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## A NEW METHOD OF DIAGNOSIS AND TREATMENT OF CHRONIC RECURRENT RHINOSINUSITIS

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**Abstract.** Chronic sinusitis is a chronic inflammation of the mucous membrane of the nasal cavities. The study was conducted in the otolaryngology department and 110 patients treated with chronic recurrent rhinosinusitis in stationary conditions for 2021 years were selected. The average age of patients: up to 17-70 years. During the examination, all patients were divided into 3 groups depending on the degree of remission of the disease: I group – mild remission (n=46), II – moderate severity (n=33), III – severe remission (n=31). For the purpose of CRRS treatment, patients were divided into two groups: group I patients were treated only with standard therapy, group II patients were treated with a drug of definite and pomegranate seed oil (to drink 6 drops of pomegranate seed oil per day) in addition to standard therapy.

**Keywords:** chronic rhinosinusitis, cytokines, interleukin, derinate.

**Introduction.** Rhinosinusitis - inflammation of the nasal mucosa and paranasal sinuses, characterized by two or more signs, one of which is obstruction of the nasal cavity or the appearance of a discharge from the nose, may be accompanied by the following signs: headache, pressure or pain in the face, decrease or loss of smell, the appearance of signs of intoxication [1-4]. According to European guidelines (EPOS 2012; ICAR: RS, 2016), rhinosinusitis is diagnosed by two or more signs and objective data: endoscopic signs (presence of mucopurulent discharge in the nasal passage, swelling of the mucous membrane of the middle nasal passage) and magnetic resonance imaging (changes mucosa of the otomeatal complex and/or adjacent nasal cavities). Because,

Currently, much attention is paid to the structures that control the immune system. The ratio of CD4+ and CD8+ T-lymphocytes in peripheral blood is called the “immunomodulatory index”. Depending on the disease, the value of this indicator changes upward or downward [5-8].

Determining the severity of the course of rhinosinusitis is also very important. One way to determine the severity of the course of the disease is a visual analogue scale (VAS). In accordance with the procedure for this method, patients will be assisted and asked to set their symptoms on a scale of 0 to 10 points [9-19], mild severity is considered when patients score from 0 to 3 points, moderate severity is from 3 to 7 points, and moderate severity is from 7 to 10 points. The severity of rhinosinusitis can also be determined by clinical signs. The absence of temperature in mild rhinosinusitis, mild nasal discharge, nasal congestion, cough have very little effect on the quality of life in patients there is no pain in the area of the adjacent nasal cavities and no complications are observed. The following symptoms correspond to the moderate severity of the disease: body temperature not higher than 38 ° C, severe nasal congestion, runny nose and cough with nasal discharge, which clearly affect the quality of life of patients, a feeling of heaviness in the area adjacent to the nose of the

cavities is formed by nodding or tilting the head , complications are observed in the middle ear. In a severe degree of the disease, the following signs are revealed: an increase in body temperature above 38 ° C, pronounced painful symptoms of rhinosinusitis, which clearly affect the quality of life of patients (nasal congestion, nasal discharge, cough), constant pain in the area of the nasal adjacent cavities, aggravated by nodding, tilting and percussion of the head,

**Purpose of the study.** In chronic recurrent rhinosinusitis, the severity of the course of the disease is determined and new methods of treatment are recommended.

**Material and research methods.** The study was conducted in the Department of Otorhinolaryngology of the Bukhara Regional Multidisciplinary Medical Center and 110 patients with chronic recurrent rhinosinusitis (CRRS) were selected, who underwent inpatient treatment during 2021. Average age of patients: 17-70 years.

Clinical studies of all patients, including the collection of complaints and anamnesis, general examination, palpation and percussion of the paranasal sinuses, laboratory (general blood count, biochemical blood test, immunogram: serum immunoglobulins (IgM, IgG, IgA, IgE), interleukins (IL-1 $\beta$  , IL-4, IL-6 IL-8, IL-10, TNFa, IFN), from instrumental methods - rhinoscopy and endoscopic rhinoscopy of the nasal cavities (Stema - 0°,30°,45°,70° angled rigid endoscopes were used ), a visual analogue scale (VAS) to determine the intensity of pain.

During the examination, all patients were divided into 3 groups depending on the degree of the course of the disease: group I - mild severity (n=46), II - moderate severity (n=33), III - severe severity (n=31).

**Research results.** When separating patients according to the severity of the disease, the method of randomized differentiation was used. When using this method, it will be necessary to take into account the features that affect the results of the check, and take into account the even distribution of these features among the people being checked. These signs include: increased or decreased body temperature, the degree of development of sinusitis (nasal congestion, the appearance of nasal discharge), the absence of local pain in the region of the lateral nasal cavities, the absence of a systemic inflammatory process, depending on laboratory indications (leukocytosis, increased ESR, increased CRP ), assessment of the quality of life of patients according to VAS (Table 1).

