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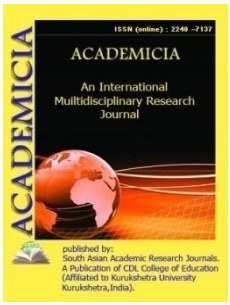

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MICRO ELEMENTAL IMBALANCE IN IRRITABLE BOWEL SYNDROME AND ITS CORRECTION

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ABSTRACT

The prevalence of IBS is very high and varies between 10-20% in different countries. As a result of the study, the imbalance of the elements in the tissues of patients with IBS was detected using the method of gamma spectrometry in the hair. Decreased levels of Ca, Mg, Fe, Zn, Cu, I, Mn, Co in patients with IBS compared to healthy people, and the elements P, Se, As, Ni are reliable. found to increase. Patients with IBS were corrected with element-preserving drugs such as Ca, Mg after the detection of element imbalance in the tissues. Positive results were obtained after complex treatment, and As in the tissues was reliably reduced.

KEYWORDS: *Irritable Bowel Syndrome, Elemental Balance, Essential And Toxic Elements.*

INTRODUCTION

Irritable bowel syndrome (IBS) is the most diagnosed gastrointestinal disease in the 21st century, as well as the most common cause of referral to gastroenterology clinics. Various mechanisms and theories related to IBS etiology have been proposed, but currently the most accepted biopsychological model for IBS is that IBS is the result of an interaction between psychological, behavioral, social, and environmental factors. There are no specific tests for the diagnosis of IBS [1,2].

The prevalence of this pathology is very high and varies from 10–20% in different countries [3,4,5]. The complexity of managing IBS patients is related to the heterogeneity of clinical manifestations that require a differential approach in the treatment of different patients [6]. This makes the study of this problem very relevant [7].

A recent revision of the Rome IV consensus (2016) identified time criteria and diagnostic criteria for IBS - recurrent abdominal pain, at least once a week for the previous 3 months, associated with 2 or more symptoms / factors: 1) defecation; 2) change in stool frequency; 3) change in the form of feces. However, anamnestic symptoms should be noted in the last 6 months or more, in the absence of clear anatomical and physiological limitations during routine clinical examination [8,9].

The complexity of treating patients with IBS is that the factors that cause the disease and the mechanisms of development are individual. The most important risk factors for IBS are: female gender (risk is 4 times higher); age (30-40 years); place of residence (megacities); education (higher, humanitarian); professional affiliation (mental workers and cultural workers); social environment (non-full-blooded families, orphanages); low levels of social support [10].

Deviations in the intake of macro- and micronutrients into the body can reduce or increase IBS ability to adapt and resist [11, 15, 17]. In this regard, in medicine more and more attention is paid to the study of the micronutrient status of the human body and the development of methods to correct IBS disorders in various diseases [12,13, 16, 19].

To study the elemental state, it is necessary to have an idea of what tissue and in what form the element under study is found in the maximum amount, because the deposition of chemically important elements is closely related to their biochemical functions [14, 18, 20].

Thus, the study of risk factors and the main etiopathogenetic mechanisms of the formation of intestinal affect syndrome among the population is of particular importance due to their prevalence and serious psychoemotional disorders. According to the study, nonspecific manifestations of ionic balance in the tissues of the gastrointestinal tract, liver and fluid environment in experimental gastric ulcers, according to the authors, in the ulcer zone, an increase in the concentration of Se in the intestine, gastric juice - Se, Mg, Si, chromium (Cr), blood - Ca, in the gastric and intestinal juice - Zn, in the small intestine - Mg, Na, Fe, Mn and a number of other important elements.

The purpose of the study

To study the status of chemical elements in patients with different forms of IBS and its correction.

Material and research methods

The study was conducted in the gastroenterology department of BRMMC (Bukhara Regional Multidisciplinary Medical Center) and all patients treated with IBS in an inpatient setting for 2017-2019 were selected. The diagnosis of IBS was made based on IV Roman criteria (2016), using the Bristol fecal forms scale to determine the clinical form of IBS (Blake M.R., Raker J.M., Whelan K., 2016). Determination of the composition of chemical elements was carried out in the laboratory of the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan.

