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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

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IMPORTANCE OF GUT MICROBIOTA ANALYSIS IN ASSESSING CLINICAL-LABORATORY SEVERITY LEVELS OF INTESTINAL IRRITATION SYNDROME

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✓ Resume

The study was carried out in the Polyclinic and gastroenterology department of the Bukhara regional Multidisciplinary Medical Center, and 90 patients were selected who were examined in an outpatient setting with irritable bowel syndrome (IBS). Patients with IBS were divided into two groups: the diarrheal-dominant type of its (IDS – D-43 patients) and the constipation – dominant type (IBS-C-43 patients). Gut microbiota analysis on its weight levels showed that moderate to severe patients with mild levels had normal enzymatic activity and a decrease in lactozonegative bacteria was noted. From conditionally pathogenic Enterobacteria-E. Coli levels have been observed to increase at moderate to severe levels of IBS, from staphylococci to St. Aureus was only identified in patients with severe levels of IBS. Bifidobacteria and lactobacilli, which are considered beneficial bacteria, were noted in patients with moderate to severe IBS levels.

Keywords: irritable bowel syndrome, intestinal symptoms, intestinal microbiota, intestinal dysbiosis

ICHAKLAR TIRNASH XUSUSIYATI SINDROMINING KLINIK-LABORATORIYA OG'IRLIK DARAJASINING DARAJASINI BAHOLASHDA ICHAK MIKROBIOTALARINI TAHLIL QILISHNING AHAMIYATI

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✓ Rezyume

Tadqiqot Buxoro viloyati ko'p tarmoqli tibbiyot markazining Poliklinika va gastroenterologiya bo'limida o'tkazildi va irritable ichak sindromi (IBS) bilan ambulator sharoitda ko'rikdan o'tgan 90 nafar bemor tanlab olindi. IBS bilan og'rigan bemorlar ikki guruhga bo'lingan: uning diareya-dominant turi (IDS - D-43 bemorlar) va ich qotishi - dominant turi (IBS-C-43 bemorlar). Og'irlik darajasi bo'yicha ichak mikrobiotasini tahlil qilish shuni ko'rsatdiki, engil darajadagi o'rtacha va og'ir bemorlarda normal fermentativ faollik mavjud va laktozonegativ bakteriyalarning kamayishi qayd etilgan. Shartli patogen Enterobakteriyalardan-E. Coli darajalari IBSning o'rtacha va og'ir darajalarida ortishi kuzatilgan, stafilokokklardan Sankt-Aureusgacha faqat IBSning og'ir darajasi bo'lgan bemorlarda aniqlangan. IBS darajasi o'rtacha va og'ir bo'lgan bemorlarda foydali bakteriyalar deb hisoblangan bifidobakteriyalar va laktobakteriyalar qayd etilgan.

Kalit so'zlar: irritable ichak sindromi, ichak belgilari, ichak mikrobiotasi, ichak disbiyozi

Relevance

Irritable bowel syndrome (IBS) is a biopsychosocial disorder consisting of the sum of functional disorders in the intestines that are not explained by organic changes [1,4,5].

Analysis of modern data on the etiology and pathogenesis of functional pathology of the digestive tract allows us to express an opinion about the concept of the formation of the disease, which, undoubtedly, is due to not one, but several etiological factors, and in turn, these factors are associated



with not one, but several pathophysiological mechanisms. And the complexity of controlling such patients is that in each individual case, the combination of etiopathogenetic mechanisms is individual. Today, among them, the following are of urgent importance: socioeconomic status, hereditary predisposition, the possibility of the appearance of the disease in the children of parents with IBS, psychological aspects, hypersensitivity of internal organs, gastrointestinal tract disorders, changes in the neuroendocrine system (brain-intestinal axis), low-grade-inflammation, the concept of IBS after infectious disease, microflora imbalance and, finally, nutritional factors [2,3,6,7].

The purpose of the study is to assess the clinical-laboratory severity levels of the disease in the types of intestinal irritation syndrome accompanied by diarrhea and constipation predominance.

