UDC 616.329/.333-008.6+616.248]-036-07-053.5

Y.V. Karpushenko, T.V. Frolova, N.M. Drobova, O.M. Ashcheulov

Comorbidity and impact of bronchial asthma to gastroesophageal reflux disease in children

Kharkiv National Medical University, Ukraine

Modern Pediatrics. Ukraine. (2024). 4(140): 34-38. doi: 10.15574/SP.2024.140.34

For citation: Karpushenko YV, Frolova TV, Drobova NM, Ashcheulov OM. (2024). Comorbidity and impact of bronchial asthma to gastroesophageal reflux disease in children. Modern Pediatrics. Ukraine. 4(140): 34-38. doi: 10.15574/SP.2024.140.34.

Gastroesophageal reflux disease (GERD) is a highly comorbid disease with bronchial asthma (BA). The relationship between GERD and BA is complicated and controversial.

Aim: to analyze impact factors of BA and GERD in children with comorbid pathology for the further development of early diagnostic and preventive measures.

Materials and methods. 81 children (aged 6 to 18 years) were involved in the study and divided into two groups: children with GERD and BA as a main group (n=27) and children with GERD and without allergy as a control group (n=54). The verification of diagnoses was carried out according to the unified clinical protocols of medical care. The results were processed using nonparametric statistical methods.

Results. Esophageal motility disorders (EM) were detected in 100% of patients with BA, regardless of the severity. Inflammatory changes of the esophageal mucosa (EM) were equally frequently detected in patients with mild and moderate persistent BA, and were absent in patients with severe BA. GERD was diagnosed in 44.4% of patients with BA. 25.0% of patients had the erosive form of GERD, 25.0% — non-erosive GERD, 50.0% — endoscopically negative GERD, in the control group — 33.0%, 35.0%, 32.0% respectively.

Conclusion. All patients with BA had esophageal motility disorders. GERD was diagnosed in 44.4%. Inflammatory changes of EM (erosive and non-erosive forms of GERD) were detected in 22.0% of patients with mild and moderate forms of BA, and in severe forms of BA — endoscopically negative GERD. The frequency of inflammatory changes reached 68.0% in the control group.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of the institution indicated in the work. The informed consent of children's parents was obtained for conducting the studies.

No conflict of interests was declared by the authors.

Keywords: GERD, bronchial asthma, allergy, children, comorbidity.

Гастроезофагеальна рефлюксна хвороба та бронхіальна астма в дітей: коморбідність та взаємовплив

Ю.В. Карпушенко, Т.В. Фролова, Н.М. Дробова, О.М. Ащеулов

Харківський національний медичний університет, Україна

Гастроезофагеальна рефлюксна хвороба (ГЕРХ) є високо коморбідним до бронхіальної астми (БА) захворюванням. Їхній взаємозв'язок є складним та дискусійним.

Мета: проаналізувати фактори взаємовпливу БА та ГЕРХ у дітей із коморбідною патологією для подальшої розробки ранніх діагностичних та профілактичних заходів.

Матеріали та методи. До дослідження залучено 81 дитину віком від 6 до 18 років. До основної групи увійшло 27 дітей із ГЕРХ та супутньою БА, до контрольної групи — 54 дитини без алергії та з наявною ГЕРХ. Верифікацію діагнозів виконано згідно з уніфікованими клінічними протоколами медичної допомоги. Результати опрацьовано методами непараметричної статистики.

Результати. Моторні порушення встановлено у 100% пацієнтів із БА незалежно від ступеня важкості. Запальні зміни слизової оболонки стравоходу (СОС) однаково часто виявлено в пацієнтів із легким та середньоважким перебігом БА та відсутні в пацієнтів із важкою формою захворювання. ГЕРХ діагностовано у 44.4% хворих на БА. 25.0% пацієнтів мають ерозивну форму ГЕРХ, 25.0% — неерозивну ГЕРХ, 50.0% — ендоскопічно негативну ГЕРХ, у групі контролю — 33.0%, 35.0% 32.0% відповідно.

