



Eating Habits, Anxiety and Depression in Patients with Irritable Bowel Syndrome: Clinical and Laboratory Comparisons

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Aim: to assess the level of stress hormones (cortisol in saliva), neurotransmitters (serotonin in blood serum, dopamine in blood plasma) in relation to eating habits, anxiety and depression levels in patients with IBS.

Materials and methods. An open cohort prospective study was conducted with the inclusion of 263 patients with an established diagnosis of IBS, among them 189 (71.9 %) women and 74 (28.1 %) men. The average age of patients with IBS was 29 [25; 35] years. The control group included 40 healthy volunteers. All individuals included in the study were assessed for diet and eating habits using the WHO CINDI program questionnaire, "Information on Nutrition and Eating Behavior", the severity of anxiety and depression according to the HADS questionnaire, the level of specific anxiety in relation to gastrointestinal symptoms according to the VSI questionnaire, quality of life according to the IBS-QoL questionnaire. In addition, the enzyme immunoassay method was used to assess the levels of cortisol in the morning and evening portions of saliva, serotonin in the blood serum and dopamine in the blood plasma.

Results. Among patients with IBS there is a statistically significantly higher level of cortisol in the morning and evening portions of saliva ($U = 19.5, p < 0.001$ and $U = 111.5, p < 0.001$, respectively), serotonin in blood serum ($U = 269.0, p = 0.042$) and lower plasma dopamine levels ($U = 93.5, p = 0.0002$) compared with controls. The mean salivary cortisol level among patients with IBS was 45.39 [29.86; 70.10] ng/ml in the morning and 19.21 [13.98; 23.50] ng/ml in the evening, while in the group of healthy individuals it was 19.0 [16.5; 21.7] and 9.7 [8.5; 10.5] ng/ml, respectively. The average content of serotonin in blood serum in patients with IBS was 188.78 [150.41; 230.32] ng/ml, among healthy individuals — 142.80 [130.52; 154.15] ng/ml. The average content of dopamine in blood plasma in patients with IBS was 28.83 [20.08; 41.54] ng/ml, in healthy individuals — 58.20 [48.15; 66.62] ng/ml.

Conclusion. In patients with IBS the secretion of the stress hormone (cortisol) and neurotransmitters (serotonin, dopamine) is closely related to the nature of nutrition, the level of anxiety and depression, and is also associated with the clinical variant and severity of the course of the disease.

Keywords: irritable bowel syndrome, cortisol, serotonin, dopamine, neurotransmitters, stress hormone, anxiety, depression, eating habits

Conflict of interest: the authors declare no conflict of interests.

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Пищевые привычки, уровень тревоги и депрессии у пациентов с синдромом раздраженного кишечника: клинко-лабораторные сопоставления

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Цель исследования: оценить уровень гормонов стресса (кортизол в слюне), нейромедиаторов (серотонин в сыворотке крови, дофамин в плазме крови) во взаимосвязи с пищевыми привычками, уровнем тревоги и депрессии у пациентов с СРК.

Материалы и методы. Проведено открытое когортное проспективное исследование с включением 263 пациентов с установленным диагнозом СРК, среди них 189 (71,9 %) женщин и 74 (28,1 %) мужчины. Средний возраст пациентов с СРК составил 29 [25; 35] лет. В контрольную группу вошли 40 здоровых добровольцев. Всем включенным в исследование лицам проводилась оценка рациона питания и пищевых привычек по опросникам WHO CINDI program questionnaire, «Информация о питании и пищевом поведении», выраженности тревоги и депрессии по опроснику HADS, в том числе уровня специфической тревоги в отношении гастроинтестинальных симптомов по опроснику VSI, качества жизни по опроснику IBS-QoL. Кроме того, ме-

тодом иммуноферментного анализа проводилась оценка уровней кортизола в утренней и вечерней порциях слюны, серотонина в сыворотке крови и дофамина в плазме крови.

Результаты. Среди пациентов с СРК, по сравнению с лицами группы контроля, отмечается статистически значимо более высокий уровень кортизола в утренней и вечерней порциях слюны ($U = 19,5$, $p < 0,001$ и $U = 111,5$, $p < 0,001$ соответственно), серотонина в сыворотке крови ($U = 269,0$, $p = 0,042$) и более низкий уровень дофамина в плазме крови ($U = 93,5$, $p = 0,0002$). Среднее значение уровня кортизола в слюне среди пациентов с СРК составило 45,39 [29,86; 70,10] нг/мл в утренние часы и 19,21 [13,98; 23,50] нг/мл в вечерние, тогда как в группе здоровых лиц — 19,00 [16,50; 21,70] и 9,70 [8,50; 10,50] нг/мл соответственно. Среднее значение уровня серотонина в сыворотке крови среди пациентов с СРК составило 188,78 [150,41; 230,32] нг/мл, дофамина в плазме — 28,83 [20,08; 41,54] нг/мл, среди здоровых лиц — 142,8 [130,52; 154,15] и 58,20 [48,15; 66,62] нг/мл соответственно.