Materials and methods

The study was carried out in the Polyclinic and gastroenterology department of the Bukhara regional Multidisciplinary Medical Center, and 90 patients were selected who were examined with IBS in an outpatient setting. The diagnosis of IBS was made based on the criteria of Rome IV (2016). The average age of patients is 34.6 ± 0.9 years.

Patients with IBS were divided into two groups: the diarrheal-dominant type of its (IBS – D-43 patients) and the constipation – dominant type (IBS-C-47 patients).

Total blood to all patients, general stool analysis, stool examination into hidden blood, blood biochemical analysis, intestinal microbiota analysis, cytokine analysis - IL-1 β , IL-4, IL-6, IL-10, α -TNF (Vektor-Best reagents), fekal calprotectin (de medi tec reagents) and cortisol analysis in the blood, from instrumental examinations - esophagofibrogastrroduodenoscopy (FUGINON. FUGI FILM EPX-2500, 2014, Japan; FUGI FILM-EG-530pf, 2014, Japan), colonoscopy (FUGI FILM-EG-530fl, 2014, Japan), ultrasound of internal organs (Vivid s-60, 2014, Norway).

Results and analyses

After patients with its-like syndrome were excluded from the study, 98 patients diagnosed with IBS were enrolled in the follow-up program.

Table 1. Results of gut microbiota analysis, $M \pm m$

Microorganisms	1 gr the number of microorganisms in the stool		
	IBS (n=90)	Control group (n=30)	P
Salmonella-Shigella	0	0	0
Intestinal sticks with normal enzymatic activity	$10^6 \pm 0,2$	$10^7 \pm 0,1$	0,00337
Lactozonegative intestinal sticks	$10^4 \pm 0,2$	$10^5 \pm 0,07$	0,68613
Intestinal sticks with hemolytic activity	0	0	0
Other conditionally pathogenic Enterobacteria (E. coli).	$10^5 \pm 0,2$	$10^4 \pm 0,2$	0,00006
Staphylococci (St. aureus).	$10^{0,2} \pm 0,1$	0	0,15799
Staphylococci (St. epidermidis, St. saprophyticus)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	u/r
Enterococcus	$10^5 \pm 0,0$	$10^5 \pm 0,0$	u/r
Yeast-like fungi	$10^4 \pm 0,1$	$10^4 \pm 0,03$	0,08150
Bifidobacteria	$10^6 \pm 0,2$	$10^7 \pm 0,05$	0,00008
Lactobacilli	$10^5 \pm 0,1$	$10^6 \pm 0,05$	0,00761
Bacteria that do not form enzymes (NGOB)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	u/r

Note: IBS is an irritable bowel syndrome; u/r is unreliable.

Thirty healthy people were included in the control group to obtain regulatory information. The median age for those in the control group was 29.3 ± 1.02 years. The study was carried out simultaneously. IBS type of clinical rejection was clinically identified, as well as retrospectively, taking into account data on Anamnesis and the results of a study of medical records. In order to determine the nature of the disease, gut microbiota analysis was performed on all patients involved in the examination and those in the control group (Table 1).

Data from table 1 showed that Salmonella-Shigella and hemolytically active intestinal rods were not detected in patients with IBS and those in the control group. Patients were observed to have normal enzymatic activity and a reliable decrease in the number of lactose-free intestinal rods in 1 gr feces compared to those in the control group ($p=0.00337$ and $p=0.68613$, respectively).

In addition, from conditionally pathogenic Enterobacteria - E. Coli and staphylococci - St. aureus increase in the amount of aigeis was found ($p=0.00006$ and $p=0.15799$, respectively).

It was observed that the amount of Bifidobacteria and lactobacilli in 1 gr of feces belonging to the group of beneficial bacteria decreased compared to the control group ($p=0.00008$ and $p=0.00761$, respectively).

In order to get more in-depth information, we have also analyzed intestinal microbiota among IBS clinical types. The results of the analysis are presented in Table 2.

