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O.Yu. Belousova[1], Vaidotas Urbonas[2], L.V. Kazarian[1]

The influence of serotonin on the formation of clinical symptoms of functional gastrointestinal disorders in children

[1]Kharkov National Medical University, Ukraine
[2]Vilnius University, Faculty of Medicine Institute of Clinical Medicine Clinic for Children's Diseases

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According to the Rome IV consensus (2016), functional gastrointestinal disorders (FGIDs) are disorders of the interaction between the gut and the brain. A crucial role in the realization of this mechanism is played by the key neurotransmitter serotonin.

Aim — to investigate the influence of serotonin on the formation of clinical symptoms in children with FGIDs.

Materials and methods. Under observation were 72 children aged 10–18 years with FGIDs. The Group I consisted of 30 children with combined functional dyspepsia (FD) and irritable bowel syndrome (IBS), the Group II included 42 children with FD. A control group of 20 healthy children was established. The diagnosis of FD and IBS was established based on the analysis of clinical symptoms according to the Rome IV criteria (2016). The severity of clinical symptoms was assessed using the Likert scale from 0 to 5 points. The study of serotonin content in whole blood was conducted using a fluorometric method after adsorption on carboxymethylcellulose.

Results. The intensity of abdominal pain and the severity of dyspeptic syndrome in children with combined FD and IBS is higher than in children with FD ($p<0.01$; $p<0.05$, respectively). The serotonin content in whole blood in children with FGIDs is lower than in healthy children ($p<0.001$). In children with combined FD and IBS, the serotonin content is lower than in children with FD ($p<0.05$). Reverse correlation links were found between serotonin content and the intensity of pain syndrome ($r=-0.7$), the severity of dyspeptic syndromes ($r=-0.5$), constipation ($r=-0.7$), and diarrhea ($r=0.7$).

Conclusions. The obtained research results indicate the influence of serotonin on the formation of clinical symptoms in children with FD and combined FD and IBS.

The research was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Local Ethics Committee of the participating institution. The informed consent of the patient was obtained for conducting the studies.

No conflict of interests was declared by the authors.

Keywords: functional gastrointestinal disorders, functional dyspepsia, combined functional dyspepsia and irritable bowel syndrome, children, serotonin.

Вплив серотоніну на формування клінічних симптомів функціональних шлунково-кишкових розладів у дітей

О.Ю. Бєлоусова[1], Vaidotas Urbonas[2], Л.В. Казарян[1]
[1]Харківський національний медичний університет, Україна
[2]Вільнюський університет, медичний факультет Інституту клінічної медицини клініки дитячих хвороб

Відповідно до Римського консенсусу IV (2016), функціональні шлунково-кишкові розлади (FGIDs) — це розлади взаємодії між кишечником і мозком. Вирішальну роль у реалізації цього механізму відіграє ключовий нейромедіатор серотонін.

Мета — вивчити вплив серотоніну на формування клінічних симптомів у дітей із FGIDs.

Матеріали та методи. Під спостереженням перебували 72 дитини віком 10–18 років із FGIDs. Першу дослідницьку групу становили 30 дітей із поєднаною функціональною диспепсією (ФД) та синдромом подразненого кишечника (СПК), другу — 42 дитини з ФД. До контрольної увійшло 20 здорових дітей. Діагноз ФД і СПК встановлювали на підставі аналізу клінічних симптомів за IV Римськими критеріями (2016). Виразність клінічних симптомів оцінювали за шкалою Лайкерта від 0 до 5 балів. Дослідження вмісту серотоніну в цільній крові проводили флюорометричним методом після адсорбції на карбоксиметилцелюлозі.

Результати. Інтенсивність абдомінального болю та вираженість диспептичного синдрому в дітей із поєднаною ФД і СПК є вищими, ніж у дітей із ФД ($p<0,01$; $p<0,05$, відповідно). Вміст серотоніну в цільній крові дітей із FGIDs нижчий, ніж у здорових дітей ($p<0,001$). У дітей із поєднаною ФД і СРК вміст серотоніну нижчий, ніж у дітей із ФД ($p<0,05$). Виявлено зворотні кореляційні зв'язки між вмістом серотоніну та інтенсивністю больового синдрому ($r=-0,7$), вираженістю диспепсичних синдромів ($r=-0,5$), закрепів ($r=-0,7$), діареї ($r=0,7$).

