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Upper airway allergic diseases diagnostics and allergic and non-allergic bronchial asthma phenotype clarification at the specialized medical care level

Key words: *bronchial asthma, phenotype, allergic rhinitis, polyposis ethmoiditis, specialized medical care.*

In modern practical medicine, diagnosis of bronchial asthma (BA) is relevant for determining its phenotypes. The entire arsenal of diagnostic research and phenotyping is carried out to achieve one goal – successful treatment of this pathology, achievement of normal quality of life of patients [1], [11], [12].

Well known clusters of demographic, clinical and/or pathophysiological characteristics of asthma are often referred to as «asthma-phenotype». Some phenotypes of the disease for a long time remain not diagnosed, and therefore have a difficult course and are bad-treated. In 2014–2016, new recommendations were issued by the European Respiratory Society and the American Thoracic Society for Severe Asthma [11], [12]. The main changes affected the definitions, refinements of diagnostic algorithms, approaches to therapy, which are not yet available in the domestic Order number 868 MOH Ukraine of 10.08.2013 «On the approval and implementation of medical and technical documents on the standardization of medical care in bronchial asthma» [5].

The most common asthma phenotypes are:

– allergic asthma, which is characterized by eosinophilic inflammation of the airways. Patients with this phenotype of asthma respond well to treatment with inhaled corticosteroids (ICS) and omalizumab;

– non-allergic asthma – asthma is not associated with allergies. Patients have a reduced response to ICS;

– late onset asthma occurring in adulthood, predominantly in women and requiring the use of higher doses of ICS;

– asthma with fixed bronchial obstruction, which is associated with respiratory remodeling processes;

– asthma with obesity.

Separately defines asthma with other concomitant diseases that aggravate the course of asthma [1], [12].

There is currently no common definition of specific phenotypes of asthma. Nevertheless, certain characteristics of certain phenotypes are identified, the effects of which can contribute to targeted and more effective treatment of patients. To determine the phenotype in each particular case, a comprehensive examination of the patient is required. Each level of medical care has its own capabilities [1], [4].

At the primary medical care level, the doctor can collect a thorough history of the disease by using special questionnaires and questionnaires on the symptoms, the level of asthma control, the response to previous treatment, the need for ambulance drugs, concomitant pathology [4]. A spirometric study with the bronchodilator test, available at the primary medical care level, makes it possible to determine the presence and degree of broncho-obstruction, which is also a marker of severe asthma [14], [15], [17]. However, the possibilities of the primary care unit can not provide full information on the main causes of the severe course of asthma, but they are sufficient to recommend patients undergo a follow up in specialized medical care facilities for the purpose of the final establishment of the phenotype of the disease and the appointment of an individually selected pathophysiologically grounded therapy.

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The most common phenotype is allergic asthma. Often, allergic asthma is associated with allergic rhinitis and polyposis, which aggravate the course of asthma [8], [10]. Therefore, at the stage of specialized medical care for patients with a possible diagnosis of allergic asthma it is advisable to consult an otolaryngologist and immunological examination.

The aim of the study was – to conduct additional examination at the specialized medical care level for the patients with a possible phenotype of allergic bronchial asthma (BA) found at the primary medical care level, by consulting an otolaryngologist to clarify the allergic diseases (allergic rhinitis (AR), polyposis ethmoiditis (PE) found at the preliminary stage) and the study of immunological indices of local inflammation of the lower respiratory tract.

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Object of research

The study was coordinated with the local Medical Ethics Committee of the NIPhP NAMS, participants were familiarized with the study protocol and signed an informed consent form to participate in the study.

At the primary medical care level, 160 patients with severe asthma were examined. According to the anamnesis, clinical and functional study and additional questionnaires, the probable phenotypes of the disease were isolated: allergic asthma – in 112 (70,0%) patients (with allergic rhinitis – in 41 (25,6%), polyposis ethmoiditis – in 15 (9,4%)) and non-allergic asthma – in 48 (30,0%).

Methods of research – questionnaires, clinical, X-ray, immunological, statistical.

