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SOME INDICES OF METABOLISM IN CHILDREN WITH IRRITABLE BOWEL SYNDROME AND CO-EXISTING OVERWEIGHT

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In this article, we demonstrate the data on clinical course features of irritable bowel syndrome in children of school age with normal weight as well as co-existing overweight. Also, we conducted an assessment of certain indices of lipid and carbohydrate metabolism in these conditions. Clinical features of irritable bowel syndrome with overweight include duration of the disease (6.5±0.5 months), female sex (30 vs. 5 children, χ^2=5.1429, p<0.05), abdominal pain syndrome (85 % vs. 65 %, p<0.05), intermittent diarrhoea and constipation (62.5 % vs. 90 %, p<0.05), and bloating (77.5 % vs. 50 %, p<0.05). Initial signs of impaired carbohydrate metabolism were detected: an increase in the level of C-peptide (4.5±0.01 and 2.5±0.03, p<0.05) and NOMA index (3.41±0.02 and 2.86±0.01, p<0.05). The given data indicate deviations from the norm of the evaluated indicators of certain types of metabolism in school-age children with irritable bowel syndrome and overweight that will be reversible in case of adequate therapy.

Key words: children, irritable bowel syndrome, overweight, faecal calprotectin.

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СТАН ОКРЕМИХ ПОКАЗНИКІВ ОБМІНУ У ДІТЕЙ ІЗ СИНДРОМОМ ПОДРАЗНЕНОГО КИШЕЧНИКА ТА НАДЛИШКОВОЮ ВАГОЮ

В статті наведені дані про особливості перебігу синдрому подразненої кишки у дітей шкільного віку, на тлі нормальної та надлишкової маси тіла, а також проведено оцінку окремих показників ліпідного та вуглеводного обмінів при цій патології. Встановлено, що до клінічних особливостей обстежуваних дітей належать: тривалість (6,5±0,5 місяців), жіноча стать (30 і 5 дітей, χ^2=5,1429, p<0.05), больовий абдомінальний синдром (85 % і 65 %, p<0,05), чергування діареї та закрепу (62,5 % і 90 %, p<0,05) та метеоризм (77,5 % і 50 %, p<0,05). Інтенсивність больового синдрому була вищою у групі дітей із надлишковою масою тіла (6,5±0,5 і 4,3±0,1 балів, p<0.05). Виявлені початкові ознаки порушення вуглеводного обміну: зростання рівня С-пептиду (4,5±0,01 і 2,5±0,03, p<0.05) та індексу HOMA (3,41±0,02 і 2,86±0,01, p<0.05). Наведені дані свідчать про відхилення від норми показників окремих видів обміну в дітей із синдромом подразненої кишки на фоні надмірної маси тіла, які матимуть зворотній характер за умови адекватної терапії через рік від моменту спостереження.

Ключові слова: діти, синдром подразненої кишки, надлишкова маса тіла, фекальний кальпротектин.

The study is a fragment of the research project “Health state and features of adaptation in children in the Prykarpattya region with somatic disease, and its prevention”, state registration No. 0121U111129.

Functional gastrointestinal (GI) disorders and in particular irritable bowel syndrome (IBS) are one of the biggest concerns in paediatric gastroenterology globally taking into account the prevalence among children of school age (7 till 30 % according to the data of different authors), and its medical and psychosocial burden [1, 2, 7, 8].

At the same time, considering a comprehensive approach to the assessment of some chains of the pathogenesis, and major clinical symptoms of functional gastrointestinal disorders, we would like to note the presence of multiple blank spots in research of this field, especially when concomitant overweight or obesity is present [6, 8].

Based on data by WHO experts and novel research Global Burden of Disease Study (Imperial College London) [6, 7] the overall incidence of overweight in the world during the last three decades has increased by 27.5 % among adults and 47.1 % in children [7, 8]. In experts’ opinion, if the current trend

persists, by the end of 2022 the number of children with overweight will be greater than the number of their peers with healthy body weight [3, 4, 7].

A literature review on this topic showed that the data regarding the clinical course of IBS in children and adolescents with overweight and obesity are lacking [5, 10, 11]. There is not enough focus on the evaluation of metabolic disorders in children with mentioned comorbidities [2, 3, 12].