Висновки. Отримані результати свідчать про вплив серотоніну на формування клінічної симптоматики в дітей із ФД та поєднанням ФД і СПК.

Дослідження виконано згідно з принципами Гельсінської декларації. Протокол дослідження ухвалено комісією з біоетики вказаної в роботі установи. На проведення дослідження отримано інформовану згоду пацієнтів.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: функціональні шлунково-кишкові розлади, функціональна диспепсія, комбінована функціональна диспепсія та синдром подразненого кишечника, діти, серотонін.

Prevalence of functional gastrointestinal disorders (FGIDs) varies in children aged up to 4 years from 5.8% to 40%, and in children aged 4–18 years from 19% to 40% [11]. According to the Rome IV consensus review of 2016, FGIDs are disorders of the gut-brain interaction [4]. Serotonin plays a significant role in the functioning of the gut-brain axis, acting as a key neurotransmitter at both ends of this axis [12]. Serotonin is a mediator of the metasympathetic part of the autonomic nervous system, as well as a neurotransmitter produced in the brain (5%) and enterochromaffin cells of the intestines (95%). It is stored in platelets and plays an important

role in performing certain functions and reactions of the body [5].

It is known that serotonin acts through numerous types of receptors and plays a role in some nervous and psychological disorders, as well as gastrointestinal dysfunctions. The most common types of receptors in the gastrointestinal tract are 5-HT3, 5-HT4, and 5-HT7 [1]. Serotonin enhances peristalsis and propulsive contractions of the intestines by acting on the 5HT3 receptor, while it reduces motility by acting on the 5HT4 receptor [6,10].

Research results do not provide a clear answer about the nature of serotonin's impact on the formation of clinical symptoms in functional dyspepsia. Reports are conflicting, with some indicating a decrease in blood serotonin levels in patients with functional dyspepsia, while others suggest an increase [2,9]. The influence of the serotonergic system on the clinical course of «overlap syndrome» of irritable bowel syndrome (IBS) and functional dyspepsia (FD), especially in children, remains insufficiently studied.

The ***aim*** of the research — to study the impact of serotonin on the formation of clinical symptoms in children with FGIDs.

Materials and methods of the research

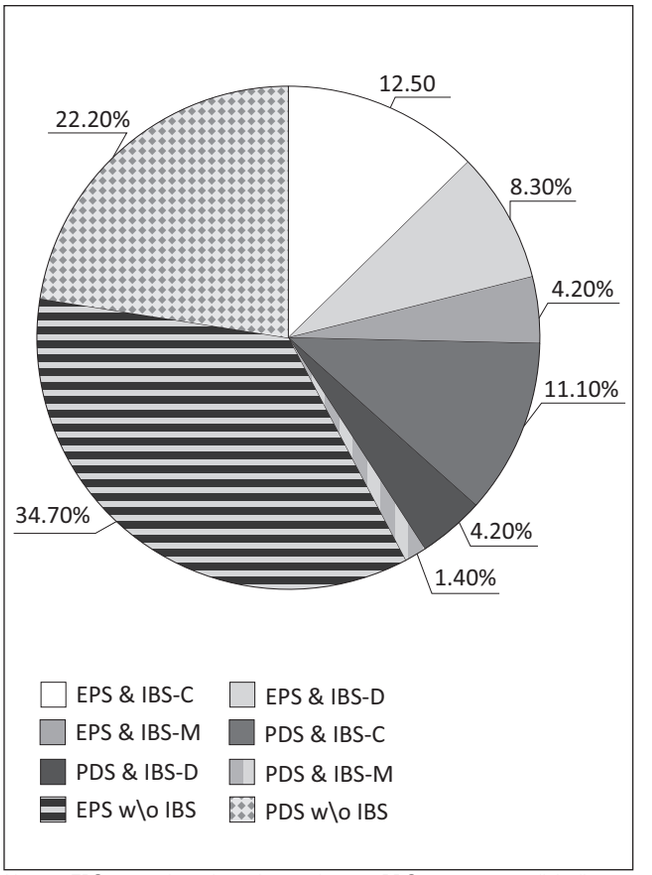
72 children aged 10–18 years with FGIDs were under observation. The Group I comprised 30 children with combined FD and IBS, and the Group II included 42 children with FD. A control group of 20 healthy children was established. The diagnosis of FD and IBS was determined based on clinical symptoms according to the Rome IV criteria (2016) [3]. The severity of clinical symptoms was assessed using the Likert scale: 0 — absence of the symptom, 1 — mild expression (1 point), mild — 2 points, moderate — 3 points, severe — 4 points, and very severe — 5 points [13]. The study of serotonin content in whole blood was conducted using a fluorometric method after adsorption on carboxymethylcellulose [7].

