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REVIEW OF DIAGNOSTIC METHODS FOR HELICOBACTER PYLORI ASSOCIATED GASTROINTESTINAL PATHOLOGY IN CHILDREN

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Abstract:

The authors conducted a review of modern studies on the diagnosis of diseases of the gastrointestinal tract, non-invasive methods of examination of Helicobacter pylori associated gastrointestinal pathologies. The results of numerous studies by foreign and domestic authors are systematized.

Keywords: Helicobacter pylori, gastrointestinal pathology, saliva, gastrointestinal tract, diagnosis

Timely accurate diagnosis of the disease is a key step in making the correct diagnosis to the patient and choosing an adequate allergy therapy. In pediatric practice, the issue is even more acute: early detection of a sensitizing agent prevents the development of multiple sensitization. Examination of patients with allergies includes several stages: collection of anamnesis of the disease, clarification of hereditary predisposition, in case of confirmation of the allergic nature of symptoms, a laboratory instrumental examination of the patient is carried out, the purpose of which is to search for specific allergens responsible for the development of the disease. Available tools for allergy diagnosis, including in pediatrics, are evaluation of the effectiveness of elimination measures, in vivo (skin tests) and in vitro testing to determine the level of allergen-specific IgE antibodies circulating in the blood serum [3,5].

The variety of causes causing the development of allergic diseases, complex pathogenesis, and the uneven response of patients to the therapy provided the basis for the identification of phenotypes and endotypes of allergic diseases [2,8,12].

The spectrum of plant allergens, both pollen and food, causing dominant sensitization, has regional characteristics. The formation of a sensitizing profile largely depends on the place of birth and residence of a person. The reaction to all plant allergens develops over several years when inhaling pollen from plants growing in a particular geographical region. Therefore, when collecting anamnesis, it is very important to clarify where a person usually lives, where he spends his vacation and what plant foods he prefers to eat. Component diagnostics – a new method of detecting IgE antibodies to molecular components - opens a new era in allergology. The use of whole allergenic extracts from natural sources does not make it possible to accurately diagnose various clinical conditions caused by the same sensitizing mixed source. Accurate objective prediction of systemic reactions, including life-threatening ones, is possible only when analyzing component diagnostics [1,4,13].

Often, gastrointestinal symptoms are combined with IdE-dependent reactions from the skin, eyes, respiratory tract, as well as anaphylactic reaction. GIA can be combined with skin lesions and manifest in the form of vomiting, nausea, abdominal pain, diarrhea. At the same time, PA symptoms may occur already in the maternity hospital in the case of prescribing mixtures based on cow's milk. Depending on the immunological mechanism, the following types of gastrointestinal hypersensitivity are distinguished. IgE-mediated gastrointestinal manifestations of PA include immediate gastrointestinal hypersensitivity and OAS. In clinical practice, mixed hypersensitivity is increasingly encountered, according to this variant, eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis and eosinophilic gastroenterocolitis are realized. Among non-IgE-dependent allergic diseases of the digestive tract, enterocolitic syndrome, proctocolitis induced by dietary proteins, food enteropathy and celiac disease should be distinguished.

Most symptoms of allergy to BCM are associated with the skin (for example, atopic dermatitis); the gastrointestinal tract (for example, vomiting, diarrhea, constipation); and the respiratory tract (for example, wheezing, sneezing) - or more general, such as colic. However, none of these symptoms are specific or definitive in nature. This can lead to overdiagnosis, undiagnosis or misdiagnosis of the disease, causing significant suffering among parents and infants. Allergy to BCM is most often confused with lactose intolerance, childhood colic, GERD or functional gastrointestinal disorders, which leads to untimely diagnosis, repeated consultations and inaccurate management. In addition, given that allergy to BCM remains a subject of debate and controversy in terms of diagnosis, and given the lack of definitive guidelines, it remains a significant burden from a

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clinical point of view. Thus, since allergy to BCM is easily missed, making a correct and early diagnosis while minimizing the burden on the patient and family remains a difficult task [10,14,17].
Consequently, there is an urgent need for such a tool as the assessment of symptoms associated with cow's milk allergy as CoMiSS – a scale of symptoms associated with cow's milk, which helps diagnose this condition in infants. CoMiSS includes parameters such as general, dermatological, gastrointestinal and respiratory symptoms, and takes from 5 to 15 minutes to diagnose [6, 9, 11].