The purpose of the study was to provide an assessment of clinical course features, and some indices of carbohydrate and lipid metabolism in children of school age with irritable bowel syndrome in the setting of overweight.

Materials and methods. We examined 80 children aged 7 to 17 years with irritable bowel syndrome (IBS) who were hospitalised in the Public Nonprofit Enterprise "Ivano-Frankivsk Regional Children`s Clinical Hospital of Ivano-Frankivsk Oblast Council" during 2017–2022 years. The control group included 30 children of the same age.

The diagnosis of irritable bowel syndrome was verified according to the Order of the Ministry of Health of Ukraine No. 59 "On Adoption of Unified Clinical Protocols of Medical Care for Children with Digestive Disorders", and Rome IV Criteria (2016) [13]. As the main sign of the stool shape, we took the Bristol Stool Scale [7, 8, 14].

The overweight was diagnosed due to Order of the Ministry of Health of Ukraine No. 55 "On Adoption of Treatment Protocols of Children with Endocrine Disorders" (https://www.cdc.gov/growthcharts/clinical_charts.htm).

The severity evaluation of clinical signs of irritable bowel syndrome was made regarding the total score (each symptom assessed from 0 to 3) made by us. These are: pain in the umbilical area and along the colon, bloating, the prevalence of constipation or diarrhoea, intermittent disorders of defaecation.

Interpretation: if the total score is 0 to 2, the overall symptom expression is low, 3 to 5 corresponds to high expression, and 5 to 10 corresponds to very high expression of the symptoms.

Study inclusion criteria: consent of the patient, and parents; confirmed diagnosis of irritable bowel syndrome and overweight.

Criteria of non-inclusion: anaemia, increased ESR, inflammatory changes in the full blood count, body weight loss within the last three weeks, melena and other particles in the stool, and epidemiological history (contact with SARS-CoV-2, parasitic or acute bowel infection in a patient).

We noninvasively quantified the level of the biomarker such as faecal calprotectin (method of the solid-phase immune enzyme assay in the laboratory "DILA", the reference age range (after three years of age) is below 50 mcg/gram).

We also assessed glucose and glycated haemoglobin levels in the blood of the examined children (analyzer and test-system Cobas 6000, Roche Diagnostics (Switzerland). The reference value for glycated haemoglobin is 4.8-5.9 %, and for the glucose in the capillary blood it is 3.38-5.55 mmol/L. We calculated the insulin resistance index using the standard formula: HOMA-IR=fasting insulin level x fasting glucose/22.5.

The concentration of the blood lipids was determined via the enzymatic colourimetric method using the reagents "SpineLab" (total cholesterol, cat. No.: 4.010–100 mL; HDL-cholesterol, cat. No.: 4.008-100 mL; triglycerides, cat. No.: 4.012-100 mL).

The examined children were randomized into two groups. The first group included 40 children of school age with IBS and normal weight (n=40), and the second one included 40 children with the same diagnosis and overweight (n=40). The control consisted of 30 virtually healthy children of the same age.

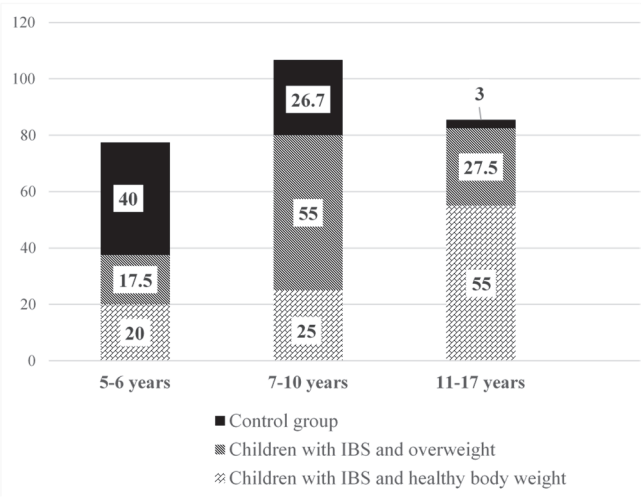

Fig. 1. Age structure of the examined patients with IBS and the control group, n=110

The main principles of bioethics were maintained by: the informed parental consent, the Declaration of Helsinki of The World Medical Association "Ethical Principles for Medical Research Involving Human Subjects" (USA).