Statistical data processing was performed using the SPSS 19.0 software package. The statistical analysis was conducted using both quantitative and qualitative variables. Qualitative data were presented as percentages, while quantitative data were presented as mean and standard error (M±m). The Student's t-test and the χ^2 test were used for comparing indicators in independent samples. The Pearson correlation coefficient was utilized to identify correlation relationships. The critical significance level for testing statistical hypotheses in the study was set at 0.05.

Results of the research and discussion

According to the findings of the conducted study, more than half of the patients with FGIDs were female (55.5%). The average age of the children at the time of examination was 13.1±0.39 years.

Clinical variants of the disease course were identified in children with FGIDs based on the presence of symptoms (Figure 1). In the group of children with FD, 25 (34.7%) patients exhibited epigastric pain syndrome (EPS), and 16 (22.2%) patients had postprandial distress syndrome (PDS). Among children with the «overlap syndrome», EPS symptoms combined with IBS symptoms with a predominance of constipation (IBS-C) were observed in 9 (12.5%) patients, with IBS symptoms with a predominance of diarrhea (IBS-D) in 6 (8.3%) children, and with a mixed form of IBS (IBS-M) in 3 (4.2%) children. In children with PDS, symptoms of IBS-C were present in 8 (11.3%) cases, IBS-D in 3 (4.2%) patients, and only 1 (1.4%) patient exhibited IBS-M.



Notes: EPS — epigastric pain syndrome; PDS — postprandial distress syndrome; IBS-C — predominance of constipation; IBS-D — predominance of diarrhea; IBS-M — mixed form of IBS; w\o — without.

Fig. 1. Variants of the clinical course of FGIDs in children

Table 1

The frequency of dyspeptic symptoms in children with functional gastrointestinal disorders (%)

Dyspeptic symptom	Combined functional dyspepsia and IBS (the Group I) n=30		Functional dyspepsia (the Group II) n=42	
	N	%±m	n	%±m
Feeling of fullness after eating	8	18.2±5.8	16	24.2±5.3
Feeling of early satiety	9	20.5±6.6	10	15.2±4.4
Nausea	19	43.1±7.5	21	31.8±5.7
Belching	15	34.1±7.1*	6	9.1±3.5
Abdominal bloating	14	31.8±7.2*	7	10.6±3.8
Vomiting	4	9.1±4.3	8	12.1±4.0
Hiccup	6	13.6±5.2	11	16.6±4.6

Note: * — statistically significant difference (p<0.05) between the indicators of the Group I and the Group II.

Table 2

The serotonin levels in the blood of children depending on the clinical variant of functional dyspepsia and the «overlap syndrome» of functional dyspepsia and social-psychological correction (μmol/L)

IBS variants	Combined FD and IBS N=30		FD N=42		Control Group N =20
	EPS n=18	PDS n=12	EPS n=26	PDS n=16	
IBS-C	1.22±0.02***,##	1.15±0.03**,^	1.36±0.02*	1.37±0.02*,3)	1.47±0.02[4)]
IBS-D	1.33±0.02*	1.22±0.01**,^^			
IBS-M	1.26±0.03*,#	–			

Notes: 1) difference in indicators compared to the control group: * — p<0.05; ** — p<0.01; *** — p<0.001; 2) difference in indicators in children with SEB in the Groups I and II: # — p<0.05; ## — p<0.01; 3) difference in indicators in children with PPDS in the Groups I and II: ^ — p<0.05; ^^ — p<0.01; 3) the average serotonin level in the blood of children with EPS; 4) the average serotonin level in the blood of children with PDS.

One of the main symptoms of FGIDs was abdominal pain. All children in the Group I complained of pain of varying localization (100%), while in the Group II, this symptom was noted in 35 (83.3±5.8%) children (p<0.05). The intensity of abdominal pain on the Likert scale in the Group I reached 2.7±0.13 points, which exceeded the corresponding indicator in the Group II (1.2±0.15 points) (p<0.01).

