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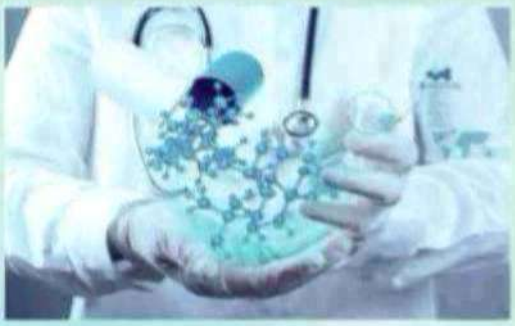

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ТИББИЁТДА ЯНГИ КУН
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NEW DAY IN MEDICINE

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LABORATORY CRITERIA FOR EVALUATING SEVERITY IN IRRITABLE BOWEL SYNDROME

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✓ ***Resume***

The scientific article summarizes the survey data of 90 patients with IBS who were examined in the polyclinic department of the Bukhara Regional Multidisciplinary Medical Center from 2022 to 2023. The average age of the patients was 33.3±1.5 years. Analysis of calprotectin levels in feces showed that the amount of calprotectin in feces also increased as the severity of the disease varied from mild to severe. As the severity of IBS increased from mild to severe, the level of pro-inflammatory cytokines IL-1β increased by 1.6 times, IL-6 by 1.4 times, and αTNF by 2.6 times, while the level of anti-inflammatory cytokines IL-10 decreased by 2.2 times.

Keywords: irritable bowel syndrome, cytokine, fecal calprotectin, cortisol.

Relevance

Functional diseases of the gastrointestinal tract develop due to the interaction of biological (disruption of intestinal patency, changes in the composition of the microbiota), psychological (emotional disorders) and social (psycho-traumatic states in youth, lack of social support) factors [1,2].

Among the functional disorders of the gastrointestinal tract, one of the most common is irritable bowel syndrome (IBS) [3]. The prevalence of IBS among the population is from 10% to 25%[4].

IBS is considered a functional disease of the gastrointestinal tract, characterized mainly by the manifestation of recurrent abdominal pain, observed at least once a week, including the following signs (two or more): associated with defecation, combined with a change in frequency and/or shape of stool. Depending on the forms of stool according to the Bristol Stool Scale, there are 3 main variants of the disease: with a predominance of diarrhea (IBS-D), with a predominance of constipation (IBS-C), and mixed (IBS-M). The fourth - non-classifiable variant of IBS, in which the diagnosis is made if the patient's complaints meet the criteria for IBS, but there is insufficient data for the diagnosis of one of the three listed options [5].

IBS significantly worsens the patient's quality of life, moreover, the disease causes significant financial damage to both the patients and the healthcare system [6].

The aim of this article is to identify and analyze laboratory criteria that can be used to assess the severity of IBS, in order to improve diagnostic accuracy and guide individualized treatment strategies.

Materials and methods

The scientific article summarizes the survey data of 90 patients with IBS who underwent examination in the polyclinic department of the Bukhara Regional Multidisciplinary Medical Center from 2022 to 2023. The average age of the patients was 33.3±1.5 years. Patients with IBS were divided into two groups: patients with IBS with a predominance of hypermotion or diarrhea - IBS-D - 43 (47.7%) and patients with IBS with a predominance of hypomotor or constipation - IBS-C - 47 (52.3%). In order to reduce the number of patients with mixed and non-classified types of IBS and to avoid statistical errors, they were not included in the study.

The examination methods were carried out in the polyclinic department of the State Medical Center, as well as in the faculty and the department of gospetal therapy. The examination methods included clinical-anamnestic, laboratory-instrumental, and prepared questionnaires.

Data processing was carried out using Microsoft Office Excel 2013, Statistica 6.0. The arithmetic mean (M) and standard deviation (m) were used to characterize quantitative indicators with a normal distribution. To characterize the quality indicators, the frequency and fractions (%) of the trait in the sample were used.

Research results and discussion

In addition to the assessment system for determining the clinical severity of the disease, laboratory severity levels (IL-1β, IL-6, IL-10, αTNF, fecal calprotectin, the level of cortisol and dysbiosis in the blood) were also included, and the assessment system was summarized. Patients scoring 21-28 points were assessed as having a severe course of the disease, patients scoring 10-20 points as having a moderate course, and patients scoring 1-9 points as having a mild course of the disease (Table 1).

Table 1

Method for determining the severity of irritable bowel syndrome

No	Main clinical signs		0 points	1 point	2 points
1.	Abdominal pain		"not too serious," rarely	"not too serious," quick	very strong, "terrible"
2.	Diarrhoea		Less than 3 times a day	3-5 times a day	more than 5 times a day
3.	Constipation		once every 2 days	once every 3-4 days	once every 5-7 days
4.	Feeling of bloating		+	++	Too toxic
5.	Feeling of incomplete bowel emptying		+	++	Too toxic
6.	False calls		sometimes	frequently	constant
7.	Mucus secretion		sometimes	frequently	constant
8.	Additional during toilet attempts		sometimes	frequently	constant
9.	IL-1β, pg/ml		0-5	5.1-12.	12.1-18.
10.	IL-6, pg/ml		0-9	9.1-12.	12.1-16.
11.	IL-10, pg/ml		5-31.	2-5	0-2
12.	αTNF, pg/ml		0-6	6.1-12.	12.1-22.
13.	Fecal calprotectin, ng/ml		0-50.	50-100	100-120
14.	Blood cortisol, nmol/l	morning	166-507	508-600	over 600
		evening	73.8-291	292-350	over 350
15.	Dysbiosis level		I	II.	III.