In order to detect and evaluate the severity of the symptoms of concomitant allergic rhinitis (AR) and polyposis ethmoiditis (PE), the patient was examined by an otolaryngologist and a synonasal outcome questionnaire SNOT-22 was requested [16]. In the objective review of ENT organs, the following common methods were used: anterior and posterior rhinoscopy, pharyngoscopy and indirect laryngoscopy [2]. To control the four main symptoms of AR (rhinorrhea, nasal congestion, itchiness in the nose, sneezing), they used a common score system – scale TNSS (Total nasal symptom score). Under this system, the symptoms of rhinitis were evaluated using a 4-level scale with values from 0 to 3, where 0 – absence of a symptom; 1 – the symptom is weakly expressed; 2 – moderate; 3 – severe manifestations of the symptom. Symptoms were evaluated by the patient in the past 24 hours and the data were taken to the patient's individual card (daily maximal = 12 points). Then the average value was calculated on a scale TNSS [8].

For a more complete understanding of the course of AR, eye symptoms that are almost always present in exacerbation of this pathology were also taken into account. Overall assessment of the severity of eye symptoms TOSS (Total ocule symptom score) includes 3 symptoms: itching, redness of the eyes and tears, which was also evaluated using the 4-level scale: 0 – no symptom; 1 – the symptom is weakly expressed; 2 – moderate; 3 – severe manifestations of the symptom (daily maximum = 9 points) [9]. Altogether 7 symptoms – T7SS (TNSS plus TOSS; daily maximal T7SS = 21) assessed the overall rhinoconjunctival symptom at AR at the time of examination.

Additional parameters for assessing the severity of symptoms are included:

– retrospective general assessment of nasal symptoms at the time of exacerbation AR –TNSS (rhinorrhea, nasal congestion, itchiness in the nose, sneezing; daily maximum = 12);

– retrospective general assessment of ocule symptoms at the time of exacerbation AR – TOSS (itching, redness of the eyes and tears; daily maximum = 9);

– retrospective general assessment 7 symptoms – T7SS (TNSS plus TOSS; daily maximum T7SS = 21), which characterizes the general rhinoconjunctival symptom complex at the time of exacerbation AR.

The study of local respiratory immunity has been performed in 50 patients with severe asthma. In 25 (50,0%) from them the probable phenotype of allergic asthma is established at the primary care level and in 25 (50,0%) – non-allergic asthma. The control group consisted of 20 healthy individuals.

Assessment of the local bronchial immunity status was carried out by studying induced sputum on its contents of leukocytes – eosinophils, neutrophils, lymphocytes and alveolar macrophages [6], [13].

The method of induced sputum was to get sputum after inhalation 3–5% hypertonic NaCl solution with a nebulizer for 5–30 minutes, during or after which the patient tries to cure sputum. When a satisfactory sample of sputum was received, the procedure was stopped [13].

Investigation of sputum was carried out not later than 2 hours after receipt of the material, during this time samples of sputum were stored at 4 °C. In the induced sputum, the percentage composition of leukocytes by content – eosinophils (Ef), neutrophils (HF), lymphocytes (LF) and alveolar macrophages (AMF) was calculated according to the generally accepted method [6]. After that, the ratio of these cells were calculated, namely, the ratio of eosinophils and neutrophils Kg, or the granulocyte ratio, which is equal to the ratio of the number of eosinophils to the number of neutrophils in the percentage when calculating the number of cells in the smears of induced sputum (Kg = Ef / Nf), and the ratio of the mononuclear amount to the amount of granulocytes Km, or the mononuclear factor equal to the ratio of the sum of the number of lymphocytes and alveolar macrophages to the sum of the number of eosinophils and neutrophils in the percentage when calculating the number of cells in the smears of induced sputum (Km = (AMF + LF) / (Ef + Nf)) [3], [7].

Patients with severe asthma were divided into groups using granulocytic (Kg) and mononuclear (Km) coefficients, namely: with the advantage of neutrophils in induced sputum Kg <0.8 and Km <1 – (neutrophilic) group, with the advantage of eosinophils – Kg> 1.2 and

Km <1 – (eosinophilic) group, with equal preference of granulocytes 1.2 ≥ Kg ≥ 0.8 and Km <1 – (mixed) group, with the advantage of mononuclear 1,2 ≥ Kg ≥ 0,8 and Km ≥ 1 – (residual) group.

Data collection and mathematical processing carried out by licensing software products included in the package Microsoft Office Professional 2003 license Russian Academic OPEN No Level № 17016297. Statistical analysis was performed using mathematical and statistical features MS Excel, and their error followed by comparison using t Student-test.

