Здоровье ребёнка

Огляд літератури / Review of Literature

UDC 616.329/33-008.6-053.2 DOI: 10.22141/2224-0551.12.2.1.2017.100991

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Gastroesophageal reflux disease in pediatric practice: current topical issues

For cite: Zdorov'ye Rebenka. 2017;12:267-72. DOI: 10.22141/2224-0551.12.2.1.2017.100991

Abstract. *In recent years, much attention has been paid to the upper digestive tract diseases in children, particularly gastroesophageal reflux disease, as a cause that has an impact on the quality of life, even in children of school age, and thereafter in young adults. Consequently, there are searches for optimization of early detection, new methods of non-invasive diagnosis, screening of this pathology in children's population in order to determine persons with risk factors and to control disease development and complicated course, as well as searches for the formation of preventive activities algorithm. Scientists came to a consensus that all examinations, which are used in pediatric practice, must be maximally available, simple and non-invasive to the extent of child's condition. The question about advisability of performing esophagogastroduodenoscopy for all patients with complaints of heartburn and with other symptoms of gastroesophageal reflux disease, the question relative to performing ultrasonography of the esophagus in children as an additional method of examination, usage of questionnaire in pediatric practice, formation of disease course prediction algorithm, and identification of preventive measures specific to every patient remain open. In order to explain their application, the developmental mechanisms of this pathology must be well-understood, and individual risk factors that may influence disease severity and disease course prediction, which occur in children in different periods of life, must be taken into account. Therefore, the goal of this research is to provide an overview of modern literature with reference to topical issues of clinical evidence, risk factors, diagnosis, prediction of gastroesophageal reflux disease course in children of different ages (regarding main causative and pathogenic factors, clinical evidence (esophageal and extra-esophageal), diagnostic methods and modern approaches to gastroesophageal reflux disease treatment).*

Keywords: *gastroesophageal reflux disease; disorders of the motor secretory function; ultrasound diagnosis; non-invasive diagnosis; risk factors; prediction of the disease course*

Introduction

Gastroesophageal reflux disease (GERD) is a chronic recurrent disease associated with disorder of motor-evacuation function of gastroesophageal area which is characterized by established esophageal and extraesophageal clinical evidence as a result of spontaneous and/or regular backflow of stomach or duodenal content into the esophagus that result in physicochemical damage of the distal segment of the esophagus [1, 2].

GERD is a current problem in modern gastroenterology specified by high disease incidence, a great number and variety of complaints raised by patients, development of severe complications (Barrett esophagus and adenocarcinoma of the esophagus) as well as necessity for long-term therapy [3].

GERD is the one of the most widespread diseases of the digestive system in Western world with typical symptoms such as heartburn, belching or retrosternal pain and constitute 15–20 % from overall population. In Asia this number is significantly less and constitutes approximately 5 % [4], though over the last years the tendency for morbidity increase is also observed.

GERD incidence in children is uncertain since application of invasive methods of examination (pH measurement and endoscopy) particularly in young children is significantly limited. In the structure of gastroenterological morbidity according to different authors it constitutes 8 to 25 % [5, 6].

The significant point is that in children the risk of digestive system diseases incidence is higher than in adults,

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disease progresses in less time with increasingly frequent and long-lasting recurrence.

Incidence rate of GERD has been noted around the world however there are significant differences in terms of its frequency in children from 8.7 to 49 %. In Ukraine the prevalence rate of GERD (0.83 ‰) and the incidence rate of GERD (0.29 ‰; 2014) are significantly less than in other countries that may indicate poor education of professionals in the matter [7].

High prevalence of heartburn as a principal symptom of GERD in the world and Ukraine in combination with invasiveness of research, high cost of diagnostics and treatment is a significant social and economic problem of State health care system. Particularly well-timed screening diagnostics and identification of disease course prediction algorithms and creating specific prophylactic events can prevent development of complications and severe forms of GERD that will significantly reduce costs for long-term treatment and improve the life quality of patients.

Pathologic gastroesophageal reflux onset can be associated with incompetence of cardia, esophagus clearance disorder, and stomach and duodenum motility disorders. Esophagus clearance disorder and gastroduodenal motility disorder are often associated with autonomic nervous system function disorder of different origin. Important favorable factors of GERD development are fatness, undifferential dysplasia of connective tissue, and sliding esophageal hiatal hernia. Contamination and ablation of Helicobacter pylori (Hp) do not play a critical role in GERD genesis [8].

Several metaanalyses showed statistically significant low prevalence of Hp when it comes to GERD [9], as well as Barrett esophagus [8, 10] or esophageal adenocarcinoma [11]. However ablation of Hp does not affect the course of already present GERD and does not influence the effectiveness of treatment with proton pomp inhibitors [12, 13].

