Analysis of Cytokine Status in Irritable Bowel Syndrome

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ABSTRACT

Currently, intestinal functional disorders are the most common pathology among patients with a gastroenterological profile.The study was conducted in the department of gastroenterology of the multidisciplinary medical center of Bukhara region, and 157 patients treated in the inpatient setting with IBS were selected. Patients with IBS were divided into two groups: non-refractory (ITSn – 68 patients) and refractory (IBSr – 89 patients) of IBS. Depending on the expression of clinical symptoms, patients with IBSn-d (diarrhea) - 38 (24.2%), IBSn-c (constipation) - 30 (19.2%), IBSr-d - 47 (29.9%) and IBSr-c was allocated to 42 people (26.7%). The results of personal research showed that in irritable bowel syndrome, which is considered a functional disease of the intestine, the imbalance of cytokines is considered to be of great importance, especially this imbalance is characterized by a decrease in the amount of anti-inflammatory cytokine IL-10.

Keywords: irritable bowel syndrome, cytokine, low-grade inflammation

Introduction. Currently, intestinal functional disorders are the most common pathology among patients with a gastroenterological profile [1].

According to the revised Rome IV criteria, this group of diseases includes irritable bowel syndrome (IBS), functional constipation, functional diarrhea, functional abdominal distension, nonspecific functional bowel disorders, and opioid-related constipation.[1,2,3,4].

The role of "low-grade mucosal inflammation" in the intestinal mucosa in some patients with IBS is actively discussed [1,5,6]. Degranulation of mast cells leads to the release of biologically active substances (leukotrienes, tryptase, heparin, prostaglandins) and stimulates the differentiation of T cells into functional effector cells. Obviously, therefore, in patients with IBS, CD3 + T cells, CD8 + T cells increase not only in the intestine, but also in the peripheral blood, which in turn causes minimal intestinal inflammation [7].

The results of studying cytokine levels in peripheral blood are conflicting. Many sources of literature indicate an increase in the level of IL-1β, IL-2, IL-6, IL-8, TNF-α, and a decrease in the level of IL-10 in blood serum. Some researchers have found normal levels of α-TNF, IL-6 and IL-10 in the blood of patients. However, there is no correlation between the amount of cytokines in the intestinal wall and peripheral blood [7-11].

The aim of the study is to evaluate the status of pro-inflammatory and anti-inflammatory cytokines and fecal calprotectin in various forms of irritable bowel syndrome.

Material and methods. The study was

conducted in the department of gastroenterology of the multidisciplinary medical center of Bukhara region, and 157 patients treated in the inpatient setting with IBS were selected. The diagnosis of IBS was made based on the Rome IV criteria (2016), and the Bristol scale of stool patterns was used to determine the clinical form of IBS. The average age of patients is 33.2±0.8 years.

Patients with IBS were divided into two groups: non-refractory (IBSn – 68 patients) and refractory (ITSr – 89 patients) of IBS. Depending on the expression of clinical symptoms, patients with IBSn-d (diarrhea) - 38 (24.2%), IBSn-q (constipation) - 30 (19.2%), IBSr-d - 47 (29.9%) and IBSr-q was allocated to 42 people (26.7%).

All patients underwent esophagogastroduodenoscopy (FUGINON. FUGI FILM EPX-2500, 2014, Japan; FUGI FILM-EG-530PF, 2014, Japan), colonoscopy (FUGI FILM-EG-530FL, 2014, Japan), stool examination for dysbacteriosis, ultrasound examination of internal organs (Vivid S-60, 2014, Norway), cytokine analysis - IL-1β, IL-4, IL-6, IL-10, α-TNF (Vekor-Best reagents) and fecal calprotectin (De medi tec reagents) were examined .

Results and discussion. Among patients with ITS, individuals with IBS with diarrhea predominated, which is not entirely consistent with literature data. Patients were divided by gender as follows: men - 70 (44.5% of the total number of research participants), women - 87 (55.5%) (Fig. 1).