Results and discussion

At the primary care level, 160 patients with severe asthma were examined. According to anamnesis, clinical and functional study and additional questionnaires, the probable phenotype of allergic asthma was isolated – in 112 (70.0%) patients. From anamnesis and questionnaire method, the probable combination of the phenotype of allergic asthma with AR was discovered in 41 (25,6 ± 3,5)% and PE – in 15 (9,4 ± 2,3)% of the patients. But at the examination of these patients at the specialized medical care level by the otolaryngologist AR was diagnosed in 55 (34,4 ± 3,8)% and PE in 6 (3,8 ± 1,5)% of the patients, which indicated the hypodiagnosis of AR and hyper diagnostics of PE at the primary care level.

In 14 (8.8)% of patients with allergic asthma, the diagnosis of AR was first established only at the stage of specialized medical care by an otolaryngologist based on an allergic history, clinical symptoms of AR, objective examination and allergic examination.

In 9 (5.6)% of the patients who at the primary care level was diagnosed with a possible diagnosis of allergic asthma associated with PE, the diagnosis of PE was not confirmed during examination by the otolaryngologist. The final diagnosis was based on objective examination of ENT organs (anterior and posterior rhinoscopy), X-ray examination of nasal sinuses, and the presence of preliminary findings by doctors-otolaryngologists).

An otolaryngologist survey and clinical examination of patients with BA combined with AR and PE revealed that all patients associated an exacerbation of nasal symptoms with allergens and respiratory infections. The seasonal symptoms of the disease were noted in 28 (50.9 ± 6.7)% of patients with AR and 2 (33.3 ± 19.2)% with the PE. It was found that only for 23 (41.8 ± 6.7)% of patients with AR and for 3 (50.0 ± 20.4)% with the PE allergic tests were performed. In 17 (30,9 ± 6,2)% patients with AR and in 2 (33,3 ± 19,2)% with PE positive tests for household allergens are found, in 12 (21,8 ± 5,6)% patients with AR and in 1 (16,7 ± 15,2)% with PE – for pollen, in 7 (12,7 ± 4,5)% patients with AR – for food and in 5 (9,1 ± 3,9)% – for bacterial allergens. Positive tests for several types of allergens were determined in 13 (23.6 ± 5.7)% of patients with AR and 1 (16.7 ± 15.2)% of PE. At the same time, not all patients with allergy tests in the anamnesis food and bacterial allergens allergy tests were conducted, which indicated an inadequate examination of patients with severe BA associated with AR and PE. These patients are recommended for additional allergic examination to an allergologist.

The average duration of AR (from the time of the official diagnosis) was (15.4 ± 4.5) years, PE – (19.2 ± 8.9) years, although most patients noted the appearance of the first symptoms of AR much earlier.

All patients indicated that with aggravation, the clinical symptoms of AR arose and continued to bother more than 4 days a week or 4 weeks per year, which corresponded to the persistent course of the disease.

The severity of nasal clinical symptoms in patients with severe BA associated with AR on the scale of TNSS at the time of otolaryngologist examination was (3.98 ± 0.42) points, and at exacerbation – (6.37 ± 0.58) points ($p < 0,05$), eye symptoms on the scale of TOSS at the time of otolaryngologist examination – (1.37 ± 0.29) points, and at exacerbation – (3.13 ± 0.42) points ($p < 0.05$), which corresponded to a moderate disease course (table. 1).

The total rinoconjunctival symptomocomplex T7SS (TNSS plus TOSS) at the time of the examination was (5,25 ± 0,66) points and was significantly higher in AR exacerbation (9,33 ± 0,93) points, $p < 0,05$.

In 38 (69,1 ± 6,2)% patients with combined pathology severity of AR symptoms led to sleep disturbances, in 29 (52,7 ± 6,7)% – to a violation of daily activity, leisure and adversely affected work and education, in 35 (63,6 ± 6,5)% – to the emotional state, and in 19 (34,5 ± 6,4)% – on personal life.

The effect of synonasal symptoms on the quality of life of patients according to the results of the questionnaire SNOT-22 was almost identical in patients with asthma with AR and PE. SNOT-22 synonasal score in patients with asthma with AR at the time of review was (37,7 ± 2,9) points, and with PE – (32,2 ± 7,9) points, $p > 0,05$.

In 26 (47,3 ± 6,7)% examined petients AR appeared before asthma. In 15 (27,3 ± 6,0)% patients asthma preceded to the AR occurrence, and in 14 (25,5 ± 5,9)% patients AR and asthma occurred simultaneously.

In this case, the patients, in whom AR appeared first, noted that after they had been prescribed basal BA therapy with high doses of ICS, AR exacerbation appeared less frequently, and symptoms of AR symptoms became less pronounced.