Выводы. У пациентов с СРК секреция гормона стресса (кортизол) и нейромедиаторов (серотонин, дофамин) находится в тесной взаимосвязи с характером питания, уровнем тревоги и депрессии, а также ассоциирована с клиническим вариантом и степенью тяжести течения заболевания.

Ключевые слова: синдром раздраженного кишечника, кортизол, серотонин, дофамин, нейромедиаторы, гормон стресса, тревога, депрессия, пищевые привычки

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Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders (FGID), which is characterized by recurrent abdominal pain associated with disruption of the usual bowel activity, with the exclusion of other causes that can explain these symptoms [1, 2]. The global prevalence of IBS is estimated at about 10–15 % with a range of variation from 1.1 % to 35.5 % in different regions of the world [3]. It is well known that the disease does not affect life expectancy, while significantly reducing the quality of life, labor potential and social activity of patients [4].

It has been established that IBS is a multifactorial disease. The formation of IBS involves genetic predisposition, psychological status, stress and environmental factors such as diet, past acute intestinal infections and the use of antibacterial drugs [5]. These factors contribute to a change in the microbial landscape, activation of the immune system, development of low-level inflammation in the intestinal mucosa, an increase in the permeability of the epithelial barrier, impaired functioning of the brain-gut axis, visceral hypersensitivity and motor dysfunction and as a consequence of IBS [6, 7]. Despite the progress made in the study of IBS, the effectiveness of therapy in patients remains quite low. This requires the development of individualized patient management programs based on a comprehensive analysis of the main risk factors for the disease — eating habits, levels of anxiety and depression.

Purpose: to assess the level of stress hormones (cortisol in saliva), neurotransmitters (serotonin in blood serum, dopamine in blood plasma)

in relation to eating habits, anxiety and depression levels in patients with IBS.

Materials and methods

To achieve this goal, an open cross-sectional study was conducted, which included 263 patients over the age of 18 with an established diagnosis of IBS, in accordance with the clinical recommendations of the Russian Gastroenterological Association and the Russian Association of Coloproctologists for the diagnosis and treatment of IBS [1]. The presented study is a continuation of the previously published work [8]. Exclusion criteria from the study were organic diseases of the digestive tract, as well as other organs and systems that can occur «under the guise» of IBS, severe concomitant diseases, pregnancy or lactation, any psychiatric diseases, refusal to participate in the study. The study protocol was approved by the Local Ethics Committee of the Omsk State Medical University.

Among the patients included in the study 189 (71.9 %) were women and 74 (28.1 %) were men. The average age of patients with IBS was 29 [25; 35] years. The average duration of the disease was 26 [15; 42] months. 84 (31.9 %) were diagnosed with IBS with a predominance of diarrhea (IBS-D), 92 (34.8 %) — IBS with a predominance of constipation (IBS-C), 71 (26.9 %) — IBS with mixed variant of motor impairment (IBS-M), in 16 (6.4 %) — unclassified variant of IBS (IBS-U). Due to the small sample size of patients with IBS-U and the absence of specific characteristics

of the group, these patients were combined into one group with patients with IBS-M. Mild course of the disease was diagnosed in 110 patients (41.9 %), moderate — in 99 (37.6 %), severe — in 54 (20.5 %). Patients with IBS constituted the main study group. The comparison group included 40 healthy individuals matched in sex and age with the participants in the main group.

A digital version of the Visual Analogue Scale (VAS) was used to assess the severity of IBS symptoms (abdominal pain, constipation, diarrhea, bloating, and flatulence) over the past 4 weeks. The structure of the diet among the respondents was assessed according to the WHO CINDI program questionnaire [9], food preferences and availability of various food products — according to the questionnaire «Information on Nutrition and Eating Behavior», developed at the Department of Hygiene, Human Nutrition, Omsk State Medical University Ministry and recommended for conducting sociological studies of public health [10]. To assess the severity of anxiety and depression we used the hospital anxiety and depression scale HADS (The hospital Anxiety and Depression Scale) developed by A.S. Zigmond, R.P. Snaith for the primary detection of depression and anxiety in general medical practice [11]. The level of specific anxiety in relation to gastrointestinal symptoms in IBS was determined using the VSI (Visceral Sensitivity Index) proposed by J. Labus et al. [12, 13]. The quality of life of patients was assessed according to the IBS-QoL (Irritable Bowel Syndrome Quality of Life) questionnaire [14].

In addition, all patients and individuals of the comparison group on the basis of the Central Scientific Research Laboratory of Omsk State Medical University underwent a laboratory study to determine the level of cortisol in saliva, serotonin in blood serum and dopamine in blood plasma by enzyme immunoassay. The cortisol content in saliva determined using the Cortisol Saliva ELISA test system (Diagnostics Biochem Canada Inc, Canada). The serotonin content in the blood serum determined using the Serotonin ELISA test system (IBL, Germany). The dopamine content in blood plasma determined using the Dopamine ELISA test system (IBL, Germany).

