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Analysis of the structure of comorbidity in children with gastrointestinal tract pathologies

Diseases of the gastrointestinal tract take the second place in the structure of somatic pathology in children and adolescents. The number of cases of comorbid pathology also tends to increase. The combination of the most common diseases can be both random and causal relationship, the determination of which is important for improving the health care of the child population.

Objective — to analyse of comorbidities in children with gastrointestinal diseases based on the results of the city specialized children's gastroenterological department work.

Materials and methods. The performance indicators of Kharkiv City Children's Clinical Hospital No19 for the period from 01.01.2019 to 31.12.2019 were studied. During 2019, 2633 children aged 5 to 18 years (average age: 10.6 ± 2.9 years) with diseases of the digestive system were hospitalized.

Results. The presence of comorbidity was established in 73.6% of children. The most common among children with diseases of the gastrointestinal tract were manifestations of diseases of the nervous system — 31.8%. Diseases of the endocrine system — 15.4% and cardiovascular system — 15.7% were equally represented. A fairly common pathological condition in patients with gastrointestinal diseases was anemia, which was established in 8.1%. Visual impairment was found in 2.7% children, which coincides with the prevalence of this pathology among the general children's population.

Conclusions. The leading place is held by the gastroduodenal pathology, notably chronic gastroduodenitis. The presence of comorbidity from other organs and systems was established in 73.6% of children with gastrointestinal diseases. The most common comorbidity in diseases of the gastroduodenal zone are diseases of the nervous system. The greatest chances of combining pathological conditions with the development of comorbid pathology are diseases of the gastroduodenal zone and nervous system, intestines and autoimmune thyroiditis, gastroesophageal reflux diseases and obesity. The results suggest the necessity of additional examination of children with gastrointestinal pathology in order to early diagnosis of comorbidity and provide the required comprehensive assistance.

Keywords: comorbidity, children, diseases of the gastrointestinal tract.

The incidence of diseases of the digestive system gradually increases in the structure of somatic pathology. Nowadays, diseases of the gastrointestinal tract (GIT) have come out on the second place among diseases both the adult population and children and adolescents [4, 6]. A study of children's health in Ukraine over the past decade has also demonstrated an increase in the prevalence of

digestive diseases by 18.6% [4, 9]. Thus, according to the latest statistics data, GIT diseases are 49.97 per 1000 children in Ukraine as a whole, and 52.97 in the Kharkiv region in the structure of morbidity of school-age children [1].

Quite often, patients with gastrointestinal pathology have comorbid or concomitant diseases as digestive as other systems of an organism. This leads

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to a potential interconnection of pathological conditions, which induces the expansion of therapeutic tactics for the management of patients, taking into account multi-organ involvement. The combination of the most common diseases can be accidental and predefined causality relationship, the determination of which is important for improving medical care for the child population [10, 17]. The pathology of the digestive system leads to a significant dysregulation of vitamin-mineral metabolism, reducing in the content of essential and increasing in toxic trace elements, an imbalance of vitamins. These are a significant factors for the formation of endocrine pathology, as a goiter under conditions of mild iodine deficiency [7]. Patients with functional disorders of the GIT (functional dyspepsia, irritable bowel syndrome) quite often have thyroid disorders in the form of structural changes and an alterations in the functional activity of the thyroid gland [7]. Insufficiency of gastromucoprotein secretion during gastrointestinal diseases leads to anemia [14]. According to the literature, patients with gastroesophageal reflux diseases (GERD) are often overweight or diagnosed with obesity [8, 13, 19]. A large number of children with GERD have symptoms of autonomic dysfunction and a predisposition to neurosis [11]. Other diseases are not directly related to gastrointestinal pathology, but they are complicating the general condition of the patient [10]. Studying the variants and prevalence of comorbidities in children with diseases of the digestive system becomes relevant, considering the negative interaction of diseases, the necessity to expand therapy and an individual approach when prescribing treatment.

Objective — to analyse of comorbidities in children with gastrointestinal diseases based on the results of the city specialized children's gastroenterological department work.