From the anamnesis it is known that in the past all the patients were treated with endonazal glucocorticosteroids (GCS) with positive treatment efficacy. After the appointment of basal asthma therapy with high doses of ICS, the need for endonasal GCS has decreased in 24 (43,6 ± 6,7)% patients with concomitant AR and in 2 (33,3 ± 19,2)% patients with PE. Montelukast in the complex treatment of AR took only 1 patient. Decongestant drops in the nose at the time of inspection were used only by 5 (9.1 ± 3.9)% of patients with severe asthma with AR, other treatment (systemic antihistamines, physioprocedures, nasal saline solutions) were used by 5 (9,1 ± 3,9)% patients with AR and 2 (33,3 ± 19,2)% with PE.

Most patients, except for AR, had 1 or 2 other concomitant ENT illnesses. Regarding chronic purulent haymoroethmoiditis, 7 (12,7 ± 4,5)% of patients with asthma and AR and 2 (33,3 ± 19,2)% with PE were treated. Two of the patients under study were operated on a chronic bilateral

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Table 1

Results of the questioning of patients with allergic asthma according to questionnaires TNSS and TOSS, (M ± m)

Indexes	Allergic asthma	
	With AR (n = 55)	With PE (n = 6)
TNSS scale at the time of inspection:	Score	Score
– rhinorrhea	1,06 ± 0,11	1,17 ± 0,44
– nasal congestion	1,26 ± 0,13	0,83 ± 0,34
– itchiness in the nose	0,81 ± 0,11	0,33 ± 0,23
– sneezing	0,85 ± 0,12	0,50 ± 0,24
TNSS scale at the time of inspection, total score	3,98 ± 0,42	2,83 ± 0,87
TNSS scale at the time of exacerbationtion:	Бали	Бали
– rhinorrhea	1,65 ± 0,15*	2,17 ± 0,44
– nasal congestion	1,81 ± 0,16*	2,33 ± 0,37*
– itchiness in the nose	1,48 ± 0,14*	1,50 ± 0,37
– sneezing	1,54 ± 0,16*	2,00 ± 0,57
TNSS scale at the time of exacerbationtion, total score	6,37 ± 0,58*	6,83 ± 1,86
TOSS scale at the time of inspection:	Бали	Бали
– itching	0,46 ± 0,11	0,0 ± 0,0
– redness of the eyes	0,35 ± 0,09	0,0 ± 0,0
– tears	0,56 ± 0,11	0,0 ± 0,0
TOSS scale at the time of inspection, total score	1,37 ± 0,29	0,0 ± 0,0
TOSS scale at the time of exacerbation:	Бали	Бали
– itching	1,02 ± 0,14*	0,83 ± 0,44
– redness of the eyes	1,07 ± 0,15*	0,83 ± 0,44
– tears	1,19 ± 0,16*	0,83 ± 0,44
TOSS scale at the time of exacerbationtion, total score	3,13 ± 0,42*	2,00 ± 1,39
T7SS scale at the time of inspection, total score	5,25 ± 0,66	2,83 ± 0,87
T7SS scale at the time of exacerbationtion, total score	9,33 ± 0,93*	8,83 ± 3,06

Note. * – a statistically significant difference between the value of the indicator at the time of the examination of the otorhinolaryngologist and the value of the same indicator during exacerbation of AR or PE (p < 0,05).

polyposis ethmoiditis (without recurrence in the next period). This complication of AR and PE as a chronic eustachiitis was observed in 20 (36,4 ± 6,5)% of patients with AR and in 3 (50,0 ± 20,4)% of patients with PE. Other concomitant diseases are presented in table 2.

Thus, additional examination at the specialized medical care level for the patients with a probable phenotype of allergic asthma with the involvement of an otolaryngologist consultation allowed to improve the accuracy of the diagnosis of the phenotype of allergic asthma with AR – by 8,8%, with PE – by 5,6%. In the studied patients, there was predominantly persistent AR of moderate severity. Among the complications of AR and PE, there were a chronic eustachitis and chronic purulent haymoroethmoiditis. Among frequent concomitant ENT pathology were chronic tonsillitis and distortion of the nasal septum – in 23 (41,8 ± 6,7)% of patients with AR, which further contributed to the deterioration of the aerodynamic properties of the upper respiratory tract in this category of patients.

To identify the nature and mechanisms of inflammation in the lower respiratory tract, an analysis of the composition of induced sputum cells in 50 patients with severe asthma was performed. In 25 (50,0%) of them in the stage of primary medical care, allergic asthma was diagnosed and in 25 (50,0%) non-allergic asthma.