Statistical result processing was conducted using a program package for general use Statistics for Windows version 6.0 (Stat Soft inc., USA).

Results of the study and their discussion. The duration of the underlying disease till the moment of admittance to the hospital was 6.5±0.5 months.

The age distribution looks like the following (Fig. 1).

As indicated by the obtained data, the rate of irritable bowel syndrome increases with the growing age. However, these data were not statistically significant.

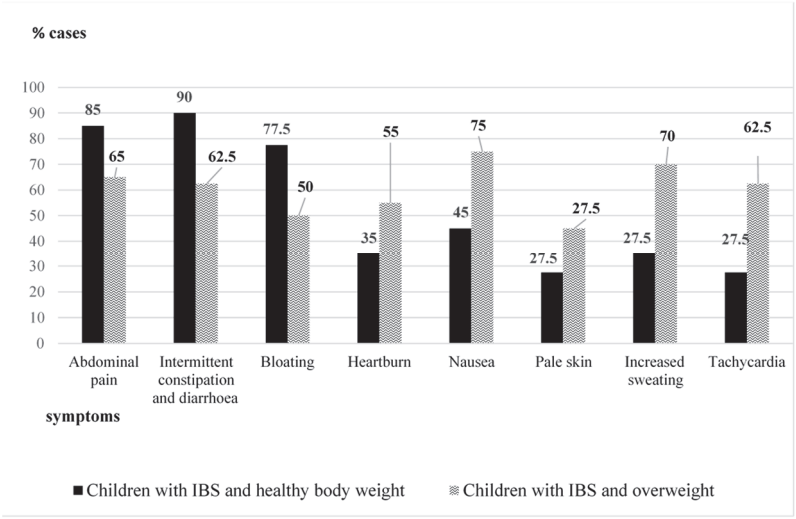

Fig. 2. The most common symptoms of IBS in children with normal weight and overweight, n=80

We have analysed the major clinical symptoms of irritable bowel syndrome in children with normal body weight and in those with overweight (Fig. 2).

The obtained results demonstrate that clinical features of IBS with overweight when compared to those with healthy weight range include: abdominal pain (85 % vs. 65 %, $p<0.05$), intermittent diarrhoea and constipation (62.5 % vs. 90 %, $p<0.05$) and bloating (77.5 % vs. 50 %, $p<0.05$).

The grade of abdominal pain that is mostly localised in the periumbilical area was more severe in children with overweight (6.5±0.5 vs. 4.3±0.1 points, $p<0.05$). Dyspepsia, in particular bloating (5.2±0.1 vs. 2.5±0.2 points, $p<0.05$), intermittent diarrhoea and constipation (5.8±0.2 vs. 3.2±0.1 points, $p<0.05$), were more intense in the second group of the examined patients.

We studied the correlation of IBS occurrence in children of the school age depending on overweight. The show that the risk of getting IBS was higher in children with overweight compared to patients with healthy body weight (35 vs. 5 CI 5.93± %; OR 1.09; RR 1.04).

The level of faecal calprotectin during the follow-up period is demonstrated in Fig. 3.