Criteria for inclusion: Conformity of the diagnosis of IBS to the IV Roman criteria, age - from 18 to 45 years, a letter of written consent. Exclusion criteria: patients older than 45 years, "anxiety symptoms" (weight loss; onset of disease in old age; nocturnal symptoms; colon cancer, celiac disease, ulcerative colitis and Crohn's disease among relatives, persistent severe abdominal pain

as the only symptom of gastrointestinal tract injury), fever, hepatitis - and splenomegaly, anemia, leukocytosis, increased ECG, the presence of occult blood in the stool, changes in the biochemical analysis of blood, steatorrhea and polyphagia).

Patients with IBS were divided into two groups: with non-refractory (IBSn - 35 people) and refractory (IBSr - 47 people) course of IBS. Of these, taking into account the leading clinical syndrome, patients with IBSn-d were identified - 21 people (25.6%), IBSn-c - 14 people (17%), IBSr-d - 28 people (34.2%), IBSr-c - 19 people (23.2%).

The composition of 25 chemical elements in the hair of patients with IBS was determined: K, Na, Ca, Mg, P, Fe, Zn, Cu, Se, I, Mn, Co, Cl, As, Sn, B, Li, N, V, S, Hg, Pb, Cd, Be, Al. Mass spectrometry method with inductively coupled plasma (ICP-MS) for the detection of chemical elements Nexion 300D (perkinelmer Inc., Shelton, CT 06484, USA), autosamplers ESI SC-2 DX4 (Elemental Scientific Inc., Omaha, NE 68122, USA) is equipped with. This practice also included Dynamic Reaction Cell (DRC) technology to eliminate most of the interference without compromising the sensitivity of analysts.

Preparation of the ICP-DRC-MS system was carried out using the manufacturer's specifications. The system is calibrated using standard solutions containing 0.5, 5, 10, and 50 mg / l copper and zinc from the Universal Data Acquisition Kit (perkinelmer Inc., Shelton, CT 06484, USA). Internal online standardization was also performed using the yttrium-89 isotope (10 mg / l, pure element Yttrium (Y) Standard, perkinelmer Inc., Shelton, CT 06484, USA).

Laboratory quality control was performed using a GBW09101 certified human hair certificate (Shanghai Nuclear Research Institute, Sinica Academy, China). Laboratory quality control practices were performed routinely before and after each analysis set.

RESULTS AND DISCUSSION

Biomaterial (hair) collection to determine the amount of chemical elements in the tissues was performed on the day the patients were hospitalized. Data obtained on the composition of chemical elements in tissues provide information on elemental balance in the broad clinical manifestations of IBS symptoms.

The distribution of ITS by type, sex, and age is given in table 1.

TABLE 1 DISTRIBUTION OF PATIENTS BY NOSOLOGY, AGE AND SEX

Groups	**Sex**				**Age**	Duration of the disease **M ± m(year)**
	Male		**Female**		**Average age M ± m(year)**	
	Ex. number	**%**	**Ex. number**	**%**		
IBSn-d(n = 21)	**11**	**52,4**	**10**	**47,6**	**24,32 ±2,3**	**3,4±1,8**
IBSn-c(n = 14)	**6**	**42,8**	**8**	**57,2**	**31,01 ± 3,4**	**5,2±2,4**
IBSr-d(n = 28)	**15**	**53,6**	**13**	**46,4**	**30,43 ± 4,2**	**6,8±2,1**
IBSr-c(n = 19)	**9**	**47,4**	**10**	**52,6**	**28,64 ± 3,8**	**7,5±2,7**
Control group (healthy) (n = 20)	**11**	**55,0**	**9**	**45,0**	**25,18 ± 3,3**	**0**

No difference was found between the age groups, and the IBS refractory type of disease duration was found to be higher than the other groups (p <0.05).

A comparison of the elements content of the elements in patients with different forms of IBS is given in table 2.