The study of the features of the immunological profile in digestive secretions (saliva, gastric juice) in a number of gastrointestinal diseases, such as chronic gastroduodenitis, celiac disease, demonstrated high informative indicators of secretory immunity, changes in which reflected the activity and depth of the pathological process in the affected organ Abdominal pain and other symptoms associated with the gastrointestinal tract, are among the most common causes pediatric consultations. To date, studies show that the organic causes of these symptoms are rare in children. Other causes, such as functional disorders, abdominal pain, are more common [7,16].

Nevertheless, abdominal pain can sometimes be caused by peptic ulcer, erosive gastritis or duodenitis, which can develop as a consequence of Helicobacter pylori infection [11, 14]. The most important thing is that complications such as peptic ulcer develop only rarely in children, compared with the adult population, and it is extremely rare for children to develop stomach cancer associated with Helicobacter pylori. In most children, Helicobacter pylori infection is asymptomatic and this disease does not play a role in functional abdominal disorders [11, 14].

For example, these studies have shown an inverse relationship between Helicobacter pylori infection and the prevalence of allergies or asthma [6,8]. Due to the mechanisms of pathogenesis of Helicobacter pylori described above, positive individuals are at increased risk of various clinical symptoms. The course of infection is variable and strongly depends on the factors of immunity of the macroorganism. In addition, the nature of the lesion of the gastric mucosa correlates with the risk of occurrence and progression of various gastric disorders [10].

Among gastrointestinal diseases, dyspepsia and peptic ulcer are often observed in clinical practice, and the detection of Helicobacter pylori, followed by eradication of infection, are decisive steps in the treatment of such disorders [2,7].

Children differ from adults regarding Helicobacter pylori infection in many aspects. Helicobacter pylori causes some extra-intestinal diseases along with gastrointestinal diseases. Although among these diseases in children, symptoms such as recurrent abdominal pain are not specific. Moreover, the role of the pathogen in growth retardation, iron deficiency anemia and bronchial asthma is still controversial. A reliable way to detect Helicobacter pylori is the most important issue that is still being actively discussed. The tests used to diagnose infection are grouped into invasive and non-invasive methods. Invasive methods include endoscopic evaluation, rapid urease test, histological method and bacterial culture seeding. Non-invasive tests include a urea breath test, a stool antigen test, serological examination and molecular diagnostic approaches. The use of the endoscopic method is a prerequisite for all invasive methods and creates difficulties in children, since it is a complex procedure and requires the patient's complicity. For this reason, noninvasive tests are widely used in children [13,15].
According to a study by Jones N.L. et al., regardless of new and improved noninvasive treatment methods, noninvasive tests are not recommended for the diagnosis of Helicobacter pylori infection in children [7, 12].
According to Kotilea K et al., most cases of infection in children are asymptomatic, and pediatric studies do not confirm the role of Helicobacter pylori in functional disorders, such as recurrent abdominal pain. The control of eradication after treatment should be based on validated non-invasive tests [10].

In addition, there are new studies conducted in 2019 by the author Hasosah M, which determined the reliability of various tests for the detection of Helicobacter pylori infection in the pediatric population. The accuracy of six different diagnostic methods was evaluated: four invasive (rapid urease test, histology, antral nodularity, culture biopsy) and two non-invasive (serological test, stool antigen test) [5,8,17].

A large prospective multicenter case-control study conducted in Spain, Italy, France and Colombia revealed a possible association between Helicobacter pylori infection and eosinophilic esophagitis. There was no significant difference in the prevalence of Helicobacter pylori infection between cases of the disease and control in children, calling into question the inverse association of Helicobacter pylori with eosinophilic esophagitis [1,3].