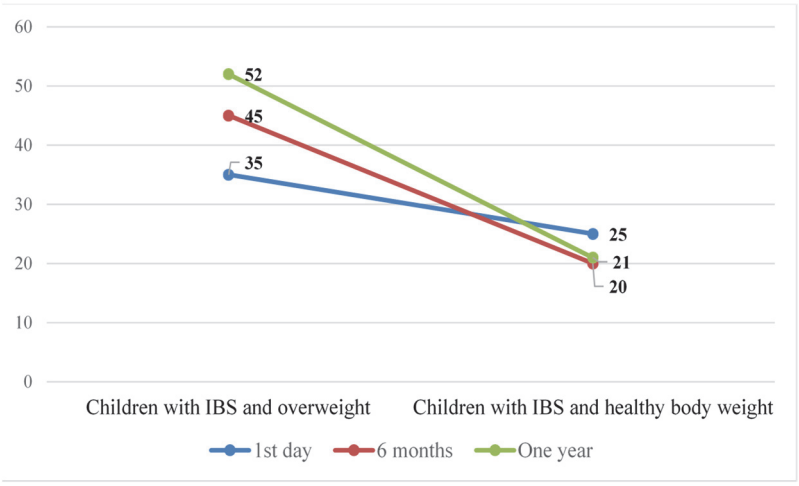

Fig. 3. The level of faecal calprotectin during the one-year follow-up, n=110

The data in the graph show that in patients with IBS and overweight after one year of the follow-up, there is a mildly elevated level of faecal calprotectin compared to reference values. Thus, this cohort of children is at risk of intestinal inflammation and should be monitored thoroughly. To evaluate some indices of carbohydrate metabolism, we measured glucose levels and glycated haemoglobin in the blood of school-age children with normal weight and those with overweight (Table 1).

Table 1

Some indices of carbohydrate metabolism in children with IBS and normal weight or co-existing overweight, n=110 (M±m)

Parameters	Healthy subjects (n=30)	Examined children (n=80)	
		Children with IBS and overweight (n=40)	Children with IBS (n=40)
Plasma glucose, mmol/L	4.45±0.09	5.24±0.01*	5.01±0.14**
Glycated hemoglobin in blood, %	4.9±0.02	6.6±0.05*	5.1±0.02**
Insulin, mcU/mL	3.9±0.06	5.5±0.05*	4.0±0.02**
HOMA Index	2.86±0.01	3.41±0.02*	2.95±0.02**
C-peptide, ng/mL	2.5±0.03	4.5±0.01*	1.8±0.03**

Note: *Statistical significance of differences between the parameters in children with IBS vs. healthy children ($p<0.05$), ** Statistical significance of differences between the parameters in children with IBS and overweight vs. patients with normal weight vs. healthy children ($p<0.001$).

By the analysis of the data in the Table 3, we would like to point out initial signs of carbohydrate disorders in patients with IBS with co-existing overweight, such as: elevation of C-peptide (4.5±0.01 vs. 2.5±0.03, p<0.05) and HOMA index (3.41±0.02 vs. 2.86±0.01, p<0.05). The latter shows the tendency to the increase of tissue insulin resistance with probable increase of the risk of diabetes mellitus type 2 and cardiovascular events in the future. At the same time, plasma glucose and glycated haemoglobin levels in the examined patients were maintained within the normal range.

We conducted the assessment of blood lipid profile in patients with IBS and control group (Table 2).

Table 2

Indices of lipid metabolism in children with IBS and normal weight or co-existing overweight, n=110

Parameters	Healthy subjects (n=30)	Examined children (n=80)	
		Children with IBS and overweight (=40)	Children with IBS (n=40)
Total cholesterol, mmol/L	2.68±0.09	4.53±0.8*	3.48±0.11**
HDL-cholesterol, mmol/L	1.49±0.05	0.67±0.06*	1.18±0.04**
TG, mmol/L	0.15±0.03	1.36±0.05*	0.89±0.05**
LDL-cholesterol, mmol/L	2.06±0.03	3.09±0.05*	2.38±0.06**
VLDL-cholesterol, mmol/L	0.18±0.01	0.56±0.05*	0.32±0.02**

Note: * Statistical significance of differences between the parameters in children with IBS vs. healthy children (p<0.05), ** Statistical significance of differences between the parameters in children with IBS and overweight vs. patients with IBS and normal body weight (p<0.05)

As indicated by the obtained data, in children with IBS and co-existing overweight there are signs of dyslipoproteinemia due to increased levels of total cholesterol, triacylglycerols, low-density and very-low-density lipoproteins, and the decline of high-density lipoproteins compared to healthy children. Herewith, triglyceride level in children with IBS and co-existing overweight (1.36±0.05 mmol/L) were higher if compared to healthy children (0.15±0.03 mmol/L) and showed 2.7 times higher levels than in the control group. Values of total cholesterol in children with IBS and overweight reached the level of 4.53±0.11 mmol/L and were 1.7 times higher than in the control group (2.68±0.09 mmol/L). This refers also to low-density and very-low-density lipoproteins. In children with IBS and overweight, the level of LDL-cholesterol was 1.5 times higher (3.09±0.05 mmol/L) than in children of the control. As well, the level of VLDL-cholesterol was 3.1 times higher than in healthy children (0.56±0.02 mmol/L). Based on the evaluation of HDL-cholesterol, we concluded that its level was 2.2 times lower in children with IBS and overweight compared to healthy children (0.67±0.06 mmol/L vs. 1.49±0.05 mmol/L, respectively).