Statistical analysis of the obtained data was carried out using the Microsoft Excel and Statistica v.6.1 software packages (Russian version). For all quantitative traits in the compared groups, the arithmetic mean and standard errors of the mean, as well as the median (Me), 25 % and 75 % percentiles (P25 and P75, respectively) were evaluated. Due to the presence of a distribution other than normal, the Mann-Whitney test (U), the Kruskal-Wallis test (H) were used to compare

independent groups. For the analysis of qualitative data (nominal, ordinal, rank) and analysis of frequencies, Pearson's χ^2 test was used. The degree of relationship between the two variables was established by the Spearman correlation analysis with the determination of the rank correlation coefficient (r_s). Results were considered statistically significant at $p < 0.05$.

Results and discussion

When analyzing the clinical symptoms of the disease, the presence of abdominal pain associated with a violation of the frequency of stools and/or the shape of feces was recorded in all patients. The average severity of abdominal pain according to VAS among the patients included in the study was 5 [3; 7] points. Motility disorders according to the type of constipation were recorded in 166 (63 %) patients, according to the type of diarrhea — in 157 (59.7 %), while isolated constipation syndrome occurred in 92 (34.8 %) patients, diarrhea syndrome — in 84 (31.9 %), alternating constipation and diarrhea — in 87 (33.1 %). The average severity of constipation according to VAS was 3 [1; 6] points, diarrhea — 4 [1; 6]. In addition, in 221 (84.0 %) patients with IBS, when questioned, they reported the presence of flatulence or bloating. The average severity of the flatulence according to the VAS was 4.5 [3; 7] points.

When analyzing eating habits and preferences, it was found that patients with IBS experience various kinds of taste preferences. For example, among patients with IBS-D, an addiction to salty foods ($\chi^2 = 33.87$, $p < 0.001$), with IBS-C — to sweet ($\chi^2 = 23.41$, $p < 0.001$) and flour products ($\chi^2 = 36.85$, $p < 0.001$). Patients with IBS were less likely to experience cravings for meat food ($\chi^2 = 43.89$, $p < 0.001$) and they are characterized by low consumption of meat and meat products ($\chi^2 = 7.21$, $p = 0.0072$) compared with healthy individuals. In the group of patients with IBS 9 (3.4 %) did not eat meat and meat products at all, 104 (39.6 %) ate them 1–2 times a week, 131 (49.8 %) — 3–4 times per week and only 19 (7.2 %) — 5 times or more per week.

Another feature of the nutrition of patients with IBS included in our study was the low consumption of milk and dairy products ($U = 142.5$, $p < 0.001$). 66 (25.1 %) patients with IBS reported a complete refusal to consume milk and dairy products. The total amount of milk and dairy products consumed decreased as the severity of abdominal pain ($\chi^2 = 11.55$, $p < 0.001$) and diarrhea ($\chi^2 = 15.38$, $p < 0.001$) increased. Patients with IBS are characterized by low consumption of vegetables ($U = 206.5$, $p < 0.008$) and fruits ($U =$

247.0, $p < 0.024$) compared with healthy individuals. The daily amount of fresh vegetables and fruits consumed in the main group was 150 [100; 200] and 75.0 [40.0; 140.0] g/day and in the control group — 300.0 [250.0; 350.0] and 200.0 [200.0; 250.0] g/day, respectively. Individuals of the main group showed increased salt intake ($\chi^2 = 16.237$, $p = 0.0002$). 30 (11.41 %) patients with IBS always add salt to cooked food, even without trying it, another 151 (57.41 %) add salt to food if they consider it not salty enough. The highest salt intake was observed among patients with IBS-D ($\chi^2 = 19.74$, $p < 0.001$).

In patients with IBS eating disorders were more often recorded: 112 (42.6 %) patients eat only 1–2 times a day, 161 (61.2 %) reported episodes of frequent overeating in the evening, 154 (58.6 %) reported about limiting time for food intake, 57 (21.7 %) reported not being able to eat regularly. Fearing the onset of symptoms patients with IBS visit catering places less frequently ($\chi^2 = 33.51$, $p < 0.001$), while only 20 (7.63 %) take food from home with them.

When analyzing the data of the HADS questionnaire signs of anxiety and depression were statistically significantly more common in the group of patients with IBS ($\chi^2 = 14.82$, $p = 0.0006$ and $\chi^2 = 8.15$, $p = 0.0169$, respectively). Signs of anxiety (8 or more points on the HADS-A subscale) were detected in 207 (78.7 %) patients with IBS, signs of depression (8 or more points on the HADS-D subscale) in 128 (48.6 %). The total score on the HADS-A anxiety subscale among patients with IBS was 9 [8; 12], according to the HADS-D depression subscale — 8 [4; 10], while among healthy individuals — 3 [0.75; 3.5] and 1 [1; 2], respectively ($U = 238.0$, $p = 0.0192$ and $U = 178.5$, $p = 0.0033$). Patients with IBS-D had a significantly higher score on the HADS-A subscale and IBS-C on the HADS-D subscale ($U = 291.5$, $p = 0.0009$ and $U = 342.5$, $p = 0.0043$, respectively). The prevalence of signs of anxiety and depression increased as the severity of the disease increased ($\chi^2 = 43.24$, $p < 0.001$ for anxiety and $\chi^2 = 40.63$, $p < 0.001$ for depression).