TABLE 2 THE COMPOSITION OF CHEMICAL ELEMENTS IN DIFFERENT FORMS OF IBS

№	Element		Control group n=20	IBSn n=17	IBSr n=33	Limit of the norm (mkg/g)
Essential (vital) chemical elements						
1	K	Potassium	812,3	746,4	804,1	40-2000
2	Na	Sodium	746,2	763,5	722,6	50-2000
3	Ca	Calcium	978,3	311,1#	294,3#	200-2000
4	Mg	Magnesium	125,7	65,2#	64,8#	20-200
5	P	Phosphorus	152,8	209,3#	215,4#	120-200
6	Fe	Iron	27,8	6,85#	7,21#	7-40
7	Zn	Zinc	234,6	120,4#	118,7#	125-400
8	Cu	Copper	21,3	8,4#	9,5#	9-40
9	Se	Selenium	0,9	2,0#	2,1#	0.25-2
10	I	Iodine	5,3	4,4	5,1	0.15-10
11	Mn	Manganese	1,2	0,55	0,52	0.15-2
12	Co	Cobalt	0,21	0,005#	0,008#	0.004-0.3
13	Cr	Chromium	0,4	0,06	0,05	0.004-1
Toxic, relatively toxic and relatively essential chemical elements						
14	As	Arsenic	0,04	0,9#	1,0#	<1
15	Sn	Olovo	0,912	1,13	0,987	<3
16	B	Bor	1,691	1,862	1,742	<5
17	Li	Lithium	0,02	0,005	0,01	<0/1
18	Ni	Nickel	0,127	1,23#	1,25#	<2
19	V	Vanadium	0,06	0,05	0,04	0.005-0.1
20	Si	Silicon	30,16	27,31	29,71	11-70
21	Hg	Mercury	0,204	0,313	0,286	<1
22	Pb	Lead	0,871	0,478	0,693	<5
23	Cd	Cadmium	0,009	0,006	0,007	<0.25
24	Be	Beryllium	0,0003	0,0003	0,0002	<0.003
25	Al	Aluminum	8,26	6,28	12,86	<25

Note: IBSn –norefractor IBS; ITSr - refractory IBS; # is the difference between the control group values (p<0.05)

When analyzing table 2, it can be seen that the essential chemical elements content of hair in patients with IBSr was significantly reduced compared to the control group and IBSn, and the amount of some toxic elements was increased. To get a more accurate result, we divided the patients into two subgroups: IBS patients with chemical elements imbalance and without chemical elements imbalance (table 3).

TABLE 3 COMPARISON OF THE AMOUNT OF CHEMICAL ELEMENTS IN PATIENTS WITH IBS WITH MICRONUTRIENT IMBALANCE AND MICRONUTRIENT IMBALANCE

№	Element		IBS with chemical elements imbalance n=32	IBS without chemical elements imbalance n=50	p
Essential (vital) chemical elements					
1	K	Potassium	823,1	775,3	0,001
2	Na	Sodium	752,6	743,1	0,01
3	Ca	Calcium	981,4	302,7	0,001
4	Mg	Magnesium	125,7	65,0	0,01
5	P	Phosphorus	152,8	212,4	0,001
6	Fe	Iron	18,4	7,03	0,008
7	Zn	Zinc	231,3	119,5	0,001
8	Cu	Copper	21,5	8,9	0,001
9	Se	Selenium	1,2	2,0	0,0001
10	I	Iodine	5,3	4,7	0,01
11	Mn	Manganese	1,32	0,53	0,001
12	Co	Cobalt	0,23	0,006	0,0001
13	Cr	Chromium	0,21	0,06	0,06
Toxic, relatively toxic and relatively essential chemical elements					
14	As	Arsenic	0,04	1,0	0.0001
15	Sn	Olovo	0,912	1,008	
16	B	Bor	1,691	1,812	
17	Li	Lithium	0,02	0,015	0,001
18	Ni	Nickel	0,127	1,24	0,05
19	V	Vanadium	0,06	0,05	0,001
20	Si	Silicon	30,16	28,51	
21	Hg	Mercury	0,204	0,299	0,002
22	Pb	Lead	0,571	0,585	0,05
23	Cd	Cadmium	0,007	0,007	0,03
24	Be	Beryllium	0,0002	0,0003	
25	Al	Aluminum	5,01	9,57	0,001

The study found that 8 of the 25 chemical elements (Ca, Mg, Fe, Zn, Cu, I, Mn, Co) were significantly reduced in patients with IBS than in healthy people. Quantitative differences between only 13 elements (Na, K, Cr, Sn, B, Li, V, Si, Hg, Pb, Cd, Be, Al) were not detected in the hair of patients and control group. It was found that the amount of the remaining 4 chemical elements (P, Se, As, Ni) increased compared to healthy people. Changes in the quantitative composition of chemical elements in tissues in IBS are determined by a complex of functional disorders of the gastrointestinal tract, including motor-evacuation, impaired intestinal absorption and selection of chemical elements, which eventually leads to the appearance of clinical signs.