**Table 1**

**Distribution of patients by clinical groups**

	<b>I group (n=46)</b>	<b>II group (n=33)</b>	<b>III group (n=31)</b>	<b>Control group (n=20)</b>
<b>Body temperature</b>	36,5±0,08	37,7±0,06	38,4±0,05	36,6±0,01
p-compared with group I		p<0,001	p<0,0001	
p-compared with the II group			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Many differences of	<b>p&lt;0,001</b>			
<b>Difficulty breathing through the nose</b>	++	+++	+++	-

Screen flow through the nose	+	++	+++	-
Local pain	-	++	+++	-
Number of leukocytes, 10 <sup>9</sup> /l	7,1±0,09	10,5±0,089	13,3±0,07	5,9±0,12
p-compared with group I		p<0,001	p<0,0001	
p-compared with the II group			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Many differences of	<b>p&lt;0,001</b>			
<b>ESR</b>	8,8±1,03	10,9±2,03	23,8±3,6	6,5±0,7
p-compared with group I		p<0,001	p<0,0001	
compared with the p-II group			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Many differences of	<b>p&lt;0,001</b>			
<b>SRP</b>	25±3,6	34±2,7	62,2±5,6	7,2±2,0
p-compared with group I		p<0,001	p<0,0001	
p-compared with the II group			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Many differences of	<b>p&lt;0,001</b>			
<b>VAS</b>	1,8±0,5	5,9±0,9	8,7±0,6	0
p-compared with group I		p<0,001	p<0,0001	
p-compared with the II group			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Many differences of	<b>p&lt;0,001</b>			

A mild course of the disease was detected in 46 patients. The mean age of the patients was 17-65 years. Sinusitis of the maxillary cavity was detected in 40 patients, frontal sinusitis in 3 patients, sphenoiditis in 1 patient, mixed sinusitis in 2 patients. The average severity of the disease was detected in 33 patients, whose average age was 18-70 years. Sinusitis of the maxillary cavity was detected in 19 patients, frontal sinusitis in 5 patients, sphenoiditis in 1 patient, aralgic sinusitis in 8 patients. Severe disease was detected in 31 patients, and the average age of patients is 17-69 years. Sinusitis of the maxillary cavity was detected in 9 patients, frontal sinusitis in 3 patients, sphenoiditis in 3 patients, mixed sinusitis in 16 patients.

IL-1 $\beta$  causes and controls the inflammatory process, while IL-10 is its antagonist. The ratio of inflammatory and anti-inflammatory cytokines in serum provides information about systemic inflammatory activity. Inflammatory cytokines IL-1 $\beta$  and anti-inflammatory IL-10 determine the degree of expression of the inflammatory process. We studied these indicators depending on the severity of rhinosinusitis (table 2).

Table 2

**Chronic recurrent rhinosinusitis results before cytokine treatment by severity (M ± m)**

Sitokinlar	I group (n=46)	II group (n=33)	III group (n=31)	Control group (n=20)
Cytokines	14.6±3.75	33.1±4.6	62.11±7.2	4.05±0.3
<b>IL-1β</b>		p<0.001	p<0.0001	
p-compared with group I			p<0.001	
p-compared with the group II	p<0.001	p<0.001	p<0.001	
p-compared with the control group	<b>p&lt;0.001</b>			
Comparison of many	3.04±1.39	17.12±2.41	13.02±1.31	1.65±0.2
<b>IL-4</b>		p<0.001	p<0.001	
p-compared with group I			p<0.01	
p-compared with the group II	p<0.05	p<0.001	p<0.001	
p-compared with the control group	<b>p&lt;0.1</b>			
Comparison of many	24.81±2.29	19.28±1.8	15.96±6.37	6.87±0.5
<b>IL-6</b>		p<0.01	p<0.001	
p-compared with group I			p<0.001	
p-compared with the group II	p<0.05	p<0.001	p<0.001	
p-compared with the control group	<b>p&lt;0.1</b>			
Comparison of many	20.27±2.4	17.6±2.58	13.1±2.50	7.16±1.7
<b>IL-8</b>		p<0.01	p<0.001	
p-compared with group I			p<0.001	
p-compared with the group II	p<0.05	p<0.01	p<0.001	
p-compared with the control group	<b>p&lt;0.1</b>			
Comparison of many	20.21±4.23	14.32±4.26	9.18±2.31	3.11±0.4
<b>IL-10</b>		p<0.001	p<0.001	
p-compared with group I			p<0.001	
p-compared with the group II	p<0.001	p<0.001	p<0.001	
p-compared with the control group	<b>p&lt;0.001</b>			
Comparison of many	17.69±1.18	13.01±2.46	8.98±0.7	4.45±0.6
<b>γINT</b>		p<0.01	p<0.05	
p-compared with group I			p<0.01	
p-compared with the group II	p<0.05	p<0.01	p<0.05	
p-compared with the control group	<b>p&lt;0.5</b>			

In the first group, a significant increase in the amount of anti-inflammatory cytokines IL-10 was found compared to II, III and control groups (p<0.001). It was found that the number of inflammation-inducing cytokines IL-1β was significantly reduced (p<0.001) compared with II, III and control groups. Accordingly, the inflammatory reaction also corresponds to a mild degree.