The indicator of specific gastrointestinal anxiety according to the VSI questionnaire was statistically significantly higher in the group of patients with IBS than in the group of healthy individuals ($U = 1.0$, $p = 0.0000$). The VSI index among patients with IBS was 49 [38; 58] points. The highest VSI index was found in patients with IBS-D — 53.0 [46.7; 66.3], compared with patients with IBS-C and IBS-M — 48.0 [40.0; 57.0] and 46.0 [35.0; 58.5] respectively.

At the same time patients with IBS had a lower quality of life ($U = 0.0$, $p = 0.0000$). The total

IBS-QoL in the main group was 67.6 [54.4; 86.7], in the control group — 100.0 [99.6; 100.0]. The lowest IBS-QoL was found in the IBS-D group — 61.8 [54.2; 81.1], in the IBS-C group the indicator was 66.2 [50.0; 87.5], in the IBS-M group — 68.0 [59.6; 86.8].

Patients with IBS showed an increase in the content of cortisol in the morning and evening portions of saliva, compared with the control group ($U = 19.5$, $p < 0.001$ and $U = 111.5$, $p < 0.001$, respectively). The mean salivary cortisol level among patients with IBS was 45.39 [29.86; 70.10] ng/ml in the morning and 19.21 [13.98; 23.50] ng/ml in the evening. The mean salivary cortisol level in the group of healthy individuals was 19.0 [16.5; 21.7] ng/ml in the morning and 9.7 [8.5; 10.5] ng/ml in the evening. A higher level of cortisol in the morning is physiological, however it should be noted excessive reactivity in relation to the production of morning (basal) cortisol in patients with IBS included in our study.

It is known that stress and autonomic dysfunction of the nervous system are closely related to the development of IBS through the activation of the hypothalamic-pituitary-adrenal system [15–18]. Under the influence of various physical or psychological stimuli, the secretion of the hormone cortisol by the adrenal cortex increases, which regulates the body's response to stress, visceral sensitivity and motility at the level of the colon [16, 17]. It has been established that cortisol stimulates the immune response along the Th2 pathway in the colon mucosa, resulting in an increase in the number of mast cells [19, 20]. Histamine, serotonin and proteases released during mast cell degranulation cause excitation of afferent neurons of the enteric nervous system and development of gastrointestinal symptoms [21, 22].

In our study the secretion of morning and evening cortisol in the subjects of the main group increased with the severity of IBS (Table 1).

Of particular interest is the analysis of the ratio of levels of morning and evening cortisol. Among persons in the control group it is 1.96, which is comparable to that among patients with mild IBS — 1.9. As the severity of IBS increases the ratio increases to 2.87 for moderate IBS and 3.45 for severe IBS. This indicates a violation of the mechanisms of regulation of the production of stress hormones with maximum reactivity in people with severe IBS.

When comparing patients with IBS by groups, depending on the subtype of the disease, the highest level of morning (basal) and evening (stress) cortisol was found in patients with IBS-D (Table 2).

When analyzing eating habits, it turned out that people with high levels of cortisol in saliva

Table 1. The average content of cortisol in the morning and evening portion of saliva among patients with IBS depending on the severity of the disease and in healthy individuals

Таблица 1. Среднее содержание кортизола в утренней и вечерней порции слюны среди пациентов с СРК в зависимости от степени тяжести заболевания и у здоровых лиц

Group Группа	Morning cortisol, ng/ml Кортизол утро, нг/мл	Evening cortisol, ng/ml Кортизол вечер, нг/мл
Mild course Легкое течение	30.03 [25.45; 38.16]	15.80 [11.75; 19.29]
Moderate course Среднетяжелое течение	59.32 [40.57; 71.79]	20.67 [15.22; 25.31]
Severe course Тяжелое течение	84.09 [65.76; 94.10]	24.40 [19.31; 32.46]
Healthy individuals Здоровые лица	19.00 [16.50; 21.70]	9.70 [8.50; 10.50]

Note: differences between groups are statistically significant $H = 56.18$, $p < 0.001$ for the morning portion and $H = 28.95$, $p = 0.03$ for the evening portion.

Примечание: различия между группами статистически значимы. $H = 56,18$, $p < 0,001$ для утренней порции и $H = 28,95$, $p = 0,03$ для вечерней порции.

have an addiction to salty foods ($\chi^2 = 4.10$, $p = 0.043$) and spicy snacks ($\chi^2 = 4.65$, $p < 0.001$), which also contain excess salt. Perhaps this is due to the fact that an increase in the content of cortisol during activation of the hypothalamic-pituitary-adrenal system under conditions of chronic stress is associated with an increase in Na excretion in the urine, which leads to hyponatremia and the emergence of a physiological need to replenish electrolyte reserves in the body [23].

High levels of cortisol in the morning portion of saliva in the IBS-D group correlated with the severity of the disease ($r_s = 0.682$, $p < 0.005$), higher anxiety scores on the HADS-A subscale ($r_s = 0.697$, $p < 0.001$), higher index VSI ($r_s = 0.708$, $p < 0.001$) and lower quality of life according to the IBS-QoL questionnaire ($r_s = -0.496$, $p < 0.05$).