It is well known, that functional gastrointestinal diseases, in particular, irritable bowel syndrome, are commonly found in overweight people; but there is scarce data regarding its prevalence in children [5, 7].

However, irritable bowel syndrome seems to be among the leading reasons for the visits to a pediatric gastroenterologist; and appearance of recurrent abdominal pain in early age very often precedes the development of irritable bowel syndrome in adolescent period [8]. Certainly, combination of this illness with obesity worsens clinical course, and quality of patient's life [6].

According to one prospective study, overweight adolescents might have higher rate of admissions to the hospital (20.8 % vs. 7.6 %, p = 0.01), and much more prominent clinics, compared to patients with normal body weight and GIT symptoms [10]. The results of our study also correlate with the data mentioned above, while the frequency of abdominal pain, as we observed, is higher in the group of children with combined pathology (85 % and 65 % cases, p<0.05).

According to obtained results, symptoms of dyspepsia, for instance, flatulence (5.2±0.1 vs. 2.5±0.2 points, p<0.05), intermittent diarrhea and constipation (5.8±0.2 vs. 3.2±0.1 points, p<0.05) usually occur in patients with normal weight. It does not quite correlate with recent scientific literature, which emphasizes the lower frequency of the mentioned clinical symptoms in children with the isolated course of irritable bowel syndrome [8].

There are a lot of risk factors in the origin of irritable bowel syndrome in children and adolescents, such as the gut-brain axis interactions, the influence of stress factors, and the consumption of certain foods and beverages, including alcohol and coffee. [8, 9, 15]. We also consider the overweight to be a prominent risk factor for the development of functional intestinal disorders. Also, we take into account the assessment of nutritional status in a childhood. Our statements are confirmed by the literature data [14].

Sex distribution in our study shows the prevalence of girls among the patients with overweight, unlike in healthy subjects (30 vs. 5 children, χ^2=5.1429, p<0.05), which correlates with the literature data [2, 5]. But we did not find some age features to be a significant factor in development of this illness.

Initial signs of lipid distress syndrome we have revealed in our investigation. It correlates with the studies provided earlier [12].

Conclusions

1. The clinical features of irritable bowel syndrome in children with overweight include: female sex (30 vs. 5 children, χ^2=5.1429, p<0.05), disease duration up to 6.5±0.5 months, prevalence of abdominal pain (85 % vs. 65 %, p<0.05), intermittent diarrhoea and constipation (62.5 % vs. 90 %, p<0.05) and bloating (77.5 % vs. 50 %, p<0.05). Abdominal pain was more severe in children with overweight (6.5±0.5 vs. 4.3±0.1 points, p<0.05). At the same time, dyspepsia, in particular bloating (5.2±0.1 vs. 2.5 ±0.2 points, p<0.05), intermittent diarrhoea and constipation (5.8±0.2 vs. 3.2 ±0.1 points, p<0.05), were more expressed in the second group of the examined patients.

2. In children with IBS in the setting of overweight, initial signs of lipid distress-syndrome were spotted, such as: increased total cholesterol, triacylglycerol, low- and very-low-density lipoproteins along with decline in high-density lipoproteins.

3. There is a slight increase in the level of faecal calprotectin compared to the reference values. It is possible to assign this category of children to the risk group for development of intestinal inflammation, and to focus on more thorough follow-up of this group of patients.

4. In children with irritable bowel syndrome and co-existing overweight, initial signs of impaired carbohydrate metabolism were detected: an increase in the level of C-peptide (4.5±0.01 vs. 2.5±0.03, p<0.05) and NOMA index (3.41±0.02 vs. 2.86±0.01, p<0.05). The given data indicate deviations from the norm of the evaluated indicators of certain types of metabolism in school-age children with irritable bowel syndrome and overweight that will be reversible in case of adequate therapy.

Prospects of further research. Development of clinical management algorithms regarding children with irritable bowel syndrome with overweight aimed at comprehensive risk assessment and prevention of complications.

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