Table 2 Results of gut microbiota analysis, $M \pm m$

Microorganisms	1 gr the number of microorganisms in the stool		
	IBS-D (n=43), %	IBS-C (n=47), %	P
Salmonella-Shigella	0	0	0
Intestinal sticks with normal enzymatic activity	$10^5 \pm 0,2$	$10^6 \pm 0,1$	0,21453
Lactozonegative intestinal sticks	$10^4 \pm 0,1$	$10^4 \pm 0,07$	0,78258
Intestinal sticks with hemolytic activity	0	0	0
Other conditionally pathogenic Enterobacteria (E. coli).	$10^5 \pm 0,2$	$10^5 \pm 0,2$	0,13104
Staphylococci (St. aureus).	$10^{0,3} \pm 0,1$	$10^{0,06} \pm 0,1$	0,12888
Staphylococci (St. epidermidis, St. saprophyticus)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	u/r
Enterococcus	$10^5 \pm 0,0$	$10^5 \pm 0,0$	u/r
Yeast-like fungi	$10^4 \pm 0,1$	$10^4 \pm 0,03$	0,22153
Bifidobacteria	$10^6 \pm 0,2$	$10^7 \pm 0,05$	0,00030
Lactobacilli	$10^5 \pm 0,1$	$10^5 \pm 0,05$	0,00194
Bacteria that do not form enzymes (NGOB)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	u/r

Note: IBS-D is diarrhea – dominated intestinal irritation syndrome; IBS-C is constipation – dominated intestinal irritation syndrome; u/r is unreliable.

A comparison of gut microbiota among its clinical types found a decrease in the amount of intestinal rods and Bifidobacteria with normal enzymatic activity in its accompanied by diarrhea predominance ($p=0.21453$ and $p=0.00030$, respectively). Other microorganisms did not detect deviations in my quantity.

It is possible to reflect on intestinal dysbiosis, depending on whether the pathogenic, conditionally pathogenic and beneficial microorganisms in the colon have increased or decreased. Table 3 presents the results of the analysis of dysbiosis levels in IBS patients and those in the control group.

When compared with rates of intestinal dysbiosis, level I dysbiosis was more noted in those in the control group compared to those with IBS (38.8% and 100%, respectively). Also, dysbiosis levels II and III were only reported in patients with IBS (43.3% and 17.9% respectively). Normal microflora, on the other hand, was not reported in both patients and those in the control group.

A more thorough analysis was carried out in order to determine the degree of dysbiosis among IBS clinical types (Figure 1).

Table 3

Dysbacteriosis levels in different types of intestinal irritation syndrome, %

Degree of dysbiosis	IBS (n=90)	Control group (n=30)
Grade I	35 (38,8)	30 (100)
Grade II	39 (43,3)	0 (0)
Grade III	16 (17,9)	0 (0)
Normal microflora	0 (0)	0 (0)

Note: # - difference between control group indicators ($p < 0.05$).