When assessing the level of serotonin in the blood serum, the indicators in the main group

were statistically significantly higher than those in the control group ($U = 269.0$, $p = 0.042$). The mean value among patients with IBS was 188.78 [150.41; 230.32] ng/ml, among healthy individuals — 142.80 [130.52; 154.15] ng/ml.

Serotonin (5-hydroxytryptamine or 5-HT) is synthesized in enterochromaffin cells of the intestine and combines the properties of a hormone and a neurotransmitter [24]. 5-HT provides a link between the central nervous system and the enteric nervous system of the intestine, and is necessary for the normal functioning of the digestive tract [25]. Impaired 5-HT synthesis is associated with activation of mucosal immune cells, increased permeability of the intestinal epithelial barrier, development of visceral hypersensitivity, and changes in colonic motility [26, 27]. It is also interesting that 5-HT plays an important role in determining quorum sensing (QS), a signaling mechanism for how gut bacteria interact with each other. Dysfunction

Table 2. The average content of cortisol in the morning and evening portion of saliva among patients with IBS depending on subtype of the disease and in healthy individuals

Таблица 2. Среднее содержание кортизола в утренней и вечерней порции слюны среди пациентов с СРК в зависимости от подтипа заболевания и у здоровых лиц

Group Группа	Morning cortisol, ng/ml Кортизол утро, нг/мл	Evening cortisol, ng/ml Кортизол вечер, нг/мл
IBS-D СРК-Д	62.48 [36.49; 87.03]	21.30 [15.03; 29.40]
СРК-З IBS-C	32.39 [26.03; 54.41]	15.70 [10.73; 19.36]
IBS-M СРК-СМ	53.84 [33.39; 69.62]	19.90 [16.87; 23.80]
Healthy individuals Здоровые лица	19.00 [16.50; 21.70]	9.70 [8.50; 10.50]

Note: differences between all groups are statistically significant $H = 45.96$. $p < 0.001$ for the morning portion and $H = 38.42$, $p = 0.02$ for the evening portion.

Примечание: различия между группами статистически значимы. $H = 45.96$. $p < 0.001$ для утренней порции и $H = 38.42$, $p = 0.02$ для вечерней порции.

of the serotonin pathway can potentially change the composition of the intestinal microbiota and determine the nature and severity of IBS [28].

Statistically significant differences were found in the analysis of serotonin levels in groups by IBS subtypes ($H = 72.63$, $p < 0.001$). The highest level was found among patients with IBS-D — 235.50 [205.47; 293.05] ng/ml, the lowest among patients with IBS-C — 123.01 [109.02; 150.72] ng/ml. The average content of serotonin in blood serum in patients with IBS-M was 200.35 [168.53; 230.32] ng/ml. The average content of serotonin in the blood serum of IBS patients by groups depending on the subtype and among healthy individuals is shown in Figure 1.

Our results are consistent with data from other studies, which reported that increased production of serotonin plays an important role in the pathophysiology of IBS-D [29]. It has been established that serotonin increases the frequency and strength of propulsive bowel contractions through stimulation of 5HT3 receptors [30]. One of the evidences for the role of excessive secretion of serotonin in the development of IBS-D is the proven efficacy of the 5-HT3 receptor antagonist alosetron in women with IBS-D [31, 32].

There were no statistically significant differences in serotonin levels between groups of patients with IBS depending on the severity of the disease ($H = 6.29$, $p = 0.3049$). However, the

increase in serotonin levels with increasing severity of IBS was statistically significant in the group of patients with IBS-D ($H = 65.29$, $p < 0.001$). The lowest serum serotonin content in the group of patients with IBS-C was observed in patients with a severe course of the disease — 96.88 [76.24; 105.80] ng/ml and this was significantly lower not only compared with patients with mild and moderate IBS-C ($H = 20.38$, $p = 0.028$), but also compared with healthy individuals ($U = 304.5$, $p = 0.002$).

Elevated serotonin levels correlated with stool frequency ($r_s = 0.627$, $p = 0.0004$), severity of abdominal pain ($r_s = 0.458$, $p = 0.003$) and with disease severity ($r_s = 0.741$, $p = 0.0001$) among patients with IBS-D.