Materials and methods

The performance indicators of the Kharkiv City Children's Clinical Hospital No 19 for the period from 01.01.2019 to 31.12.2019 were studied. The time period was chosen taking into account the full load of the medical institution, before the limitations of the working timetable due to the COVID-19 pandemic and wartime in Ukraine. During 2019, 2633 children aged 5 to 18 years (average age: 10.6 ± 2.9 years) with diseases of the digestive system were hospitalized. Diagnoses of diseases were established in accordance with the existing unified clinical protocols of medical care for children with diseases of the digestive system (Order of the Ministry of Health No 59 of 29.01.2013) [3].

The presence of comorbidities was established by the results of an additional examination of patients by a paediatric neurologist, cardio-rheumatologist, ophthalmologist, and endocrinologist. Electrocardiography, ultrasound, electroneurophysiological research was conducted to clarify the state of internal organs.

Mathematical data processing was carried out by the method of variation statistics. The data are verified against the Gaussian normal distribution law data. The frequency indicators of the prevalence of pathological conditions, the reliability of differences according to Fisher's criterion were determined. When comparing two quantities, the difference between them was considered reliable at the achieved level $p < 0.05$.

The criterion of the χ^2 for the quadrilateral conjugate table with the correction for the continuity of the Yates; standard error of chances estimation and its confidence interval was determined to odds ratio (OR) of the development of pathological conditions. For the level of significance (α), when comparing statistical hypotheses, the probability of rejecting the null hypothesis at its correctness of 5% ($\alpha = 0,05$) was accepted.

Results and discussion

The analysis involved the case history of 2633 persons, of which 51.7% (1362) are boys, 48.3% (1271) are girls.

Availability of comorbidities is established in 1939/2633 (73.6%) children. The most common among children with GIT pathologies were manifestations of diseases of the nervous system (NS) — 837/2633 (31.8%). Diseases of the endocrine system (endocrinopathy) — 406/2633 (15.4%) and the cardiovascular system (CVS) — 413/2633 (15.7%) were equally represented. A fairly common pathological condition in patients with gastrointestinal diseases was anaemia, which was established in 213/2633 (8.1%). Visual impairment was found in 70/2633 (2.7%) children, which coincides with the prevalence of this pathology among the general children's population [16].

Patients were divided into groups, according to pathological changes of the GIT to study the structure of comorbidity with consideration of the type of lesions of the gastrointestinal tract. The largest group was patients with gastroduodenal diseases: 1781/2633 (67.64%) (group I, Table). Functional dyspepsia was diagnosed in 763/2633 (28.9%), organic diseases of the organs of the gastroduodenal zone, namely: chronic gastroduodenitis, stomach ulcer and/or duodenal ulcer, in 1018/2633 (57.15%) patients. It should be noted that organic diseases of

the gastroduodenal zone are mostly presented with chronic gastroduodenitis. The group II consisted of children with the bile-duct tract and liver pathology — 759/2633 (28.82 %). The main part in this group was occupied by functional disorders of the gallbladder and sphincter Oddi. In most cases, the detected changes were associated with the anatomical features of the development of the gallbladder. Intestinal diseases were in third place in the structure of gastrointestinal diseases and amounted to 139/2633 (5.27 %) (group III). Gastroesophageal reflux disease (GERD) among hospitalized children was diagnosed in 62/2633 (2.35 %) (group IV).

In children with the gastroduodenal zone's pathology diseases of the nervous system 628/1781 (35.3 %) and anemia 154/1781 (8.6 %) were significantly more common than in patients with other gastrointestinal lesions. Thus, the chances of stratification of neurological disorders in children from this group are almost 5 times higher than in children with

intestinal diseases 14/139 (10.1 %) (OR 4.86; 95 % CI 2.78–8.52, $p = 0.000$). The chances of developing anemia were significantly higher than in patients with diseases of the biliary tract and liver 42/759 (5.5 %) (OR 1.62; 95 % CI 1.14–2.30, $p = 0.009$) respectively. This emphasizes quite significant shifts in homeostasis even in functional gastrointestinal disorders in childhood, given the multifactorial pathogenesis of anemia in children [18].