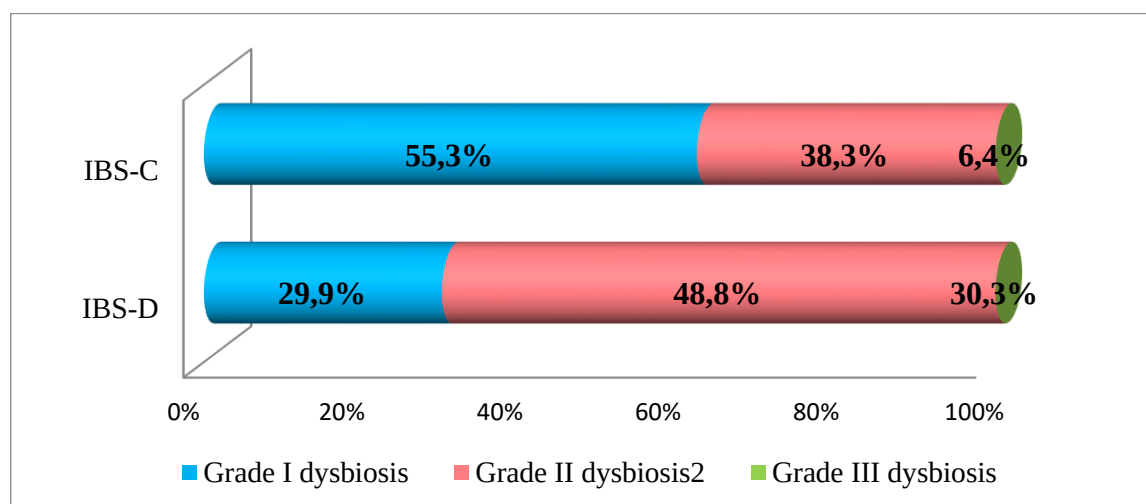


Figure 1. The rate of dysbiosis corresponding to clinical types of IBS, %

Table 4

Blood microbiota analysis results by IBS severity levels, $M \pm m$

Microorganisms	IBS severity levels		
	Light (n=32)	Middle heavy (n=37)	Sever (n=21)
	1 gr the number of microorganisms in the stool		
Salmonella-Shigella	0	0	0
Intestinal sticks with normal enzymatic activity	$10^7 \pm 0,3^{* \wedge}$	$10^5 \pm 0,1$	$10^5 \pm 0,2$
Lactozonegative intestinal sticks	$10^5 \pm 0,1^{* \wedge}$	$10^4 \pm 0,2$	$10^4 \pm 0,2$
Intestinal sticks with hemolytic activity	0	0	0
Other conditionally pathogenic Enterobacteria (E. coli).	$10^4 \pm 0,2^{* \wedge \wedge}$	$10^5 \pm 0,2$	$10^6 \pm 0,2$
Staphylococci (St. aureus).	0	0	$10^{0,6} \pm 0,2^{\#}$
Staphylococci (St. epidermidis, St. saprophyticus)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	$10^4 \pm 0,0$
Enterococcus	$10^5 \pm 0,0$	$10^5 \pm 0,0$	$10^5 \pm 0,0$
Yeast-like fungi	$10^4 \pm 0,07$	$10^4 \pm 0,1$	$10^4 \pm 0,1$
Bifidobacteria	$10^7 \pm 0,1^{* * \wedge \wedge \wedge}$	$10^6 \pm 0,1^{\wedge \wedge}$	$10^4 \pm 0,1$
Lactobacilli	$10^6 \pm 0,1^{* \wedge \wedge \wedge}$	$10^5 \pm 0,07$	$10^3 \pm 0,1$
Bacteria that do not form enzymes (NGOB)	$10^4 \pm 0,0$	$10^4 \pm 0,0$	$10^4 \pm 0,0$

Note: patients with moderate to severe levels of statistical reliability compared to indicators: * - $p < 0.05$; * * - $p < 0.01$; * * * - $p < 0.001$, patients with severe levels of statistical reliability compared to indicators: $\wedge$ - $p < 0.05$; $\wedge \wedge$ - $p < 0.01$; $\wedge \wedge \wedge$ - $p < 0.001$; # - $p < 0.01$.

When dysbiosis levels were analyzed among IBS clinical types, Grade I dysbiosis dominated the constipation-dominated type of IBS (n=26.5-55.3%). Grade II and III dysbiosis, on the other hand, demonstrated dominance in the diarrheal dominant type of IBS (n=21.48.8% and n=13.30.3%, respectively). Due to these changes, it can be assumed that the colon is associated with a decrease in resistance to colonization in the mucous membrane and exacerbates it.

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

Gut microbiota analysis on IBS severity levels showed that moderate to severe patients with mild levels had normal enzymatic activity and a decrease in lactosonegative bacteria was noted ($p<0.05$). From conditionally pathogenic Enterobacteria-E. Coli levels have been observed to increase at medium-heavy and severe levels of IBS ($p<0.05$, $p<0.01$), from staphylococci to St. aureus was found only in patients with severe levels of IBS ($p<0.01$). Bifidobacteria and lactobacilli, considered beneficial bacteria, were reported in patients with moderate to severe IBS levels ($p<0.05$, $p<0.01$, $p<0.001$).

Conclusion

Thus, at mild levels, dysbiosis of grade I at IBS, dysbiosis of grade II at Medium-Heavy IBS, and dysbiosis of grade III at heavy its were caused.

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