Patients with low levels of serotonin in the blood serum more often prefer fatty foods ($\chi^2 = 9.89$, $p = 0.002$), eat meat and meat products less often ($\chi^2 = 11.25$, $p = 0.027$). It is known that fats inhibit the synthesis of serotonin, while proteins stimulate being a source of the essential amino acid L-tryptophan, which is necessary for the synthesis of 5-HT [33]. In addition, it has been shown that a decrease in the intake of tryptophan with food is accompanied by a decrease in the number of bacteria of the genus *Lactobacillus* [34]. These bacteria are the main producers of short-chain fatty acids, the decrease in the content of which is associated with

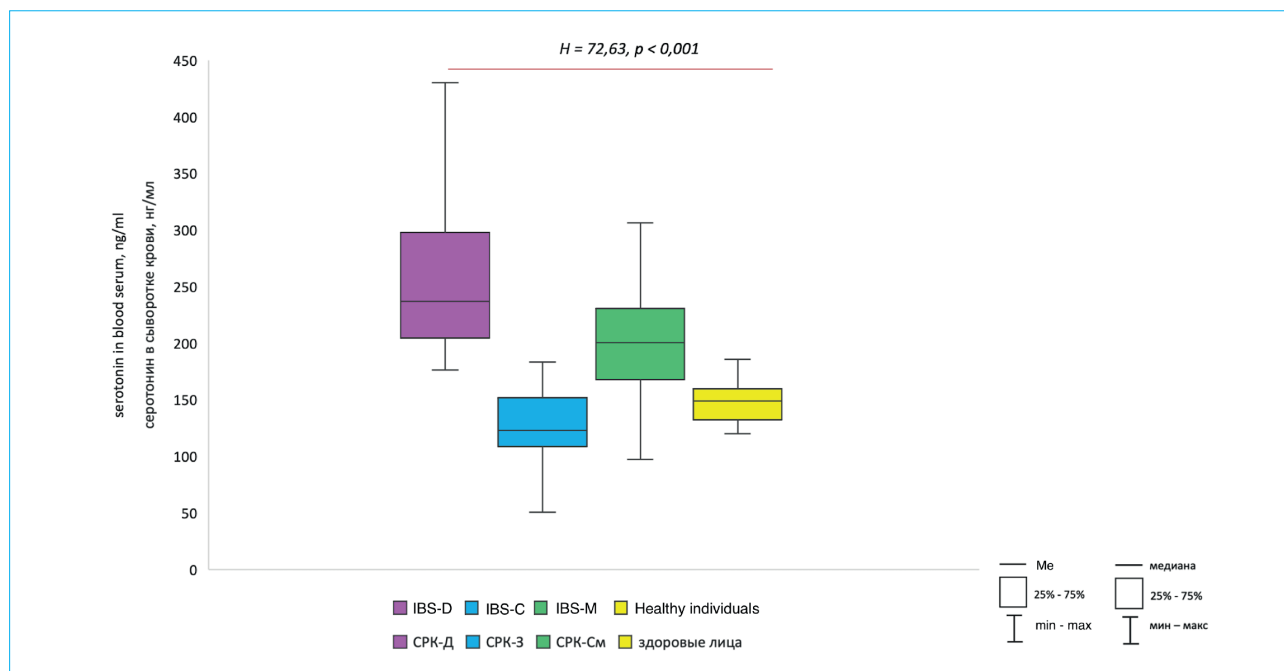


Fig. 1. The average content of serotonin in the blood serum of patients with IBS by groups depending on subtype of the disease and among healthy individuals

Рис. 1. Среднее содержание серотонина в сыворотке крови пациентов с СРК по группам в зависимости от подтипа заболевания и среди здоровых лиц

the development of visceral hypersensitivity and motor disorders in patients with IBS [35].

In our study patients with IBS also had a statistically significantly lower level of dopamine in blood plasma — 28.83 [20.08; 41.54] ng/ml than in healthy individuals — 58.20 [48.15; 66.62] ng/ml ($U = 93.5$, $p = 0.0002$). The data obtained do not contradict the results of other studies, which show that patients with IBS are characterized by a reduced level of dopamine in blood plasma and urine [36, 37] and the use of levodopa or dopamine agonists improves both gastrointestinal and extraintestinal symptoms of IBS [38]. It is known that dopamine a precursor of norepinephrine and adrenaline is an excitatory neurotransmitter of the central nervous system associated with the perception of chronic pain and the development of depression [39, 40]. Research in the field of physiology shows that dopaminergic mechanisms are also important in the regulation of the motility of the digestive tract [41]. In humans, dopamine inhibits upper intestinal motility but stimulates colonic motility. These opposing effects on motility suggest the presence of heterogeneous populations of dopaminergic receptors along the digestive tract. It has been established that the inhibitory effect of dopamine is realized by acting on D1 receptors of smooth muscle cells that regulate muscle relaxation and dopamine receptors on postganglionic cholinergic neurons, where it prevents the release

of acetylcholine. Stimulating effect is mediated by D2 receptors on presynaptic postganglionic sympathetic neurons, where dopamine inhibits the release of noradrenaline [42].

When comparing indicators depending on the subtype of IBS a statistically significantly lower level of dopamine in blood plasma was obtained among patients with IBS-C — 19.55 [11.38; 25.88] ng/mL ($H = 84.51$, $p < 0.001$). The average content of dopamine in blood plasma among patients with IBS-M was 30.10 [23.78; 39.98] ng/ml, among patients with IBS-D — 42.29 [30.63; 52.12] ng/ml. The average content of dopamine in blood plasma among patients with IBS by groups depending on the subtype of the disease and among healthy individuals is shown in Figure 2.