Among the dyspeptic symptoms characteristic of FD, children in both groups complained equally about a feeling of early satiety (p>0.05) and a feeling of fullness in the postprandial period (p>0.05) (Table 1). Among the additional symptoms in children, nausea, vomiting, hiccups were noted, and their frequency did not differ between the groups (p>0.05). Belching and meteorism were likely more frequently observed in children in the Group I (p<0.05).

Despite the fact that most of the dyspeptic symptoms occurred with equal frequency in the groups, the severity of the disease course was higher in the group of children with combined pathology. The severity of the dyspeptic syndrome according to the Likert scale in the Group I was 2.13±0.14 points, which exceeded this indicator in the Group II (1.26±0.17 points) (p<0.05).

The severity of the clinical course in children of the Group I was also influenced by the presence of bowel disorders: constipation was observed in 17 (56.6%) patients, and diarrhea in 9 (30%) patients. A mixed form of bowel disorder was noted in 5 (13.3%) children.

The average serotonin level in the blood of children with FGIDs was 1.31±0.01 μmol/L, which was significantly lower compared to the control group's 1.47±0.02 μmol/L (p<0.001). Reverse correlation relationships were found between the serotonin content in the blood of children with FGIDs and the intensity of abdominal pain (r=-0.8), as well as between the serotonin content in the blood and the severity of the dyspeptic syndrome (r=-0.5).

In children with FD and IBS, the average serotonin level in the blood was 1.22±0.1 μmol/L, which was likely lower than in the control group (1.47±0.02 μmol/L) (p<0.001) and in children with FD alone (1.36±0.02 μmol/L) (p<0.05). In the Group I children, a reverse correlation relationship was found between the serotonin content in the blood and the severity of constipation (r=-0.7), and a positive correlation was found with the severity of diarrhea (r=0.7).

Serotonin level was studied in children with different variants of functional dyspepsia and «overlap syndrome» of FD and IBS (Table 2).

As seen from Table 2, in all variants of the «overlap syndrome», the blood serotonin level

is lower than in children with FD without the «overlap syndrome». It is noteworthy that regardless of the clinical variant of FD accompanied by IBS symptoms, the serotonin level was more decreased in children with constipation compared to those with diarrhea.

Literature contains conflicting data regarding the serotonin content in the whole blood of children with functional gastrointestinal symptoms. Our obtained results demonstrate a decrease in blood serotonin levels in children with FGIDs compared to healthy children, which is consistent with some literature findings [2]. We confirmed that in children with the «overlap syndrome», serotonin levels are decreased to a greater extent than in children with functional dyspepsia, correlating with the greater severity of clinical symptoms. Our findings also align with literature suggesting varying effects of serotonin on different types of bowel disorders in children [8,14,]. We found that in children with combined FD and IBS, blood serotonin levels are lower in those with constipation than in those with diarrhea.

Thus, the obtained results support the influence of serotonin on the formation of clinical symptoms in children with FD and the overlap syndrome of FD and IBS.

Conclusions

The course of functional gastrointestinal disorders in children is associated with a reduction in blood serotonin levels, more significantly so in Group I.

The severity of clinical symptoms correlates with blood serotonin levels, confirming its pathogenetic role.

The article is our original work and does not violate the copyrights of others. It has not been previously published or submitted to the editorial board of another journal.

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Відомості про авторів:
Бєлоусова Ольга Юріївна — д.мед.н., проф., зав. каф. педіатрії та дитячої гастроентерології ННІПО Харківського НМУ. Адреса: м. Харків, вул. пр. Науки, 4; тел./факс: +38 (057) 707 72 93. https://orcid.org/0000-0003-4983-1713.
Urbonas Vaidotas — д.мед.н., проф. Клініки дитячих хвороб Інституту клінічної медицини медичного факультету Вільнюського університету, Литва. https://orcid.org/0000-0002-7779-5484.
Казарян Лариса Володимирівна — аспірант каф. педіатрії та дитячої гастроентерології ННІПО Харківського НМУ. Адреса: м. Харків, пр. Науки, 4. https://orcid.org/0000-0002-4286-5606.
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