In patients of the second group, the same increase in cytokines IL-10 and IL-1 $\beta$  was found compared with groups I, III and control ( $p < 0.001$ ). In patients of the second group, clinical signs appear in accordance with the inflammatory response, which corresponds to the moderate degree of the disease.

In patients of the third group, a clear increase in inflammation-inducing cytokines IL-1 $\beta$  ( $p < 0.001$ ) was found, which, in turn, induce and control the immune response and activate the systemic inflammatory response. It was noted that the anti-inflammatory cytokines IL-10 decreased more pronounced than other groups ( $p < 0.001$ ), indicating the activity of the inflammatory process.

In order to treat CRRS, patients were divided into two groups: patients of group I were treated only with standard therapy, and patients of group II were treated with derinate and pomegranate seed oil in addition to standard therapy (drink 6 drops of pomegranate seed oil per day). In order to normalize the level of inflammation-causing and anti-inflammatory cytokines in patients, derinate and pomegranate seed oil were used (table 3).

**Table 3**

**Outcomes after cytokine treatment in chronic recurrent rhinosinusitis (M  $\pm$  m)**

Cytokines	I group (before treatment, n=110)	II group (after standard treatment, n=55)	III group (standard treatment+derinate+pomegranate seed oil, n=55)	Control group (n=20)
<b>IL-1<math>\beta</math></b>	36,6 $\pm$ 3,81	26,1 $\pm$ 4,9	17,11 $\pm$ 7,5	4,05 $\pm$ 0,3
p-compared with group I		$p < 0,001$	$p < 0,0001$	
p-compared with the group II			$p < 0,001$	
p-compared with the control group	$p < 0,001$	$p < 0,001$	$p < 0,001$	
Comparison of many	<b><math>p &lt; 0,001</math></b>			
<b>IL-4</b>	11,04 $\pm$ 1,42	9,12 $\pm$ 2,5	7,02 $\pm$ 1,28	1,65 $\pm$ 0,2
p-compared with group I		$p < 0,001$	$p < 0,0001$	
p-compared with the group II			$p < 0,001$	
p-compared with the control group	$p < 0,001$	$p < 0,001$	$p < 0,001$	
Comparison of many	<b><math>p &lt; 0,001</math></b>			
<b>IL-6</b>	15,18 $\pm$ 2,3	20,28 $\pm$ 1,9	38,96 $\pm$ 6,4	6,87 $\pm$ 0,5
p-compared with group I		$p < 0,001$	$p < 0,0001$	
p-compared with the group II			$p < 0,001$	
p-compared with the control group	$p < 0,001$	$p < 0,001$	$p < 0,001$	

Comparison of many	<b>p&lt;0,001</b>			
<b>IL-8</b>	13,11±2,5	19,6±2,61	28,1±2,53	7,16±1,7
p-compared with group I		p<0,001	p<0,0001	
p-compared with the group II			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Comparison of many	<b>p&lt;0,001</b>			
<b>IL-10</b>	30,13±4,18	19,32±4,31	11,18±2,26	3,11±0,4
p-compared with group I		p<0,001	p<0,0001	
p-compared with the group II			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Comparison of many	<b>p&lt;0,001</b>			
<b>γINT</b>	22,08±1,2	17,01±2,5	13,98±0,74	4,45±0,6
p-compared with group I		p<0,001	p<0,0001	
p-compared with the group II			p<0,001	
p-compared with the control group	p<0,001	p<0,001	p<0,001	
Comparison of many	<b>p&lt;0,001</b>			

While a decrease in the number of inflammatory cytokines IL-1 $\beta$  and anti-inflammatory cytokines IL-10 was found in patients with CRRS after standard therapy, a significant decrease in these indicators was found in the group of patients who received the recommended drug derinate and pomegranate seed oil in addition to standard therapy.

**Conclusion.** It was found that the determination of the number of cytokines in patients with CRRS and, accordingly, the choice of treatment method are of paramount importance. In order to normalize the level of cytokines IL-1 $\beta$  and IL-10 in patients, derinate and pomegranate seed oil were recommended in combination with standard therapy. A repeated study to compare the amount of cytokines after the end of the course of treatment showed that, compared with standard therapy, in addition to derinate and pomegranate seed oil, a significant decrease in the content of cytokines was found in the recommended group. The effectiveness of the treatment method proposed above has been proven by reducing the days of inpatient treatment and reducing the number of hospitalizations of patients.



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