The data available in the literature on changes in the content of dopamine in various clinical variants of IBS are rather contradictory. There are studies demonstrating a decrease in dopamine levels among patients with IBS-C [37] and there are studies that report a significant increase in dopamine levels in patients with IBS-C [43].

In our study plasma dopamine levels decreased with increasing disease severity ($H = 70.22$, $p < 0.001$). The average content of dopamine in the blood plasma among patients with IBS depending on the severity of the course of the disease and among healthy individuals is shown in Figure 3.

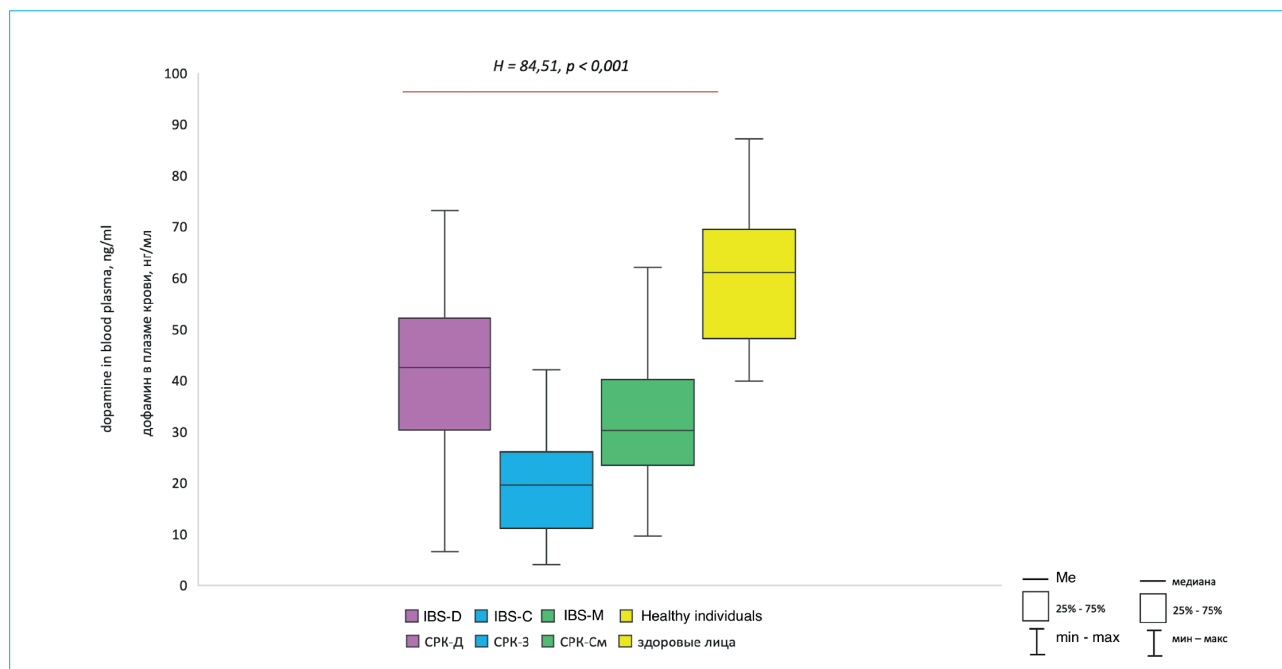


Fig. 2. The average content of dopamine in the blood plasma of patients with IBS by groups depending on subtype of the disease and among healthy individuals

Рис. 2. Среднее содержание дофамина в плазме крови пациентов с ЦРК по группам в зависимости от подтипа заболевания и среди здоровых лиц