Gastroesophageal reflux disease is characterized by complex of clinical symptoms that occur in response to backflow (reflux) of stomach content into the esophagus and proceeds with occasional recurrences and assumes progressive nature [2, 14, 15].

The symptoms of GERD are quite various and numerous, and can be esophageal and extraesophageal. Clinical implications significantly depend on age of a child and presence of comorbidity and risk factors.

Esophageal symptoms include the following: heartburn, regurgitation, belching, dysphagia, odynophagia (pain when swallowing) that occurs more frequently in the presence of erosive ulcerated lesions. Nonspecific for reflux disease symptoms that occur more rarely and can be associated with other diseases are as follows: hiccup, vomiting, sensation of lump in a throat, sensation of excessive amount of liquid in the mouth, throat irritation, burning tongue, etc. Duodenogastroesophageal reflux onset is frequently followed by bitter taste in the mouth, yellow coated tongue [16–18].

Character of clinical manifestations is influenced by changes from the side of other organs of digestive system, first of all gastroduodenal pathology which is followed by GERD in a great number of cases. Modern studies showed high frequency of GERD association with functional pathology of organs of digestive tract particularly with irritable bowel syndrome and functional dyspepsia. Frequent association of GERD with functional disorders of gastrointestinal tract is not accidental and based on their common pathophysiological mechanisms [19].

In addition to significant progression of pathology incidence and severity, GERD importance based also on extraesophageal clinical manifestations and for diagnostics they demand extended cycle of laboratorial, instrumental methods of examination and collaboration of doctors of different specialties, and in establishing diagnosis they influence the duration and the structure of treatment (Bardhan K.D. et al., 2007; Mayev I.V. and other, 2014).

Children with GERD also complain of belching that is spontaneous backflow of small amounts of food and air or only air into oral cavity. Such belching is a less specific symptom of GERD because firstly it demonstrates increase of gastric pressure and in a lesser extent depends on presence and activity of GERD [19, 20].

When it comes to heartburn, regurgitation, and belching, attention should be paid to absence of one definition of these terms. It is also necessary to admit that there is no conclusive focus on a regular pattern and frequency of heartburn as a symptom of GERD. Thus, according to Genval Cogress recommendations diagnostics of reflux disease can be performed in cases where heartburn occurs twice or more times per week. At Montreal Congress of gastroenterologists international panel which included 44 specialists from 18 countries all over the world came to a decision to consider heartburn as a symptom of GERD even if it occurs once a week [18, 21].

More than 60 % of children complain of dull pain in epigastric and substernal cavities which appears immediately after meal, increases with trunk bending and reduces after some 1.5–2 hours.

Investigators have recently started paying attention to extraesophageal (atypical) manifestations of gastroesophageal reflux disease because such clinical pattern simulates different diseases. Atypical manifestations of GERD include bronchopulmonary, otolaryngologic, cardial, and dental symptoms. At an early age the most common are extraesophageal symptoms on the part of bronchopulmonary system and ENT organs. This connection is due to similarity of anatomical relations between respiratory and digestive systems, and also the same embryological origin [21].

Pathogenesis of GERD is multiple. Understanding of these factors has been recently sufficiently improved due to understanding of acid pocket and hernia of diaphragm esophageal opening, and also interaction between these factors. In spite of recently increased understanding more investigations should be performed for better comprehension of GERD symptoms particularly in patients resistant to symptoms therapy [18, 22–24].

With one voice scientists define GERD as an acid-dependant polysystemic disease because hydrochlo-

ric acid is considered to be the main pathogenic factor. The determining risk factors of gastroesophageal reflux disease development in children include disorder of motor-evacuation function of upper digestive tract, decrease of resistance of esophageal mucous membrane to hydrochloric acid action, increase of gastric content aggressiveness, insufficient cardia (absolute or relative), increase of intragastric and intraabdominal pressure, dysfunction of autonomic nervous system, fast growth, heredity, complicated perinatal anamnesis, non-differential dysplasia of connective tissues structures and also factors of environment and lifestyle such as: overweight, harmful eating habits, absence of regular physical activity, disproportion of increase of body and esophagus, consumption of alcohol drinks, smoking in adolescence life [16, 17, 25–28].

A complicated factor is duodenogastric reflux. In alkaline (biliary) and mixed reflux inflammatory destructive changes of mucous membrane are manifested more than in isolated acid aggression. Presence of both refluxates in esophageal cavity causes risk of columnar epithelium lined lower esophagus (Barrett metaplasia) and esophageal malignancy. In particular, biliary acids increase the activity of COX-2 thereby intensifying proliferation processes [18, 29, 30].