The chances of comorbidity in children with diseases of the biliary tract and liver 480/759 (63.2 %) were 3 times higher than in patients with bowel disease 45/139 (32.4 %) (OR 3.59; CI 2.43–5.24, $p = 0.000$). Among the comorbidities, diseases of the endocrine 152/759 (20.0 %) and nervous 183/759 (24.1 %) systems were a priority. So, the chances of nervous system functioning disorders in children from this group were almost three times higher than in patients with intestinal diseases 14/139 (10.1 %) (OR 2.84; 95 % CI 1.59–5.05,

Table. Structure of comorbidity in children with GIT diseases

Comorbidities number/frequency	In general (n = 2633)	Group I (n = 1781)	Group II (n = 759)	Group III (n = 139)	Group IV (n = 62)
Total number of comorbidities	1939 (73.6 %)	1367 (76.7 %)	480 (63.2 %)	45 (32.4 %)	47 (75.8 %)
Endocrine diseases	406 (15.4 %)	227 (12.7 %)	152 (20.0 %)	4 (2.9 %)	23 (37.1 %)
Obesity	159 (7.5 %)	19 (1.1 %)	121 (15.9 %)	–	19 (30.6 %)
Diffuse goiter	167 (6.3 %)	160 (8.9 %)	5 (0.7 %)	1 (0.7 %)	1 (1.6 %)
Autoimmune thyroiditis	14 (0.5 %)	9 (0.5 %)	2 (0.3 %)	3 (2.2 %)	–
Diabetes mellitus	4 (0.2 %)	2 (0.2 %)	–	–	–
Metabolic syndrome	62 (2.4 %)	35 (1.9 %)	24 (3.16 %)	–	3 (4.8 %)
Diseases of the nervous system	837 (31.8 %)	628 (35.3 %)	183 (24.1 %)	14 (10.1 %)	12 (19.4 %)
Intracranial hypertension	274 (10.4 %)	201 (11.3 %)	65 (8.6 %)	6 (4.3 %)	2 (3.2 %)
Syndrome of autonomic dysfunction	298 (11.3 %)	229 (12.8 %)	57 (7.7 %)	4 (2.9 %)	8 (12.9 %)
Cerebral angiodystonia	252 (9.6 %)	187 (10.5 %)	59 (7.8 %)	4 (2.9 %)	2 (3.2 %)
Syncope	13 (0.5 %)	11 (0.4 %)	2 (0.3 %)	–	–
Diseases of cardiovascular system	413 (15.7 %)	300 (16.8 %)	94 (12.4 %)	8 (5.8 %)	11 (17.7 %)
Secondary cardiopathy	331 (12.6 %)	252 (14.1 %)	64 (8.4 %)	8 (5.8 %)	7 (11.3 %)
Arterial hypertension	82 (3.1 %)	48 (2.7 %)	30 (3.9 %)	–	4 (6.5 %)
Diseases of the eyes	70 (2.7 %)	58 (3.6 %)	9 (1.2 %)	2 (1.4 %)	1 (1.6 %)
Myopia	53 (2.0 %)	42 (2.4 %)	8 (1.1 %)	2 (1.4 %)	1 (1.6 %)
Amblyopia	6 (0.2 %)	5 (0.3 %)	1 (0.1 %)	–	–
Astigmatism	11 (0.4 %)	11 (0.6 %)	–	–	–
Diseases of the blood (anemia)	213 (8.1 %)	154 (8.6 %)	42 (5.5 %)	17 (12.2 %)	–