Since the content of cells in induced sputum varies, we divided the patients into groups depending on the predominant number of local defense cells and derived the ratios of these cells. Namely – the ratio of eosinophils and neutrophils Kg = Ef / Nf, or the granulocyte ratio, and the ratio of the mononuclear amount to the amount of granulocytes Km = (AMF + LF) / (Ef + Nf)), or the mononuclear factor. Thus, the first group included patients with granulocytic factor Kg which was greater than 1,2 and mononuclear Km less than 1. The second group included

Table 2

Other diseases of ENT organs in patients with asthma with AR and PE, n,% (M ± m)

Concomitant ENT pathology	Allergic asthma			
	With AR (n = 55)		With PE (n = 6)	
	abs.	%	abs.	%
Chronic purulent haymoroethmoiditis	7	12,7 ± 4,5	2	33,3 ± 19,2
Distortion of the nasal septum	23	41,8 ± 6,7	1	16,7 ± 15,2
Chronic tonsillitis	22	40,0 ± 6,6	4	66,7 ± 19,2
Chronic laryngitis	9	16,4 ± 5,0	0	0,0 ± 49,6
Phonasthenia	13	23,6 ± 5,7	3	50,0 ± 20,4
Chronic subatrophic pharyngitis	7	12,7 ± 4,5	2	33,3 ± 19,2
Chronic eustachiitis	20	36,4 ± 6,5	3	50,0 ± 20,4

Note. statistically significant difference between patients with asthma and AR or asthma with PE not revealed

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patients whose granulocyte factor was less than 0,8 and mononuclear less than 1. The third group consisted of patients with a granulocyte factor of $1,2 \geq Kg \geq 0,8$ and mononuclear less than 1, and the fourth group included patients whose mononuclear factor was greater than 1 (table 3.).

From the table below, it is evident that these groups were significantly different from each other in the content of the main cells of local protection. Thus, patients in the first group with the predominant number of eosinophils in sputum significantly differed in the content of eosinophils and neutrophils from patients in the second and third groups, in the content of alveolar macrophages from patients in the fourth group. Patients in the second group with the predominant number of neutrophils in sputum significantly differed in the content of eosinophils and neutrophils from patients in the first, third and fourth groups, with the content of alveolar macrophages – from patients in the fourth group. Patients in the third group, which included patients with the same content of granulocytes, significantly differed in the content of eosinophils and neutrophils from patients in the second and fourth groups. Finally, the patients in the fourth group with the vast majority of mononuclear cells differed in the content of eosinophils and neutrophils from patients in the first and third groups, in the content of alveolar macrophages – from patients in the first group (table 3.5).

Thus, the allocation of allergic and non–allergic phenotypes of asthma at the stage of primary care does not give a complete picture of the nature of the inflammatory process in the bronchi.

At the specialized stage of medical care, an additional study of induced sputum should be conducted, in which, depending on the redistribution of local protective cells, it is possible to determine the predominant type of cellular inflammation with the granulocytic and mononuclear factors in a particular patient, namely: with the advantage of eosinophils in induced sputum $Kg > 1$, 2 and $Km < 1$, the advantage of neutrophils $Kg < 0.8$ and $Km < 1$, with an equal preference of granulocytes $1.2 \geq Kg \geq 0.8$ and $Km < 1$, with the advantage of mononuclear $Km \geq 1$.

After immunological examination at the stage of specialized medical care, 60.0% of patients with allergic phenotype BA and two of its variants were allocated: with eosinophilic inflammation – in 20.0% of patients and mixed inflammation (with equal number of eosinophils and neutrophils in induced sputum) – in 40.0% of patients. Also, at the stage of specialized medical care, 40.0% of patients with non–allergic BA phenotype and two of its variants were allocated: with the advantage of neutrophils – in 30.0% of patients and with the advantage of LF and AMF – in 10.0% of patients.

The conducted studies indicate that an additional study of immunological indices of local inflammation (cellular composition of induced sputum in patients with severe BA) increases the effectiveness of the diagnosis of allergic and non–allergic asthma by an average of 10.0% and allows qualitative characterization of the mechanism of inflammation in the bronchus, identifying several variants of the disease, which is the basis for the appointment of pathogenetically grounded anti–inflammatory therapy.

