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COMPARISON OF INDICES OF FEROKINETICS, HEMOPOESIS AND IL-6 IN CHILDREN WITH BRONCHIAL ASTHMA

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Abstract

Asthma is the most common chronic respiratory disease in children, the urgency of which is increasing with increasing incidence. **The aim of the study.** Conduct comparisons of ferrokinetics, hematopoiesis and interleukin - 6 in children with asthma. **Materials and methods.** According to our goal, we examined 144 children between the ages of 6 and 17 who have asthma.

Results. In children with asthma who have a latent iron deficiency manifested by a decrease in ferritin <15 μg / l and a decrease in CST <20%, the risk of developing persistent moderate and severe disease is increased 1.5-fold.

The risk of developing uncontrolled asthma increased in patients who experience a decrease in CST and an increase in the level of soluble transferrin receptors by 5.2 and 3.1 times, respectively.

An increase in soluble transferrin/ferritin receptor levels above 1.5 causes a significant increase in the risk of developing uncontrolled asthma.

In children with asthma with low serum iron, the rate of interleukin - 6 increased. In addition, a negative relationship between the transferrin saturation factor of iron and the content of interleukin - 6 in serum found to be of medium strength.

Keywords: asthma, children, iron proteins.

Actuality. Asthma is the most common chronic respiratory disease in children, the urgency of which is increasing with increasing incidence. [3, 4]. In the world, up to 300 million people suffer from this pathology [1]. The incidence rates of asthma vary across countries and populations and range from 1% to 18%. However, despite current methods of diagnosis and treatment in children, this figure ranges from 5 to 10% in the population and has a steady upward trend.

It is now established that the active inflammatory process in asthma stimulates the production of high-level markers of active inflammation in patients, such as: cytokines (IL-6 IL-1b IL-8 TNF-a), acute phase proteins (CRP, fibrinogen, surfactant) protein D), cellular elements (neutrophils, monocytes, lymphocytes). It is known that most of the above proinflammatory cytokines are pathogenetic in the development of anemia. There are studies showing an association between anemia and asthma. [3]. Eissa S.A. et al. 2016 found a positive correlation between Hb, serum ferritin, and pulmonary function tests. [2]. But it has not yet been fully determined what factors influence the transition from acute inflammation to disease persistence and the subsequent interplay of iron deficiency and inflammatory activity in asthma in children. The disclosure of these mechanisms can be an important contribution to understanding the pathogenetic changes in asthma.

The aim of the study. Conduct comparisons of ferrokinetics, hematopoiesis and interleukin - 6 in children with asthma.

Materials and methods. According to our goal, we examined 144 children between the ages of 6 and 17 who have asthma. The average age of the examined patients was (9,87 ± 0,22) years. The diagnosis of asthma established in accordance with ICD10 review and order of the Ministry of Health of Ukraine for bronchial asthma in children № 868 from 08.10.2013. with recommendations from the Global Initiative for Asthma (GINA, 2019). Assessment of bronchial asthma control was performed using the AST test (Asthma Control Test, Quality Metric Incorporated, 2002).

The work started after the patient and his or her parents had obtained the consent to participate in the study in compliance with the provisions of the UN Convention on the Rights of the Child. The research materials do not contradict the International Code of Medical Ethics (1983) and the laws of Ukraine, conform to the basic bioethical standards of the Declaration of Helsinki, adopted by the General Assembly of the World Medical Association, the Council of Europe Convention on Human Rights and Biomedicine (1977).

The amount of iron in the serum was determined by the colorimetric method by reaction with ferrozine using a set of reagents "Iron" (REF No. HP012.01, TOB-NPP "Philitis-Diagnostics", Ukraine) in accordance with the instructions of the manufacturer. Total iron binding (TIB) was determined after the transfer of serum transfer of Fe3 + ions with ferrozine. Latent iron-binding ability (LIBA) or unsaturated iron-binding ability (UIBA) was defined as the difference between PZZZ and serum iron (LIBA = TIB-SI). The transferrin saturation coefficient (CST) determined by the formula: CST = SI * 100 / PO 3%. The determination of serum ferritin level was performed by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's Ferritin (ORGENTEC Diagnostika, Germany) according to the manufacturer's instructions, where a level of <15 μg / l was determined as reduced [5, 7, 8]. The content of soluble transferrin receptors (sTfR) in serum was determined by enzyme-linked immunosorbent assay (ELISA) using a standard Human sTfR ELISA kit (BioVendor, Germany) according to the manufacturer's instructions.