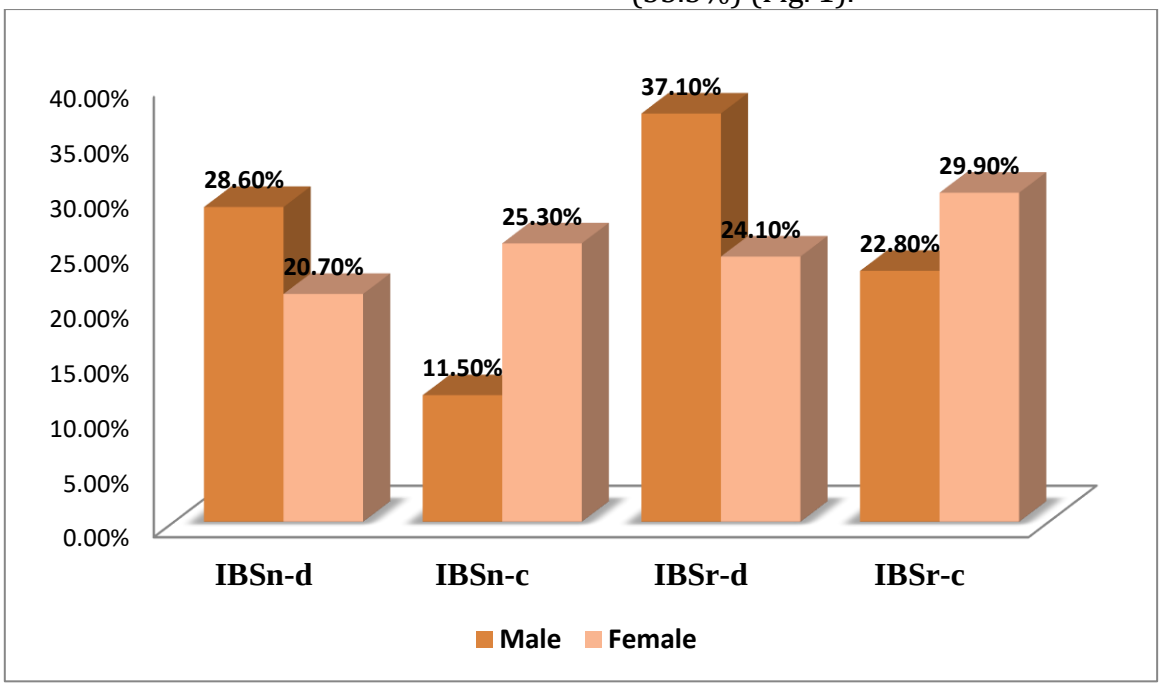

Figure 1. Gender ratio in different forms of IBS

Data from the study showed a female predominance among all IBS patients in the study, which is consistent with the literature.

In the analysis of the relationship between the type of IBS and gender, the following trends were identified. According to our data, the diarrhea-predominant type of IBS prevailed among men - in 70 patients (44.6 %). Constipation-predominant type of IBS prevailed in women - 87 (55.4%). These results are consistent with literature data.

We studied fecal calprotectin levels in 157 IBS patients and 30 healthy controls (Table 1).

Table 1

Fecal calprotectin values corresponding to types of irritable bowel syndrome

Fecal calprotectin level	IBSn-d, (%) (n=38)	IBSn-c, (%) (n=30)	IBSr-d, (%) (n=47)	IBSr-c, (%) (n=42)	Control group, (%) (n=30)
Below 50 ng/ml	11 (28,9)	26 (86,6)	4 (8,5)#*	18 (42,8)#*	30 (100)

50-100 ng/ml	27 (71,1)#	4 (13,4)#	18 (38,3)#*	23 (54,7)#*	0 (0)
100-120 ng/ml	0 (0)	0 (0)	25 (53,2)#	1 (2,5)#	0 (0)

Note: IBSn-d is a type of non-refractory IBS with diarrhea; IBSn-c - non-refractory IBS with constipation; IBSr-d - a type of refractory IBS with diarrhea; IBSr-c - refractory type of IBS with constipation;*-the difference between the indicators of the IBS patient group ($p<0.05$); #-the difference between the means of the control group ($p<0.05$).

The fecal calprotectin index prevailed in the refractory type of IBS compared to the non-refractory type. These indicators are not typical for inflammatory diseases of the intestine and correspond to the data in the literature.

A comparative analysis of pro-inflammatory and anti-inflammatory cytokines in patients with IBS revealed increased levels of pro-inflammatory cytokines - IL-1β, IL-6, α-TNF and anti-inflammatory cytokines - IL-4 and a decrease in IL-10 was found (Table 2).