Based on Table 1, all laboratory indicators were analyzed based on severity levels. Initially, the amount of fecal calprotectin in the stool was compared (Fig. 1).

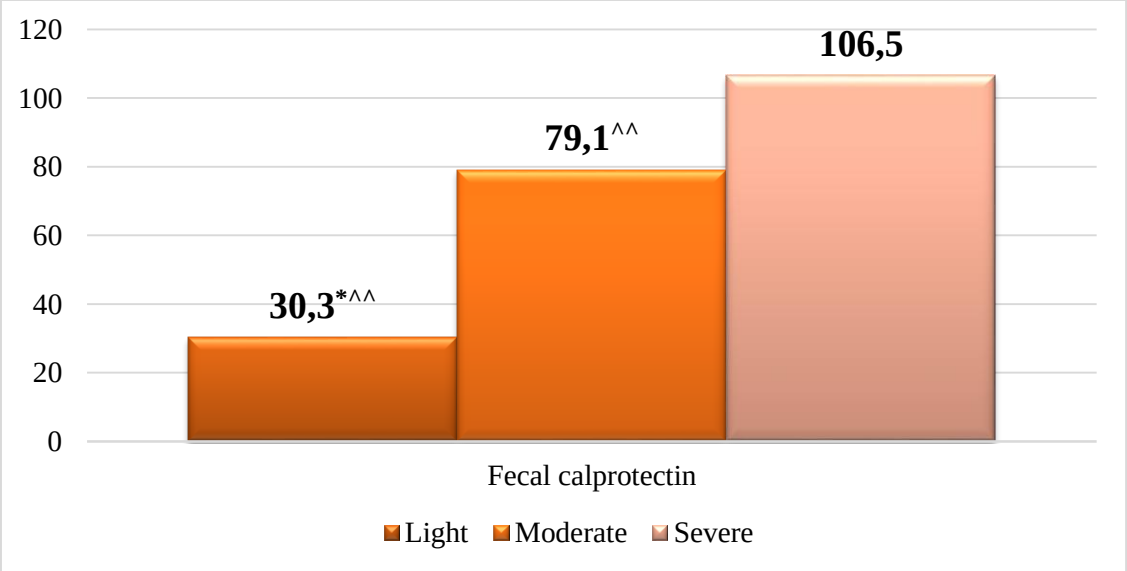

Figure 1. Fecal calprotectin indicators corresponding to the severity of IBS, ng/ml

*Note: The level of statistical significance in relation to the indicators of patients with moderate severity: * - p<0.05, the level of statistical significance in relation to the indicators of patients with severe severity: ^^ - p<0.01.*

The level of fecal calprotectin showed that as the severity of the disease varied from mild to severe, the level of fecal calprotectin also increased (30.3±2.6 ng/ml, 79.1±1.8 ng/ml, and 106.6±1.4 ng/ml, respectively).

Also, pro- and anti-inflammatory cytokines were analyzed according to their severity (Table 2).

Table 2

Cytokine analysis by disease severity, M±m, pg/ml

Cytokine levels	IBS severity levels		
	(n=32)	(n=37)	(n=21)
IL-1β	5.9±0.6***^^^	7.8±0.9^^	9.9±1.2
IL-4	2.4±0.1*^	2.1±0.1	2.1±0.1
IL-6	5.4±0.6**^^	7.2±0.7	7.3±0.8
IL-10	10.6±1.1***^^^	8.8±1.1^^	4.9±0.6
αTNF	5.6±0.6***^^^	10.5±1.08^^^	14.6±1.1

*Note: The level of statistical significance compared to the indicators of patients with moderate severity: * - p<0.05; ** - p<0.01; *** - p<0.001, the level of statistical significance compared to the indicators of patients with a severe degree: ^ - p<0.05; ^^ - p<0.01; ^^^ - p<0.001.*

Among the pro-inflammatory cytokines, the level of IL-1β was 5.9±0.6 pg/ml in the mild degree, 7.8±0.9 pg/ml in the moderate degree, and 9.9±1.2 pg/ml in the severe degree (p<0.01, p<0.001).

The level of IL-6 was 5.4±0.6 pg/ml with mild severity, 7.2±0.7 pg/ml with moderate severity, and 7.3±0.8 pg/ml with severe severity (p<0.01).

α-TNF was also 5.6±0.6 pg/ml, 10.5±1.08 pg/ml, and 14.6±1.1 pg/ml, respectively, with an increase in the severity of the disease (p<0.01, p<0.001).