As for probable pathogenic connection between GERD and Hp there are still discussions often expressing polar opinions concerning this issue. Hp is considered to be determined mostly in patients with mild disease while in severe disease (esophagitis of III–IV stages) it is found only in 16 % of patients. The comparative analysis of conservative treatment results of great number of patients suffering from GERD depending on their "helicobacter status" performed by a famous gastroenterologist from Great Britain R. Heading showed that frequency of clinical and endoscopic remission depends not on the presence or absence of Hp but on evidence of changes in esophageal mucous membrane [10]. There are no precise conclusions concerning Hp as a protective factor in respect of GERD occurrence.

Establishing of GERD diagnosis is based on combination of diagnostic criteria such as: clinical, endoscopic, histologic, roentgenologic, manometric, etc. According to world experience early diagnostics of GERD dramatically reduces risk of complications development [19, 25, 31–34].

According to international consensus GERD is a clinical diagnosis, therefore adequate correct history taking with detailed complaints allows to determine the symptoms associated with gastroesophageal reflux. Basing on national guidelines and clinical recommendations of many countries in Europe and the USA to establish primary diagnosis, to identify complications and onset of treatment at screening stage this method is the main — qualitative evaluation of clinical symptoms may be more resultant than instrumental methods of diagnostics the necessity of which should be justified due to invasiveness and difficulty of performance in children. Instrumental methods of investigation are additional or diagnosis confirming [33].

The use of different methods for studying of GERD prevalence has a number of difficulties such as high cost of large-scale investigations and lack of agreement from great part of people for invasive tests. Therefore, nowadays investigators are studying the opportunity of creation of unified questionnaire which will help to conduct a survey of patients regardless of a country where epidemiology of GERD is studied [35, 36]. Besides to determine specific clinical manifestations in children of early age connected with GERD a special questionnaire is used [2, 6, 7, 17, 33, 37].

Both in Ukraine and in the whole world the main method for determination of GERD clinical diagnosis is intraesophageal pH-metry which is performed by introducing pH-probe into distal segments of esophagus and its fixation there for a long time (pH daily monitoring). This method is characterized by high sensitivity in GERD diagnostics and helps to choose individual tactics for the case management. pH monitoring for GERD confirmation is not recommended in such cases as: in uncomplicated GERD if the results of test are not necessary in treatment or prognosis, if there is dysphagia, pain in epigastrium, when there are positive results of another methods of investigation.

Upper endoscopy of esophagus helps to confirm the presence of reflux-esophagitis and evaluate its severity. If necessary during endoscopic investigation biopsy material of mucous membrane of stomach and esophagus with further histologic evaluation is taken, it gives an opportunity to determine the stage of inflammatory process manifestations, presence of gastric metaplasia foci [19, 38].

Contrast X-ray study is a sufficiently informative method of diagnostics of diaphragm esophageal opening hernia, determination of gastrointestinal tract abnormalities which destroy its motor activity (phrenospasm, diverticula, coarctation, etc.), but this method of diagnostics is rarely used in pediatrics.

Additional methods for determination of GERD risk factors can be the following: diagnostics of reflux-esophagitis in children through echographic investigation of abdominal part of esophagus and cardial section of stomach which is performed to investigate thickening of esophageal wall, edge roughness of esophageal wall, increase in esophagus diameter after liquid contrasting (not during swallowing), widening of esophagus lumen not during swallowing; manometry of esophagus — this method helps to register pressure in different parts of esophagus, its ability to relax while swallowing, contracting function of esophagus and also to evaluate the character of peristaltic waves; impedansometry is based on measurement of electric parameters of intraesophageal environment while introducing of gastric contents into esophagus; investigation is performed with the help of intragastric impedance probe and reogastrograph.

Due to its invasiveness application of this method in children as in pH-metry is limited. Due to specialists interest regarding GERD comorbidity with another diseases of digestive organs, ENT organs, and organs of respiratory system and also with great attention to amount

increase of atypical and extraesophageal symptoms it is necessary to develop algorithms of additional individualized investigation according to identified extraesophageal symptoms.

Taking into consideration significant prevalence of GERD, variability of clinical manifestations, increase of extraesophageal symptoms, presence (sometimes combination) of risk factors which lead to GERD development or complicate its course in children and teenagers probability of serious complications development and continuous worsening of life quality determine medical and social character of gastroesophageal disease. Its actuality proves the necessity of further search in the study of pathogenesis and clinical manifestations of GERD to improve diagnostics, individualize case management and predict the course of gastroesophageal reflux disease.