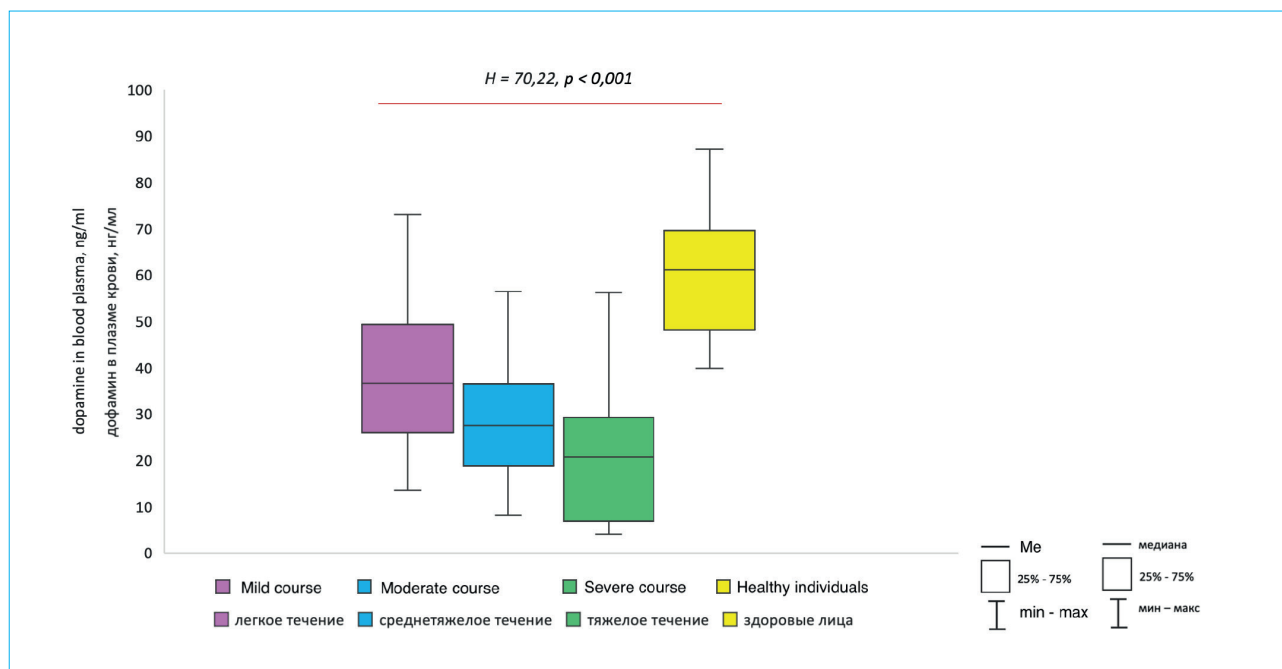


Fig. 3. The average content of dopamine in the blood plasma of patients with IBS by groups depending on severity of the disease and among healthy individuals

Рис. 3. Среднее содержание дофамина в плазме крови пациентов с СРК по группам в зависимости от степени тяжести заболевания и среди здоровых лиц

This pattern persisted in the IBS-C group ($H = 80.76$, $p < 0.001$), where among patients with mild course the plasma dopamine content was 25.44 [21.72; 30.63] ng/ml, moderate course – 14.89 [11.20; 20.20] ng/ml, severe course – 5.00 [4.06; 6.00] ng/ml.

An inverse correlation was found between the level of dopamine in the blood plasma with the severity of IBS ($r_s = -0.392$, $p = 0.005$), the severity of abdominal pain ($r_s = -0.364$, $p = 0.02$) and the severity of depression according to the HADS-D ($r_s = -0.548$, $p = 0.0004$). In addition, low dopamine levels correlated with lower quality of life on the IBS-QoL questionnaire ($r_s = 0.348$, $p < 0.05$).

When analyzing eating habits it turned out that patients with low plasma dopamine levels are characterized by cravings for sweets ($\chi^2 = 7.32$, $p = 0.012$) and confectionery ($\chi^2 = 8.35$, $p = 0.006$), low consumption of vegetables and fruits ($\chi^2 = 17.28$, $p < 0.001$), fish and seafood ($\chi^2 = 14.49$, $p = 0.002$). Moreover, they more often noted the presence of episodes of overeating ($\chi^2 = 22.51$, $p < 0.001$) and heavy meals in the evening hours ($\chi^2 = 19.04$, $p < 0.001$).

It has been found that dopamine deficiency can promote compensatory overeating to activate the reward system [44] and that carbohydrate-rich foods stimulate dopamine release [45]. It is also interesting to note that omega-3 polyunsaturated fatty acids (ω -3 PUFAs) found in fish and seafood

can modulate key properties of cell membranes and the function of transmembrane proteins [46]. Whereas a decrease in the content of ω -3 PUFA in the cell membrane is associated with a decrease in the formation and rate of oligomerization of dopamine D2 receptors [47], which play a role in the development of depressive disorders and are involved in the regulation of digestive tract motility.

Conclusions

1. Patients with IBS showed a significant increase in the level of cortisol in saliva both in the morning and in the evening portion. Cortisol secretion increased with the severity of the disease and was most pronounced in the IBS-D group, where it correlated with the severity of anxiety according to the HADS scale, a high level of specific gastrointestinal anxiety according to the VSI questionnaire and a low quality of life according to the IBS-QoL questionnaire. In addition, people with high levels of cortisol in saliva showed an addiction to salty foods and spicy snacks.

2. In patients with IBS an increase in the level of serotonin in the blood serum was revealed. The highest serum serotonin level was observed in the IBS-D group. Serotonin levels correlated with stool frequency and severity of abdominal pain, and in patients with IBS-D, also

with disease severity. In the IBS-C group a statistically significantly lower level of serotonin was observed in patients with a severe course of the disease. Patients with low levels of serotonin in the blood serum more often preferred fatty foods, less often consumed meat and meat products.

3. In patients with IBS a decrease in the level of dopamine in the blood plasma was revealed. The lowest plasma dopamine levels were found in the IBS-C group and in patients with severe disease. Low dopamine levels were associated with the severity of abdominal pain and depression according to the HADS and low quality of life

according to the IBS-QoL questionnaire. Patients with low plasma dopamine levels are characterized by cravings for sweets and confectionery, low consumption of vegetables and fruits, fish and seafood, frequent episodes of overeating and heavy meals in the evening.

Our results indicate a violation of neurohumoral regulation in patients with IBS. The secretion of the stress hormone (cortisol) and neurotransmitters (serotonin, dopamine) is closely related to the nature of nutrition, the level of anxiety and depression and determines the clinical variant and severity of the disease.

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