The index sTfR / log Ferritin (> 1.5 - latent iron deficiency) was calculated [5, 6]. External respiration function was examined by spirography on a Spirolab III apparatus. The type of respiratory distress was assessed on the basis of Vital Lung Rate (VC), forced VC (FVC), forced expiratory volume in 1 second (FEV_1), and Tiffno Index (IT).

The content of interleukin-6 (IL-6) was determined by enzyme-linked immunosorbent assay (ELISA) according to the set of "INTERLAYKIN-6-IFA-BEST" (A-8766; CJSC "Vector-Best", RF) according to the instructions of the manufacturer.

Research results. Assessing the chances of a decrease in ferrokinetics, namely the transferrin saturation factor (CST) and the level of ferritin in children with asthma, we found a significant increase in 1,552 and 1,653 times the risk of developing persistent moderate and severe disease in which the disease is affected by the disease. decrease in ferritin level, respectively ((OR = 1.552; 95% CI 1.489 - 4.085) (OR = 1.653; 95% CI 1.579 - 4.981)). In addition, in children with low CST, the chance of developing persistent severe asthma significantly increased one and a half times (OR = 1.501; 95% CI 1.027 - 3.103).

Table 1 - Assessment of the chances of developing persistent moderate and severe asthma, depending on the presence of latent iron deficiency in children with asthma

Severity of asthma	Decrease CST (N 20-50%)		Decrease transferrin level < 15 (mcg/l)	
	OR	95 % CI	OR	95 % CI
Persistent mild	1.339	0.812 – 2.209	0.939	0.817 – 1.079
Persistent moderate	1.233	0.847 – 1.796	1.552	1.489 – 4.085
Persistent severe	1.501	1.027 – 3.103	1.653	1.549 – 4.981

We also found a significant increase in the risk of developing uncontrolled asthma by 5,163 times in children with a decrease in CST (OR = 5,163; 95% CI 2,418 - 11,027). In addition, in children who experienced a decrease in ferritin levels, the odds of developing uncontrolled disease increased 1,697 times (OR = 1,697; 95% CI 1,313 –2,194).

Table 2 - Assessment of the chances of developing uncontrolled course of asthma, depending on the presence of latent iron deficiency in children with asthma

Control level of asthma	Decrease CST (N 20-50%)		Decrease transferrin level < 15 (mcg/l)	
	OR	95 % CI	OR	95 % CI
Control	0.376	0.277 – 0.510	0.094	0.034 – 0.259
Uncontrol	5.163	2.418 – 11.027	1.697	1.313 – 2.194

The association of the severity of asthma with the level of soluble transferrin receptors above 5.0 mg / l and the ratio of soluble transferrin receptors / ferritin is to increase the risk of persistent moderate and severe asthma. Thus, the risk of persistent moderate-onset disease (OR = 1.729; 95% CI 1.067 - 3.450) is increased 1.729 times and the risk of persistent severe asthma is 1.7 times higher (OR = 1.795; 95% CI 1.050 - 3.562). Also, this situation is noted with the increase of soluble transferrin / ferritin receptors, namely raising its level above> 1.5 causes a significant increase in the chance of developing persistent severe disease by 1.569 times (OR = 1.569; 95% CI 1.024 - 2.663).

Table 3 - Estimation of the chances of developing persistent moderate and severe asthma, depending on the presence of iron deficiency in children with asthma

Severity of asthma	Increase content of soluble transferrin receptors >5,0 mg/l (N: 2,2–5,0 mg/l)		Index sTfR / log Ferritin >1,5	
	OR	95 % CI	OR	95 % CI
Persistent mild	1.074	0.521 – 2.213	0.859	0.413 – 1.789
Persistent moderate	1.729	1.067 – 3.450	1.473	0.864 – 2.514
Persistent severe	1.795	1.050 – 3.562	1.569	1.024 – 2.663

Children with soluble transferrin receptor levels above 5.0 mg / L were at increased risk of developing uncontrolled asthma. Thus, the risk of uncontrolled disease course increases by 3,755 times (OR = 3,755; 95% CI 1,859 - 7,587). A similar trend is observed with the increase of soluble transferrin / ferritin receptors, namely an increase in its level above 1.5 causes a significant increase in the risk of developing an uncontrolled course of asthma, namely 4,166 times (OR = 4,166; 95% CI 2,193 - 7,913).