Table 3

Cellular composition of induced sputum in patients with severe asthma, depending on redistribution of local defense cells (M ± m)

Indexes	n	Granulocyte ratio (Ef / Nf)				Mononuclear ratio ((AMF + LF) / (Ef + Nf))			
		Ef,%	Nf,%	Kg	Kg (limits of variation)	LF,%	AMF,%	Km	Km (limits of variation)
Healthy individuals	20	3,0 ± 0,8	1,8 ± 0,5	1,70 ± 0,60	Kg > 1,5	12,4 ± 1,5	85,8 ± 3,0	16,04 ± 5,01	$K_m > 10$
Asthma with dominated Ef (I) group	10	52,0 ± 3,8$^{\lozenge\bullet\bullet}$	15,0 ± 3,6$^{\lozenge *\circ}$	6,55 ± 1,95$^{\bullet\bullet}$	Kg > 1,2	16,3 ± 2,9$^{\lozenge}$	16,3 ± 2,2$^{\lozenge\bullet}$	0,51 ± 0,07$^{\lozenge\bullet}$	$K_m < 1$
Asthma with dominated Nf (II) group	15	23,7 ± 3,3$^{\lozenge *\circ}$	59,3 ± 3,5$^{\lozenge *\circ}$	0,43 ± 0,06$^{\lozenge *\circ}$	Kg < 0,8	10,4 ± 1,9$^{\lozenge}$	7,3 ± 3,0$^{\lozenge}$	0,25 ± 0,06$^{\lozenge}$	$K_m < 1$
Asthma with equaldomination Ef and Nf (III) group	20	36,6 ± 1,5$^{\lozenge\bullet\bullet}$	35,9 ± 1,3$^{\lozenge *\bullet\bullet}$	1,03 ± 0,03$^{\bullet}$	$1,2 \geq Kg \geq 0,8$	13,7 ± 1,6$^{\lozenge}$	15,4 ± 2,1$^{\lozenge}$	0,44 ± 0,06$^{\lozenge}$	$K_m < 1$
Asthma with dominated LF and AMF (VI) group	5	11,8 ± 2,6$^{*\bullet\circ}$	19,4 ± 3,5$^{\bullet\circ}$	0,70 ± 0,30$^{*\bullet}$	Kg ≥ 0,0	17,6 ± 8,6$^{\lozenge}$	51,4 ± 8,1$^{\lozenge\bullet}$	2,30 ± 0,3$^{*\bullet\lozenge}$	$K_m \geq 1$

Note: * – statistically significant difference between patients with asthma with the advantage of eosinophils in sputum and asthma with the advantage of other effector cells of sputum ($p < 0,05$); • – statistically significant difference between patients with asthma with the advantage of neutrophils in sputum and asthma with the advantage of other effector cells of sputum ($p < 0,05$); ° – statistically significant difference between patients with asthma with the equal advantage of eosinophils and neutrophils in sputum and asthma with the advantage of other effector cells of sputum ($p < 0,05$); • – statistically significant difference between patients with asthma with the advantage of mononuclears in sputum and asthma with the advantage of other effector cells of sputum ($p < 0,05$); ◊ – statistically significant difference between patients with asthma and healthy subjects ($p < 0,05$).

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Conclusions:

1. Additional examination at the specialized medical care level for the patients with a probable phenotype of allergic asthma with the involvement of a doctor–otolaryngologist consultation increases the accuracy of the diagnosis of the phenotype of allergic asthma with allergic rhinitis – by 8,8%, with polyposis ethmoiditis – by 5,6% compared with the diagnosis of this pathology on primary health care level. In the studied patients, there was predominantly persistent AR of moderate severity. Among the complications of AR and PE, there were a chronic eustachiitis and chronic purulent haymoroethmoiditis. Among frequent concomitant ENT pathology were chronic tonsillitis and distortion of the nasal septum – in 23 (41,8 ± 6,7)% of patients with AR, which further contributed to the deterioration of the aerodynamic properties of the upper respiratory tract in this category of patients.

2. It has been established that the allocation of allergic and non–allergic phenotypes of asthma at the primary medical care level does not give a complete picture of the nature of the inflammatory process in the airways. At the specialized medical care level, an additional study of induced sputum should be conducted, in which, depending on the redistribution of local protective cells, it is possible to determine the predominant type of cellular inflammation with a granulocytic and mononuclear factors in a particular patient, namely: with the advantage of eosinophils in induced sputum Kg > 1,2 and Km < 1, the advantage of neutrophils Kg < 0,8 and Km < 1, with an equal preference of granulocytes 1,2 ≥ Kg ≥ 0,8 and Km <1, with the advantage of mononuclears 1,2 ≥ Kg ≥ 0,8 and Km ≥ 1.