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For morphological assessment of the gastric mucosa, using the updated Sydney classification, it is necessary to take at least 6 biopsies: two biopsies from the antrum and two biopsies from the stomach body, for cultivation (if available) — one biopsy from the antrum and the body, at least one biopsy from the antrum of the stomach for any urease tests and molecular analyses). It should be noted that methods based on biopsy (histology, culture, rapid urease test) can give false negative results for bleeding from the upper gastrointestinal tract. In these cases, molecular diagnostic methods are more accurate [17].

The study of the features of the immunological profile in digestive secretions (saliva, gastric juice) in a number of gastrointestinal diseases, such as chronic gastroduodenitis, celiac disease, demonstrated high informative indicators of secretory immunity, changes in which reflected the activity and depth of the pathological process in the affected organ [12,16].

Urease breath test and stool analysis for antigen with monoclonal antibodies are reliable non-invasive methods for detecting Helicobacter pylori infection. These tests are as sensitive and specific as invasive tests. In a recent Cochrane analysis of data from 99 studies, the diagnostic accuracy of four noninvasive tests for the detection of Helicobacter pylori was compared [17].

Taking into account the prevalence of Helicobacter pylori in the world, which is 53.7%. When comparing these tests indirectly, indeed, statistical data on differences in diagnostic accuracy were obtained. Recently, in individuals who have not used antibiotics or proton pump inhibitors, the results of respiratory tests are more diagnostically accurate than serology or detection of antigen in feces. According to international consensus reports, one positive noninvasive test is a sufficient reason to undergo endoscopy and histological examination [3,9].

To identify Helicobacter pylori, various diagnostic tests are offered, which have their own specific advantages and disadvantages. The histological method involves the use of several smears stained with Giemsa and the Immunostaining method to allow the pathogen to be detected [12].

Another important diagnostic method for Helicobacter pylori is a rapid urease test, which detects an increase in the pH of the reagent after adding a biopsy sample containing Helicobacter pylori to the reagent. A rapid urease test is a relatively cheap, fast, easy, specific and widely available test. Polymerase chain reaction (PCR) has also been used to detect Helicobacter pylori [7,18].

Currently, the urea breath test is the main non-invasive method for such diagnosis, gradually taking the place of endoscopy as the most suitable method for the detection of Helicobacter pylori. This test is based on the mechanism of bacterial degradation of labeled 13C or 14C urea in carbon dioxide, which can be measured in exhaled air using a mass or infrared spectrometer [11].

A less expensive option of non–invasive tests - the determination of antigen in feces, is a good alternative to the diagnosis of Helicobacter pylori. The fecal antigen can be detected by ELISA or immunochromatography. In addition, as an alternative, a promising new non-invasive method has been largely studied - urine analysis for the diagnosis of Helicobacter pylori infection. A 2017 meta-analysis involving 23 studies showed that testing for antibodies in urine samples could be a good diagnostic option. However, further research is needed to confirm the accuracy of this method. Finally, thanks to the discovery of specific serological markers, new strategies for the serological diagnosis of Helicobacter pylori infection have been developed. A recent study evaluated the accuracy of the ELISA method of the Flid - flagellar hook-associated protein (FliD) flagellar hook-associated protein as a marker of this infection [10,19].

CONCLUSION. Such a high interest in this problem is due to the fact that modern advances in the diagnosis and therapy of allergic diseases do not always satisfy patients, and many of them note the ineffectiveness of the standard treatment. Taking into account the above, it can be confidently stated that at present, differential diagnosis between non-IgE-mediated GIA and functional disorders of the gastrointestinal tract is extremely difficult. Difficulties and errors in the diagnosis of GIA are associated with both subjective and objective reasons and are explained primarily by the fact that gastrointestinal reactions to food are often delayed and occur in a non-IgE-mediated type. At the same time, knowledge of the modern classification of GIA, algorithms for diagnosis and management of various clinical forms of this pathology can significantly improve the quality of medical care for this category of patients, avoid chronicling the process and the development of severe, disabling forms of diseases.

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