Conflicts of interests. Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

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Получено 02.03.2017

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Гастроезофагеальна рефлюксна хвороба в педіатричній практиці: сучасні проблемні питання

Резюме. Останнім часом багато уваги приділяється захворюванням верхніх відділів травного тракту в дітей, зокрема гастроезофагеальній рефлюксній хворобі як причині, що призводить до порушення якості життя вже в дітей шкільного віку, а в подальшому — і в осіб молодого віку. У зв'язку з цим існують пошуки оптимізації раннього виявлення, нових методів неінвазивної діагностики, скринінгу цієї патології серед дитячого населення з метою визначення осіб із факторами ризику та запобігання розвитку захворювання та ускладненого перебігу, а також пошуки формування алгоритму профілактичних заходів. Вчені дійшли консенсусу, що всі обстеження, які використовуються в педіатричній практиці, повинні бути максимально доступними, простими та неінвазивними, наскільки це дозволяє стан дитини. Залишається відкритим питання про доцільність проведення фіброезофагогастродуоденоскопії всім пацієнтам зі скаргами на печію та іншими симптомами гастроезофагеальної рефлюксної хвороби, питання щодо застосування ультразвукової діагностики стравоходу в дітей як додаткового методу обстеження, використання опитувальників у педіатричній практиці, формування алгоритмів прогнозування перебігу захворювання та визначення профілактичних заходів індивідуально для кожного пацієнта. Щоб мати змогу обґрунтувати їх призначення, необхідно добре розуміти механізми розвит-ку цієї патології та враховувати індивідуальні фактори ризику, що можуть вплинути на тяжкість захворювання та прогнозування перебігу, які виникають у дітей в різні періоди життя. Отже, **метою** цієї роботи було подати огляд сучасної літератури з проблемних питань щодо клінічних проявів, факторів ризику, діагностики, прогнозування перебігу гастроезофагеальної рефлюксної хвороби в дітей різного віку (із питань основних етіологічних та патогенетичних факторів, клінічних проявів (стравохідних та позастравохідних), методів діагностики та сучасних підходів до лікування гастроезофагеальної рефлюксної хвороби).

Ключові слова: гастроезофагеальна рефлюксна хвороба; моторно-секреторні порушення; ультразвукова діагностика; неінвазивна діагностика; фактори ризику; прогнозування перебігу

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Гастроэзофагеальная рефлюксная болезнь в педиатрической практике: современные проблемные вопросы

Резюме. В последнее время много внимания уделяется заболеваниям верхних отделов пищеварительного тракта у детей, в частности гастроэзофагеальной рефлюксной болезни как причине, которая приводит к нарушению качества жизни уже у детей школьного возраста, а в дальнейшем — и у людей молодого возраста. В связи с этим существуют поиски оптимизации раннего выявления новых методов неинвазивной диагностики, скрининга этой патологии среди детского населения с целью определения лиц с факторами риска и предупреждения развития заболевания и осложненного течения, а также поиски формирования алгоритма профилактических мероприятий. Ученые пришли к консенсусу, что все обследования, которые используются в педиатрической практике, должны быть максимально доступными, простыми и неинвазивными,

насколько это позволяет состояние ребенка. Остается открытым вопрос о целесообразности проведения фиброэзофагогастродуоденоскопии всем пациентам с жалобами на изжогу и другими симптомами гастроэзофагеальной рефлюксной болезни, вопросы применения ультразвукового исследования пищевода у детей в качестве дополнительного метода обследования, использования опросников в педиатрической практике, формирования алгоритмов прогнозирования течения заболевания и определения профилактических мероприятий индивидуально для каждого пациента. Чтобы иметь возможность обосновать их назначение, необходимо хорошо понимать механизмы развития этой патологии и учитывать индивидуальные факторы риска, которые могут повлиять на тяжесть заболевания и прогнозирование течения, возникающие у детей в разные периоды жизни. Итак, **целью** этой работы было представить обзор современной литературы по проблемным вопросам в отношении клинических проявлений, факторов риска, диагностики, прогнозирования течения гастроэзофагеальной рефлюксной болезни у детей разного возраста (по вопросам основных этиологических и патогенетических факторов, клинических проявлений (пищеводных и внепищеводных), методов диагностики и современных подходов к лечению гастроэзофагеальной рефлюксной болезни).

Ключевые слова: гастроэзофагеальная рефлюксная болезнь; моторно-секреторные нарушения; ультразвуковая диагностика; неинвазивная диагностика; факторы риска; прогнозирование течения