3. Additional study of immunological indices of local inflammation (cellular composition of induced sputum in patients with severe BA) increases the efficiency of diagnosis of allergic and non–allergic asthma by 10,0% and allows quantitatively and qualitatively characterizing the mechanism of inflammation in the bronchi, which is the basis for the appointment of pathogenetically grounded anti–inflammatory therapy.

Список літератури

1. Фещенко Ю.І. та ін. Адаптована клінічна настанова, заснована на доказах. Уніфікований клінічний протокол первинної, вторинної (спеціалізованої), третинної (високотехнологічної спеціалізованої) медичної допомоги та медичної реабілітації. Бронхіальна астма: методичні рекомендації для практичних лікарів. Київ: Національна академія медичних наук України, 2016. 190 с.
2. Лайко А.А., Заболотний Д.І., Синяченко В.В. Обсяг і методики обстеження об'єктивного статусу дітей з ЛОР-патологією. Київ: Логос, 2000. 138 с.
3. Матвієнко Ю.О. Використання аналізу індукованного харкотиння для оцінки різних варіантів запального процесу у хворих на бронхообструктивні захворювання легень. Лабораторна діагностика. 2009. № 2 (48). С. 12–16.
4. Фещенко Ю.І. та ін. Можливості визначення фенотипів тяжкої бронхіальної астми на етапі первинної медичної допомоги. Вісник проблем біології та медицини. 2017. Вип. 3. Т. 1 (137). С. 232–242.
5. Наказ МОЗ України № 868 від 08.10.2013 р. «Про затвердження та впровадження медико-технічних документів зі стандартизації медичної допомоги при бронхіальній астмі» МОЗ України. Режим доступу: http://www.moz.gov.ua/ua/portal/dn_20131008_0868.html.
6. Предтеченский В.Е. и др. Руководство по лабораторным методам исследования, микроскопическое исследование мокроты. Москва, Медгиз, 1950. С. 278–291.
7. Спосіб діагностики патогенетичних варіантів запального процесу у хворих на тяжку персистуючу бронхіальну астму: пат. 40065 Україна. № u 200811968; заявл. 09.10.08; опубл. 25.03.09. Бюл. № 6. 8 с.
8. Яшина Л.А., Игнатьева В.И. Возможности азеластина в лечении сезонного аллергического ринита в формате нового исследования MP4001. Астма та алергія. 2013. № 1. С. 55–58.
9. Bielory L., Friedlaender M. Allergic conjunctivitis. Immunol Allergy Clin North Am. 2008. № 28 (1). P. 43–58.
10. Feshchenko Y. et al. Chronic obstructive pulmonary disease, bronchial asthma and allergic rhinitis in the adult population within the commonwealth of independent states: rationale and design of the CORE. BMC Pulmonary Medicine. 2017. Vol. 17. № 131. URL: https://bmcpulmmed.biomedcentral.com/articles.
11. Global strategy for asthma management and prevention. National Institutes of Health National Heart & Lung and Blood Institute. Bethesda, 2014. 146 p.
12. Global strategy for asthma management and prevention, 2016. URL: http://ginasthma.org/wp-content/uploads/2016/04/GINA-2016-main-report_tracked.pdf.
13. Kim C.K., Hagan J.B. Sputum tests in the diagnosis and monitoring of asthma. Ann. Allergy Asthma Immunol. 2004. V. 93. № 2. P. 112–122.
14. Lung function testing: selection of reference values and interpretative strategies. American Thoracic Society. Am. Rev. Respir. Dis. 1991. Vol. 144 (5). P. 1202–1218.
15. Quanjer P.H. et al. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur. Respir. J. 1993. Vol. 16. P. 5–40.
16. Morley A.D., Sharp H.R. A review of sinonasal outcome scoring systems – which is best? Clinical Otolaryngology. 2006. Vol. 31. P. 103–109.
17. Miller M.R., Hankinson J., Brusasco V. et al. Standardisation of spirometry. Eur. Respir. J. 2005. Vol. 26. P. 319–338.