Of the pro-inflammatory cytokines, IL-4 was 2.4±0.1 pg/ml in patients with mild ulcerative colitis, 2.1±0.1 pg/ml in patients with moderate ulcerative colitis, and 2.1±0.1 pg/ml in patients with severe ulcerative colitis (p<0.05).

It was established that the level of IL-10 decreased to 10.6±1.1 pg/ml in the mild degree, to 8.8±1.1 pg/ml in the moderate degree, and to 4.9±0.6 pg/ml in the severe degree.

Thus, as the severity of IBS increases from mild to severe, the level of pro-inflammatory cytokines IL-1β increases by 1.6 times, IL-6 by 1.4 times, and αTNF by 2.6 times, while anti-inflammatory cytokines IL-10 decrease by 2.2 times. This result indicates the importance of nonspecific inflammatory markers in patients with IBS.

The hormone cortisol, which is one of the neuroendocrine markers evaluated as a response to stress in the body, was also analyzed according to the severity of IBS (Table 3).

Table 3

Results of blood cortisol analysis, M±m, nmol/l

Cortisol in blood	IBS severity levels		
	(n=32)	(n=37)	(n=21)
Morning	344.3±16.8**^^^	528.1±16.2^^	605.4±8.8
Evening	187.6±11.6**^^	298.4±12.1^	354.3±3.6

*Note: The level of statistical significance compared to the indicators of patients with moderate severity: * - p<0.05; ** - p<0.01; *** - p<0.001, the level of statistical significance compared to the indicators of patients with a severe degree: ^ - p<0.05; ^^ - p<0.01; ^^^ - p<0.001.*

It was noted that the morning blood cortisol level increased by 1.7 times as the severity of IBS progressed from mild to severe (respectively 344.3±16.8 nmol/l, 528.1±16.2 nmol/l and 605.4±8.8 nmol/l, p<0.01, - p<0.001), and the evening indicator also increased by 1.8 times (respectively 187.6±11.6 nmol/l, 298.4±12.1 nmol/l and 354.3±3.6 nmol/l, p<0.05, p<0.01).

Determining the level of cortisol in the blood allows one to judge the activity of the sympathoadrenal system and the response to psychological stress, which is a pathogenetic factor of IBS.

In addition to the above, the composition of the intestinal microbiota was also analyzed by the severity of IBS (Table 4).

Table 4

Results of intestinal microbiota analysis, M±m

Microorganisms	IBS severity levels		
	(n=32)	(n=37)	(n=21)
Salmonella-shigella	0	0	0
E. coli with normal enzymatic activity	10^7±0.3*^	10^5±0.1	10^5±0.2
Lactose-negative E. coli	10^5±0.1*^	10^4±0.2	10^4±0.2
Haemolytically active E. coli	0	0	0
Other opportunistic enterobacteria (E. Coli)	10^4±0.2*^^	10^5±0.2	10^6±0.2
Staphylococci (St. Aureus)	0	0	$10^{0.6}$±0.2#
Staphylococci (St. epidermidis, St. saprophyticus)	10^4±0.0	10^4±0.0	10^4±0.0
Enterococcus	10^5±0.0	10^5±0.0	10^5±0.0
Yeast-like fungi	10^4±0.07	10^4±0.1	10^4±0.1
Bifidobacteria	10^7±0.1**^^^	10^6±0.1^^	10^4±0.1
Lactobacilli	10^6±0.1*^^^	10^5±0.07	10^3±0.1
Non-enzyme-producing bacteria (NGOB)	10^4±0.0	10^4±0.0	10^4±0.0

*Note: The level of statistical significance compared to the indicators of patients with moderate severity: * - p<0.05; ** - p<0.01; *** - p<0.001, the level of statistical significance compared to the indicators of patients with a severe degree: ^ - p<0.05; ^^ - p<0.01; ^^^ - p<0.001; # - p<0.01.*

Analysis of the intestinal microbiota by severity of IBS showed that in patients with moderate and severe IBS, compared to patients with mild IBS, normal enzymatic activity was noted, and a decrease in lactose-negative bacteria was noted (p<0.05). An increase in the number of opportunistic enterobacteria - E. Coli was observed in moderate and severe IBS (p<0.05, p<0.01), staphylococci - St. Aureus was detected only in patients with severe IBS (p<0.01). Bifidobacteria and lactobacteria, which are considered beneficial bacteria, were detected in patients with moderate and severe IBS (p<0.05, p<0.01, p<0.001).

Conclusion

The level of fecal calprotectin showed that as the severity of the disease varied from mild to severe, the level of fecal calprotectin also increased. As the severity of IBS increases from mild to severe, the level of pro-inflammatory cytokines IL-1β increases by 1.6 times, IL-6 by 1.4 times, and αTNF by 2.6 times, while anti-inflammatory cytokines IL-10 decrease by 2.2 times. Such a result indicates the importance of nonspecific inflammatory markers in patients with IBS. It was noted that the morning blood cortisol level increased by 1.7 times as the severity of IBS progressed from mild to severe, and the evening indicator increased by 1.8 times, respectively. Also, grade I dysbiosis occurred in mild IBS, grade II dysbiosis in moderate IBS, and grade III dysbiosis in severe IBS.

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