Table 2
Cytokine analysis in patients with irritable bowel syndrome, Me [P25;P75], pg/ml

	IL-1β	IL-4	IL-6	IL-10	α-TNF
IBS n=157	5,2 [0,39;16,28]	2,2 [0,48;3,72]	6,18 [1,91;13,98]	12,5 [1,16;30,42	6,7 [0,49;18,73]
Control group n=30	2,2 [0,582;3,827	2,3 [0,401;4,229]	3,04 [0,465;6,87]	14,7 [3,98;24,39]	1,9 [0,136;4,25]
p	p<0,005	p>0,005	p<0,005	p<0,005	p<0,005

Cytokine status in patients with IBS was analyzed by species for comprehensive information (Table 3).

Table 3
Quantitative indices of cytokines depending on the types of irritable bowel syndrome, Me [P25;P75], pg/ml

The amount of cytokines	Types of ITS			
	ITSn-d (n=38)	ITSn-q (n=30)	ITSr-d (n=47)	ITSr-q (n=42)
IL-1β	4,4 [0,25;10,24]	7,1 [1,55;11,81]	6,2 [1,21;17,11]*#	4,9 [0,39;16,28]
IL-4	2,3 [0,42;4,66]	2,4 [0,71;3,84]	2,3 [0,55;3,82]	2,1 [0,55;3,72]
IL-6	5,1 [0,26;12,55]	5,9 [0,72;11,78]	6,4 [2,24;13,92]	6,2 [1,91;13,98]
IL-10	13,5 [0,22;30,12]	9,3 [2,11;28,16]	4,5 [1,51;9,84]*#	12,4 [1,16;30,42]
α-TNF	5,2 [0,31;12,33]	6,4 [0,43;15,5]	9,2 [0,33;21,57]*#	6,9 [0,49;18,73]

Note: IBSn-d is a type of non-refractory IBS with diarrhea; IBSn-c - non-refractory IBS with constipation; IBSr-d - a type of refractory IBS with diarrhea; IBSr-c - refractory type of IBS with constipation;*-the difference between the parameters of the group of non-refractory patients ($p<0.05$); Difference between the indicators of #-refractory patient group ($p<0.05$).

When analyzing cytokines among IBS types, it was found that the amount of

inflammatory cytokines increased significantly in the refractory type compared to the non-refractory type ($p<0.05$). When the types of diarrhea and constipation were compared, insignificant deviations were found. The amount of pro-inflammatory cytokines differed between the groups. A significant decrease in IL-10 level was found in non-refractory IBS with constipation predominance ($p<0.05$), and this indicator also showed the same result in refractory IBS with diarrhea predominance ($p<0.05$).

The levels of pro-inflammatory - IL-1β, IL-6, α-TNF and anti-inflammatory - IL-4 and IL-10 cytokines were analyzed (Table 4).

Table 4

The level of cytokines according to the types of irritable bowel syndrome, %

The amount of cytokines	Types of IBS			
	IBSn-d (n=38)	IBSn-c (n=30)	IBSr-d (n=47)	IBSr-c (n=42)
IL-1β ↑	12	16	12	8
	31,2%	53,3%	25,5%	19,1%
IL-4↓	15	11	17	21
	39,5%	36,6%	36,2%	50%
IL-6↑	7	5	5	9
	18,4%	16,6%	10,6%	21,4%
IL-10↓	8	10	29	7
	21,1%	33,3%	61,7%	16,6%
α-TNF↑	13	14	18	12
	34,2%	46,6%	38,3%	28,6%

4- as shown in the table, the level of high levels of inflammatory IL-1β, IL-6 and α-TNF cytokines was noted more in refractory IBS than in non-refractory IBS. Decreased levels of the pro-inflammatory cytokines IL-4 and IL-10 were similarly more marked in refractory IBS.

Summary. Thus, literature sources and personal research results showed that in irritable bowel syndrome, which is considered a functional disease of the intestine, cytokine imbalance is considered to be of great importance, especially this imbalance is characterized by a decrease in the amount of anti-inflammatory cytokine IL-10. Such changes indicate the importance of cytokines in the pathogenesis of functional disorders, as well as the importance of systemic immune-inflammatory mechanisms in the development of IBS. Since the imbalance of cytokines manifests the dynamics and intensity of immune disorders in functional diseases of the gastrointestinal tract, the assessment of cytokine status is of important diagnostic and prognostic value.

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