References

1. Feshchenko YuI, et al. Adaptovana klinichna nastanova, zasnovana na dokazakh. Unifikovaniy klinichniy protokol pervinnoї, vtorinnoї (spetsializovanoї), tretinnoї (visokotekhnologichnoї spetsializovanoї) medichnoї dopomogi ta medichnoї reabilitatsiї. Bronkhial'na astma: metodichni rekomendatsiї dlya praktichnikh likariv (Adapted evidence-based clinical guideline. Unified clinical protocol of primary, secondary (specialized), tertiary (high-tech specialized) medical aid and medical rehabilitation. Bronchial asthma: methodical recommendations for practitioners) Kiïv: Natsional'na akademiya medichnikh nauk Ukraïni, 2016. 190 p.
2. Layko AA, Zabolotniy DI, Sinyachenko VV. Obsyag i metodiki obstezhennya ob'ektivnogo statusu ditey z LOR-patologieyu (The scope and methods of the survey of the objective status of children with ENT-pathology). Kiïv: Logos, 2000. 138 p.
3. Matvienko YuO. Vikoristannya analizu indukovannogo kharkotinnya dlya otsinki riznikh variantiv zapal'nogo protsesu u khvorikh na bronkhoobstruktivni zakhvoryuvannya legen'. Laboratorna diagnostika (The use of an induced sputum analysis to evaluate different variants of the inflammatory process in patients with bronchoobstructive pulmonary diseases. Laboratory diagnostics). 2009;2(48):12–16.
4. Feshchenko YuI, et al. Mozhlivosti viznachennya fenotipiv tyazhkoї bronkhial'noї astmi na etapi pervinnoї medichnoї dopomogi. Visnik problem biologiї ta meditsini (Possibilities of definition of phenotypes of severe bronchial asthma at the stage of primary medical care. Bulletin of Biology and Medicine). 2017;3;1(137):232–242.
5. Nakaz MOZ Ukraïni № 868 vid 08.10.2013 r. «Pro zatverdzhennya ta vprovadzhennya mediko-tekhnichnikh dokumentiv zi standartizatsiї medichnoї dopomogi pri bronkhial'niy astmi» MOZ Ukraïni (Order of the Ministry of Health of Ukraine №868 dated 08.10.2013 «On Approval and Implementation of Medical-Technical Documents for the Standardization of Medical Aid in Bronchial Asthma», Ministry of Health of Ukraine). Available from: http://www.moz.gov.ua/ua/portal/dn_20131008_0868.html.
6. Predtechenskiy VE, et al. Rukovodstvo po laboratornym metodam issledovaniya, mikroskopicheskoe issledovanie mokroty (Manual on laboratory methods of research, microscopic examination of sputum). Moskva: Medgiz, 1950. P. 278–291.
7. Sposib diagnostiki patogenetichnikh variantiv zapal'nogo protsesu u khvorikh na tyazhku persistuyuchu bronkhial'nu astmu: pat. 40065 Ukraïna (Method of diagnostics of pathogenetic variants of inflammatory process in patients with severe persistent bronchial asthma). № u 200811968; zayavl. 09.10.08; opubl. 25.03.09. Byul. № 6. 8 p.
8. Yashina LA, Ignat'eva VI. Vozmozhnosti azelastina v lechenii sezonnogo allergicheskogo rinita v formate novogo issledovaniya MR4001 (The possibilities of azelastine in the treatment of seasonal allergic rhinitis in the format of the new study MP4001). Astma ta alergiya. 2013;1:55–58.
9. Bielory L, Friedlaender M. Allergic conjunctivitis. Immunol Allergy Clin North Am. 2008;28(1):43–58.
10. Feshchenko Y, et al. Chronic obstructive pulmonary disease, bronchial asthma and allergic rhinitis in the adult population within the commonwealth of independent states: rationale and design of the CORE. BMC Pulmonary Medicine. 2017;17:131. URL: https://bmcpulmmed.biomedcentral.com/articles.
11. Global strategy for asthma management and prevention. National Institutes of Health National Heart & Lung and Blood Institute. Bethesda, 2014. 146 p.
12. Global strategy for asthma management and prevention, 2016. URL: http://ginasthma.org/wp-content/uploads/2016/04/GINA-2016-main-report_tracked.pdf.
13. Kim CK, Hagan JB. Sputum tests in the diagnosis and monitoring of asthma. Ann. Allergy Asthma Immunol. 2004;93(2):112–122.
14. Lung function testing: selection of reference values and interpretative strategies. American Thoracic Society. Am. Rev. Respir. Dis. 1991;144(5):1202–1218.
15. Quanjer PH, et al. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur. Respir. J. 1993;16:5–40.
16. Morley AD, Sharp HR. A review of sinonasal outcome scoring systems – which is best? Clinical Otolaryngology. 2006;31:103–109.
17. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur. Respir. J. 2005;26:319–338.

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