$p = 0.000$). The chances of stratification of endocrinopathy were significantly higher than in patients with gastroduodenal pathology 227/1781 (12.7%) (OR 1.71; 95% CI 1.37–2.15, $p = 0.000$) and 8 times higher than in patients with intestinal diseases 4/139 (2.9%) (OR 8.45; 95% CI 3.08–23.21, $p = 0.000$). Considering what is mentioned above, it can be assumed that diseases of the biliary tract are often caused by a violation of neurohumoral regulation, which is a consequence of diseases of the endocrine and/or nervous systems. Numerous studies have confirmed that primary biliary dysfunction is associated with somatovegetative disorders and stress factors that lead to a weakening of regulation of higher autonomic centers and neurohumoral mechanisms. Physiological regulation of rhythmic activity of the gallbladder and its sphincters depends on the condition of the autonomic nervous system, and the development of pathology is accompanied by the predominance of sympathicotonia with changes in the peripheral parts of the autonomic nervous system [11]. In this way, dyskinetic disorders are determined by a violation of the synergy of innervation associated with the sympathetic-adrenal system discoordination, and typically, are general vegetoneurosis. The leading role of the nervous system in the formation of motor disorders of the biliary tract can be explained by the features of innervation of the hepatobiliary system [5].

It should be noted that with intestinal pathology, comorbidity were found only in one third of children. However, exactly these patients had the highest number of anemia and AIT (autoimmune thyroiditis). Accordingly, the chances of anemia were higher than in children with biliary tract and liver diseases by 2 times: 17/139 (12.2%) vs. 42/759 (2.0%) (OR 2.38; 95% CI 1.31–4.31, $p = 0.006$). In turn, the chances of AIT in children with intestinal diseases were 4 times higher than in children with gastroduodenal diseases: 3/139 (2.2%) vs. 9/1781 (0.2%) (OR 4.34; 95% CI 1.16–16.23, $p = 0.005$) and 8 times higher than in children with biliary and liver diseases 2/759 (0.3%) (OR 8.35; 95% CI 1.52–39.78, $p = 0.032$). This combination should be taken into account in the work of pediatric gastroenterologists and endocrinologists, as well as become the basis for the prevention of the formation of comorbidity in children with this pathology.

The chances of overlaying comorbidity in patients with GERD were 6.5 times higher than in children with bowel disease 45/139 (32.4%) (OR 6.55; 95% CI 3.25–12.48, $p = 0.000$). The most common among children of this group were endocrine diseases 23/62 (37.1%), mostly – obesity and metabolic syndrome 3/62 (4.8%). Thus, the chances

of obesity in children with GERD 19/62 (30.6%) were significantly higher than in children with gastroduodenal diseases 19/1781 (1.1%) (OR 40.98; 95% CI 20.26–82.86, $p = 0.000$) and in children with biliary and liver diseases 121/759 (15.9%) (OR 2.33; 95% CI 1.31–4.14, $p = 0.000$). The findings are consistent with many scientific studies that show a direct correlation between overweight and the onset of symptoms of GERD [8]. Also in children with reflux disease, the ratio of the chances of having CVS diseases was significantly higher than in children with other gastrointestinal diseases. The chances of layering of the pathology of CVS in children with GERD were 3.5 times more than in children with bowel disease: 11/62 (17.7%) vs. 8/139 (5.8%) (OR 3.53; 95% CI 1.35–8.87, $p = 0.015$) respectively. The obtained results correspond with the data of other studies, according to which the factors that determine the common development of GERD and the disorders of CVS include autonomic dysregulation and syndrome of undifferentiated connective tissue dysplasia [15].

The analysis reveals that more than 70% of children with gastrointestinal diseases have comorbidity. The most common among children with diseases of the digestive system were manifestations of diseases of the nervous system. According to the literature, changes in the functioning of the autonomic nervous system, which directly affects the functional condition of the GIT, occur at exactly school-age children. Disorders of autonomic regulation can simultaneously cause clinical manifestations diseases of the digestive system as well as diseases of the nervous system [15, 17]. The parasympathetic orientation, typically, dominates in children 6–7 years. The beginning of school, a new type of activity, a different daily routine, high complexity and intensity of the school curriculum can lead to dysadaptation of the child and autonomic dysregulation. The next «peak» of manifestations of autonomic dysfunction comes to the puberty period, which is accompanied by violent emotional outbursts, psychosomatic disorders and leads to functional changes in organs and systems under the autonomic nervous system control, including and the gastrointestinal tract [1, 15]. On the other hand, a tension in the functioning of the endocrine system takes place exactly this age period, which also affects the functional condition of the GIT [7, 18]. According to available studies, disorders of neurohumoral and endocrine regulation in childhood can be a factor in the formation of the main as well as the comorbid pathology [12]. Consequently, school-age children are most vulnerable to the occurrence of diseases associated with these processes due to the formation of regulatory

mechanisms, that requires additional attention during the diagnosis and treatment of main and comorbid pathology [9].