Висновки. В усіх хворих із БА наявні моторні порушення стравоходу. У 44.4% діагностовано ГЕРХ. Запальні зміни СОС (ерозивна та неерозивна форми ГЕРХ) виявлено у 22.0% при легкій та середньоважкій формах БА, а при тяжкій формі БА — ендоскопічно негативна ГЕРХ. Частота запальних змін сягала 68.0% у контрольній групі.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом інституту. На проведення досліджень отримано інформовану згоду батьків дітей.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: гастроезофагеальна рефлюксна хвороба, бронхіальна астма, алергія, діти, коморбідність.

Introduction

According to different studies, the prevalence of gastroesophageal reflux disease (GERD) is between 55–83% in adults and 50–63% in children with bronchial asthma (BA) [2,7]. It has been shown that GERD plays a role in the development of inflammatory diseases of the upper and lower respiratory tract. The relationship between GERD and asthma is particularly complicated. It is not yet clear whether GERD is an accompanying finding or a cause of BA, or even if it is an aggravating factor [10].

In the modern world, allergic diseases have reached pandemic proportions, and their prevalence reaches 50% [5,11,16]. Considering the systemic nature of this process, various organs and systems are susceptible to pathological influence. Thus, the course of comorbid diseases takes on

a different character. Therefore, specialists in various medical fields need to take into account the allergy presence in patients. GERD is a chronic recurrent condition that arises from impaired motor-evacuation function of the digestive system organs and is characterized by repeated reflux of stomach contents into the esophagus, which can lead to inflammatory changes in its distal part [10,15]. The clinical manifestations of GERD are quite polymorphic, with distinguishing esophageal and extraesophageal symptoms that can be subtle. In childhood, these symptoms can be highly variable, considering the immaturity of the involved systems. One of such manifestations is respiratory disorders that require differential diagnosis with BA.

It is known that BA is a condition of any age that begins its path in childhood [1]. According to statistical data, the prevalence of BA in the pediatric population varies from 5–10% [3,9] to 37.6% [12,16], with a peak at school age. The gender distribution predominates among boys, but, however, with age, the difference evens out upon reaching puberty. It has been proven that social, environmental, and economic conditions play a significant role in the occurrence and spread of allergic diseases in general and BA in particular. Thus, a high incidence of BA in children is characteristic of industrial regions with unfavourable ecology, as well as urban residents [4].

The comorbidity of GERD and BA influences the course of each other, which currently sparks a lot of debates among specialists. In scientific research, it has been shown that in individuals with a primary diagnosis of GERD, but without signs of respiratory disease, there is an increase in the frequency of hospitalizations over time due to the development of bronchopulmonary pathology [4]. According to statistics, among patients with esophagitis and esophageal strictures, the risk of developing BA and exacerbations of chronic obstructive pulmonary disease is almost twice as high as in the group of patients without esophageal pathology in the medical history [5,12]. Persistent isolated cough and bronchial obstruction symptoms are often caused or provoked by GERD. Moreover, specific treatment of GERD modulates cough and dyspnea symptoms by reducing them to disappearance [11,15].

Therefore, the comorbidity of GERD and BA requires careful study, especially in children, as it will allow the development of effective diagnostic and prevention methods, as well as personalized approaches to therapy.

The aim is to improve the diagnostics and prevention of GERD in children with BA.

Materials and methods of the study

The study was conducted at the municipal non-profit enterprise «City Children's Clinical Hospital No.19» of the Kharkiv City Council and the municipal non-profit enterprise of the Kharkiv Regional Council «Regional Children's Clinical Hospital». Eighty-one children (aged 6 to 18 years) were involved and divided into two groups: children with BA and GERD as a main group (n=27) and children with GERD and without allergic pathology as a control group (n=54). The verification of allergic and gastroenterological diagnoses was carried out according to the current unified clinical protocols of medical care.

The detection of *Helicobacter pylori*was per-formed using either a rapid urease test or histological examination. Video esophago-gastroduodenoscopy with endoscopic pH monitoring was applied to assess the condition of the upper gastrointestinal tract.

The results were analyzed using nonparametric statistical methods with «Microsoft Excel» and IBM SPSS Statistics software programs.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of the institution indicated in the work. The informed consent of children's parents was obtained for conducting the studies.

Results of the study and discussions

In the main group, the majority were boys, accounting for 77.8% (n=21), as well as in the control group, where boys comprised 55.6% (n=30). According to the severity of BA, the examined children were distributed as follows: severe persistent BA — 11.1% (n=3), moderate persistent BA — 22.2% (n=6), mild persistent BA — 66.7% (n=18). All patients with BA were found to have concomitant allergic pathology, such as allergic rhinitis and/or atopic dermatitis (in all patients with severe or moderate persistent BA and in 33.0% of patients with mild persistent BA).