Table 4 - Assessment of the chances of developing an uncontrolled course of asthma, depending on the presence of iron deficiency in children with asthma

Control level of asthma	Increase content of soluble transferrin receptors >5,0 mg/l (N: 2,2–5,0 mg/l)		Index sTfR / log Ferritin >1,5	
	OR	95 % CI	OR	95 % CI
Control	0.505	0.390 – 0.655	0.334	0.236 – 0.472
Uncontrol	3.755	1.859 – 7.587	4.166	2.193 – 7.913

In the study of the relationship between ferrokinetics and the severity of asthma in the children we examined, a positive relationship found between the strength of serum iron and the level of asthma control. A negative, medium-strength relationship also found between the transferrin saturation factor of iron and the severity of asthma. In addition, a very strong positive relationship found between ferritin content and the level of asthma control. For such indicators of ferrokinetics, as the content of soluble transferrin receptors and soluble

transferrin / ferritin receptors, we established a negative relationship of weak and high strength, respectively, between them and the level of asthma control.

Table 5 - Relationship between severity and level of disease control and rates of hematopoiesis and ferrokinetics in children with bronchial asthma

Index	Severity of asthma		Control of asthma	
	r_{xy}	p_1	r_{xy}	p_2
Iron, mkmol/l	0,455	0,063	0,389	0,001
CST, %	-0,506	0,001	0,012	0,891
Ferritin, mcg/l	0,116	0,165	0,901	0,001
Soluble transferrin receptors, mg/l	-0,115	0,170	-0,394	0,001
Index sTfR / log Ferritin, mg/mg	-0,142	0,089	-0,769	0,001

As a result of studying the relationship between the severity of the course of asthma and indicators of the inflammatory response syndrome in the examined children with asthma, we have reliably established a direct (positive), medium strength relationship between the content of interleukin-6 and the severity of asthma, and a direct (positive), strong relationship between interleukin-6 content and the level of asthma control.

Table 6 - Relationship between the severity of the disease and the level of interleukin - 6 in the serum of children with asthma

	IL - 6, pg/ml
Severity of asthma	0,302 (p=0,001)
Control of asthma	0,931 (p=0,001)

When studying the relationship between hematopoiesis and ferrokinetics with inflammatory response syndrome in the examined children, we found a negative relationship of mean strength between MCV and interleukin content - 6 in serum. A negative, low strength relationship also found between serum iron content and interleukin content - 6 in serum. In addition, a negative relationship between the transferrin saturation factor of iron and the content of interleukin - 6 in serum found. There was also a negative relationship of mean strength between ferritin content and interleukin content - 6 in serum.

Table 7 - Relationship between hematopoiesis and ferrokinetics and interleukin levels - 6 in children with asthma

Index	High level of IL-6, pg/ml	
	r_{xy}	p
MCV	-0,545	0,048
Iron, mkmol/l	-0,469	0,001
CST, %	-0,528	0,001
Ferritin, mcg/l	-0,518	0,01
Soluble transferrin receptors, mg/l	0,499	0,001
Index sTfR / log Ferritin, mg/mg	0,547	0,001

For such indicators of ferrokinetics, as the content of soluble transferrin receptors and soluble transferrin receptors/ferritin, we established a positive relationship of average strength between them, and the content of interleukin - 6 in serum ((r_{xy} = 0,499 (p = 0,001)), (r_{xy} = 0.547 (p = 0.001))).

Conclusions

In children with asthma who have a latent iron deficiency manifested by a decrease in ferritin <15 μg / l and a decrease in CST <20%, the risk of developing persistent moderate and severe disease is increased 1.5-fold.

The risk of developing uncontrolled asthma increased in patients who experience a decrease in CST and an increase in the level of soluble transferrin receptors by 5.2 and 3.1 times, respectively.

An increase in soluble transferrin/ferritin receptor levels above 1.5 causes a significant increase in the risk of developing uncontrolled asthma.

In children with asthma with low serum iron, the rate of interleukin - 6 increased. In addition, a negative relationship between the transferrin saturation factor of iron and the content of interleukin - 6 in serum found to be of medium strength.

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