Based on the results of our research, the structure of diseases of the digestive system revealed the dominance of gastroduodenal diseases, in particular chronic gastroduodenitis, which is typical for children of this age group and coincides with literary data. According to available sources it is aware that among the diseases of the gastrointestinal tract in children of school age, 70–75% of them are the pathology of the stomach and duodenum. Chronic diseases of the gastroduodenal zone are detected in 100–150 per 1000 children's population [4, 5].

The analysis of patients with the most common pathological conditions of the gastrointestinal tract of childhood revealed a quite wide range of comorbidity. A strong correlation of developing diseases has been established, which should be considered by different specialists with a view to providing more qualified medical care.

Conclusions

Pathological changes of the digestive system in children remain widespread in the structure of child morbidity. The leading place is held by the gastroduodenal pathology, notably chronic gastroduodenitis.

The presence of comorbidity from other organs and systems was established in 73.6% of children with gastrointestinal diseases, most often in patients

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Аналіз структури супутньої патології в дітей із хворобами шлунково-кишкового тракту

Хвороби шлунково-кишкового тракту посідають друге місце в структурі соматичної патології в дітей і підлітків. Кількість випадків супутньої патології та коморбідних захворювань має тенденцію до збільшення. Поєднання найпоширеніших захворювань може бути як випадковим, так і зумовленим причино-наслідковим зв'язком, визначення якого має важливе значення для поліпшення медичного обслуговування дитячого населення.

Мета — проаналізувати супутню патологію в дітей із захворюваннями шлунково-кишкового тракту за результатами роботи міського спеціалізованого дитячого гастроентерологічного відділення.

Матеріали та методи. Проведено вивчення показників діяльності Харківської міської дитячої клінічної лікарні № 19 за період із 01.01.2019 р. до 31.12.2019 р. Протягом 2019 р. до лікарні було госпіталізовано 2633 дитини віком від 5 до 18 років (середній вік — (10,6 ± 2,9) року) із хворобами органів травлення.

Результати. Наявність супутніх патологічних станів встановлено в 73,6% дітей. Найпоширенішими у дітей із хворобами шлунково-кишкового тракту були вияви захворювань нервової системи (31,8%). З однаковою частотою траплялися хвороби ендокринної (15,4%) та серцево-судинної (15,7%) системи. Частим патологічним станом у пацієнтів із хворобами шлунково-кишкового тракту була анемія (8,1%). Порушення органа зору виявлено в 2,7% дітей, що збігається з поширенням цієї патології в загальній дитячій популяції.

Висновки. Провідне місце в структурі захворюваності дитячого віку посідає патологія органів гастродуоденальної зони, а саме хронічний гастродуоденіт. Наявність супутньої патології з боку інших органів і систем встановлено у 73,6% пацієнтів дитячого віку із захворюваннями шлунково-кишкового тракту. Найчастішим супутнім станом при захворюваннях гастродуоденальної зони були хвороби нервової системи. Найбільші шанси поєднання патологічних станів із розвитком коморбідної патології мають захворювання гастродуоденальної зони і нервової системи, кишечника і аутоімунний тиреоїдит, гастроєзофагеальна рефлюксна хвороба та ожиріння. Діти з патологією шлунково-кишкового тракту потребують проведення додаткового обстеження для ранньої діагностики супутніх захворювань і надання необхідної комплексної допомоги.

Ключові слова: супутня патологія, діти, хвороби шлунково-кишкового тракту.

ДЛЯ ЦИТУВАННЯ

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