An immediate hypersensitivity type of allergic reaction with sensitization to food, pollen and house dust allergens was noted in the vast majority of patients. The average value of total IgE was 371.4 IU/mL.

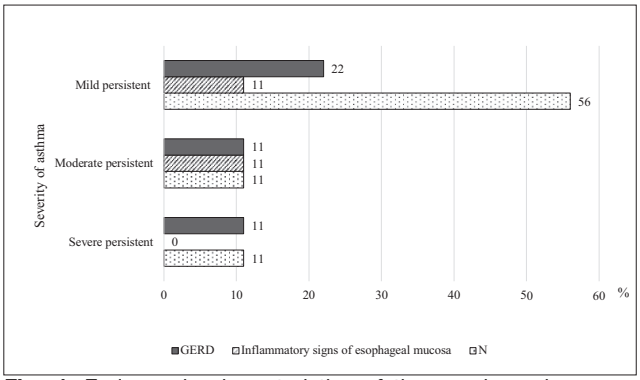

Fig. 1. Endoscopic characteristics of the esophageal mucosa depending on the severity of BA

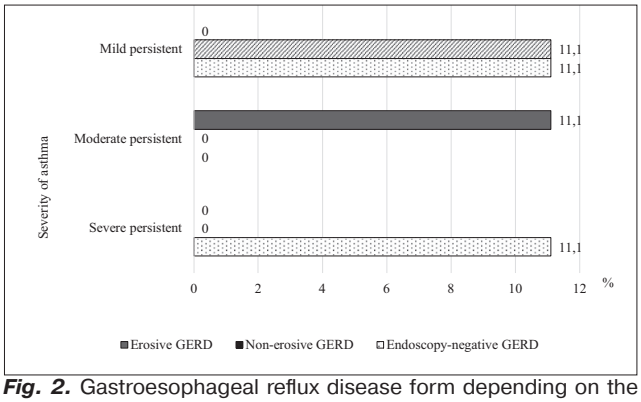

Fig. 2. Gastroesophageal reflux disease form depending on the severity of bronchial asthma

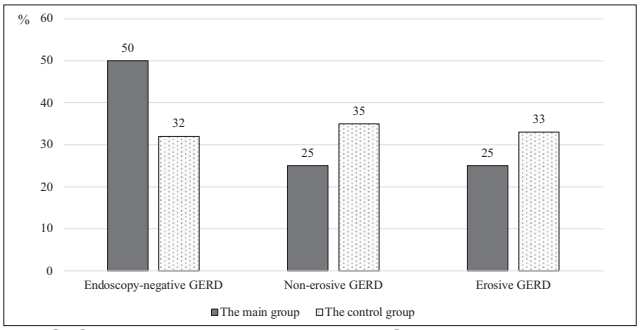

Fig. 3. Comparative characterization of GERD

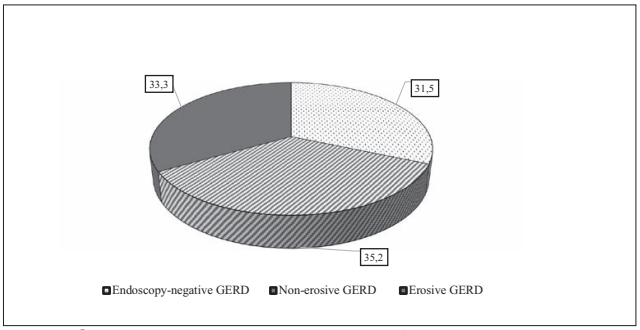

Fig. 4. GERD forms in the control group, %

The endoscopic characteristics of the esophageal motility disorders (EM) and the presence of motor disorders, depending on the severity of BA, are presented in Figure 1.

Motor disorders were detected in all patients with BA, regardless of severity. Inflammatory signs of the EM were equally common in patients with mild and moderate persistent BA but were absent in patients with severe persistent BA.

Helicobacter pylori infection was detected in one-third of patients with BA without a significant difference in disease severity. However, the *Helicobacter pylori* association in patients without BA was slightly higher, reaching 44.4% (n=12).