Increased levels of the chemical elements As and Se in patients with IBS require separate analysis. It is known that As affects the motility of the gastrointestinal tract and exacerbates spastic symptoms. The parallel increase in Se is a compensatory reaction of the body, Se has a pronounced antioxidant property due to its inclusion in the group of neurotoxic elements (Hg, Cd, Pb, Ni, etc.), neutralizes the effects of As increase, they enhance elimination, due to neuroprotective properties to smooth muscle affects.

Standard therapy in patients with a predominance of constipation includes: enriching the diet with fiber (wholemeal bread, vegetables, fruits, wheat and oat bran, the use of lactic acid products. Lactulose (duphalac) is prescribed, for which clinical efficacy has been noted. In patients with diarrhea) in the diet, the intake of fatty and gas-forming foods is limited.With this form of IBS, it is customary to prescribe loperamide, imodium plus, to which simethicone is added, a substance that absorbs gases in the intestine, as well as smecta or hydrocarbon sorbents based on activated carbon.For pain, standard therapy includes the appointment of antispasmodics: drotaverine, papaverine, mebeverine.

We identified a group of patients with IBS who received standard therapy (14 people) and a group of patients who, along with standard therapy, took measures aimed at eliminating violations of the elemental balance for a month (18 people). The division was carried out by the method of tabular randomization.

To eliminate the deficiency of calcium and magnesium, which have the greatest effect on the manifestations of pain and spastic syndrome of the gastrointestinal tract, the drug Kal-Di-Mag was used for a month, containing chelated forms of Ca and Mg (1 tablet 2 times a day with meals). To reduce the amount of toxic elements, Nutrikon-selenium was additionally prescribed, which serves as an additional source of selenium in organic form (1 t.sp 2 times a day before or during meals).The assessment of the effect of the proposed method for correcting the elemental balance in tissues was carried out on the basis of assessing the content of Mg, Ca, As and Ni in the hair of patients before treatment and after 1 month of corrective action. For comparison, parallel studies of the elemental composition of hair were carried out in 14 patients with IBS who received only standard therapy. The data are shown in table 4.

TABLE 4 CONTENT OF CHEMICAL ELEMENTS IN PATIENTS WITH IBS BEFORE AND AFTER CORRECTIVE MEASURES (MKG/G)

№	Element	Before treatment=18	**After a month of complex treatmentn=18**	P
1	Mg	65,0	115.5	0,02
2	Ca	302,7	422.0	0,01
3	Ni	1,24	0.72	0,07
4	As	1,0	0.04	0,001

As a result of the measures taken aimed at correcting the elemental balance in tissues, a significant increase in Mg and Ca (from 65.0 and 302.7 to 115.5 and 422.0) was obtained in hair in patients with IBS, as well as a significant decrease in As (from 1,0 to 0.04), these indicators

are close to those of healthy people.We did not receive significant changes when conducting studies of the content of Mg, Ca, Ni, As and Se in hair in 14 patients who received only standard therapy (before treatment and after 1 month). As a result, the effectiveness of the proposed methods for correcting elemental imbalance in tissues in IBS has been proven.

CONCLUSION

1. As a result of the study, the imbalance of the elements in the tissues of patients with IBS was detected using the method of gamma spectrometry in the hair.

2. Decreased levels of Ca, Mg, Fe, Zn, Cu, I, Mn, Co in patients with IBS compared to healthy people, and the elements P, Se, As, Ni are reliable. found to increase.

3. Patients with IBS were corrected with element-preserving drugs such as Ca, Mg after the detection of element imbalance in the tissues.

4. Positive results were obtained after complex treatment, and As in the tissues was reliably reduced.

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