased serum IgA levels (2.4±0.1 g/l), increased IgG levels (up to 16.0±0.5 g/l), and positive changes in immunological indicators were identified: IgA increased by 0.2%, while IgG decreased by 12% ($p<0.05$). In patients in the control group, no significant deviations from the norm in the content of serum immunoglobulins were observed ($p>0.05$).

When analyzing data obtained from the mucous membranes of the palate, initially identified lymphocytes were located singly, a decrease in the activity of segmented neutrophils, an increase in their number, destruction of nuclei, and a lack of phagocytic activity were noted. Microbes inside macrophages were well preserved, the cytoplasm of lymphocytes was destroyed in 90% of cases, phagocytic activity did not manifest itself in 15-20% of patients with RIA, corresponding to the third stage of the inflammatory process according to S.T. Nadzhimitdinov only in patients of group I.

Analysis of platelet data showed that the number of platelets in the peripheral blood of all patients

was within the normal range, which amounted to 180,000 and 320,000 mm3, changes were noted in their qualitative characteristics. The data obtained indicate the occurrence of a primary intravascular platelet thrombus, the main period of which is the time of appearance of the primary platelet thrombus. The quantitative indicators of platelets in patients with mild and moderate persistent RIA did not differ from those of healthy individuals. Consequently, in 82% of RIA with a mild persistent course and in 73% of RIA with a moderate persistent course, the morphofunctional parameters of platelets did not differ from those in healthy individuals. When analyzing the qualitative characteristics of platelets, depending on the degree of severity, their corresponding differences were revealed. The qualitative characteristics of the platelet change when the contents of the platelet substance are released. In RIA with mild and moderate persistent course, young, not released, functionally active platelets were detected in 55%, 65% of patients living in the hot climate of the Arid Zone, and in healthy people they were found in 50% of cases. Passive, small platelets that had completed their activity were found in 57% and 35% of patients with mild and moderate persistent RIA, respectively, and in 50% of healthy individuals.

When analyzing the thrombocytogram, it was revealed that the functional morphological properties of peripheral blood platelets provide prognostic information about intravascular platelet microthrombosis.

Thus, as a result of the study, it was established that the course of reflux-induced asthma in people living in the hot climate of the arid zone is characterized by greater severity of clinical symptoms, disturbances in functional indicators, immunity and blood coagulation system, which must be taken into account when planning treatment and preventive measures.

Conclusions:

1. In patients suffering from reflux-induced asthma living in the hot climate of the arid zone, a more severe clinical course of the disease was revealed.
2. In hot climates, patients suffering from reflux-induced asthma experience a significant decrease in bronchial patency, immunity and blood coagulation disorders with the development of severe respiratory failure.

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