GERD was diagnosed in 44.4% of patients with BA. When analyzing the variants of GERD, the following data were obtained (Figure 2).

As can be seen from the provided data, there is no correlation found between the severity of BA and structural changes in the EM associated with reflux. Erosive changes in the esophageal mucosa were detected in patients with moderate persistent BA, erythematous changes in those with mild forms, while severe forms were accompanied by the absence of visual changes in the EM, only motor disorders. Therefore, it can be assumed that the inflammatory changes in the EM are caused not so much by motor disorders as by the composition of the refluxate.

In order to assess the impact of the allergic factor specifically on the condition of the EM, the forms of GERD were compared between patients in the main and control groups (Figure 3).

As can be seen from the Fig. 3, endoscopic inflammatory changes in the EM were more frequently detected in patients without BA, while in the main group, patients had endoscopically negative form prevail in two times comparing with other forms. Thus, the specific allergic affection of the esophagus in patients of the main group is currently questionable and requires additional investigations, including immunological and histological methods which allow us to recognise specific impact factors.

When studying the distribution of GERD forms in patients without BA (Fig. 4), it is notable that there is an approximately equal distribution of forms of reflux disease, indicating the absence of influence of motor disorders on the involvement of the gastric mucosa. Likely, the duration of motor dysfunction as well as, the composition of the refluxate, are significant factors that require further investigation.

The symptoms of BA resemble extraesophageal manifestations of gastroesophageal reflux, thus

requiring verification [5,11,12]. According to literature data, the combination of BA and GERD in children leads to exacerbation of the severity of clinical manifestations, altering the course of the inflammatory process in the respiratory tract and EM with a likelihood of developing eosinophilic esophagitis, prolonging the duration of hospitalization, and disrupting symptom control of the diseases [8,6]. This mutual influence is determined by several factors. On the one hand, it involves the common embryonic origin, features of innervation and blood supply of the respiratory and digestive systems, vagal reflex reactions, resulting in the development of bronchial hyperreactivity in response to motor disorders associated with acid and pepsin reflux, or according to another hypothesis, the influence of inflammatory cytokines. On the other hand, ventilatory disorders in BA lead to an increase in pressure gradient between the thoracic and abdominal cavities, as well as uncontrolled use of systemic glucocorticosteroids and bronchodilators, which affect the tone of the lower esophageal sphincter. All these factors contribute to the development of motor disorders [11].

Esophageal motility disorders were detected in all patients with BA, while the severity of inflammatory changes observed during endoscopy varies and does not depend on the severity of the disease. Signs of inflammation of the EM are present in patients with mild persistent and moderate persistent BA, and absent in cases of severe persistent BA. Considering the significant prevalence of patients with mild and moderate persistent BA, the presence of inflammatory changes in the esophageal mucosa can possibly be explained by the composition of the refluxate.

When assessing structural changes in the esophagus in patients with BA and GERD, there is a certain progression of inflammatory changes in the EM depending on the severity of BA: in cases of mild persistent asthma, erythematous changes in the EM predominated, while in cases of moderate persistent BA, erosive changes were more prevalent. However, in patients with severe persistent BA, no visual changes in the esophagus were observed at all, only motor disorders. Such a result can be explained, on the one hand, by the small number of patients in the group with severe persistent BA, and on the other hand, by the possibility of good disease control, which requires further clarification.

Comparatively to the control group, the frequency of inflammatory changes in the EM due to GERD, according to endoscopy data, is higher in patients without comorbid BA, where the distribution by GERD forms did not show a significant difference in the presence of motor disorders. Thus, the composition of the refluxate and possibly the duration of reflux, which have not been evaluated yet, are likely to be significant factors.

Conclusions

The conducted study revealed that GERD was diagnosed in 44.4% patients with BA. All patients with BA had motor disorders of the esophagus. Endoscopic changes in the EM do not depend on the severity of BA. The non-erosive form was detected in patients with mild persistent BA, erosive form — in patients with moderate persistent BA, endoscopically negative form — in patients with severe BA, which needs clarification. The frequency of inflammatory changes of EM prevailed in patients with GERD and without BA (68.0%) according to endoscopy examination.

Prospects for further research lie in continuing to study the role of allergic pathology in pediatric patients with gastrointestinal pathology.

No conflict of interests was declared by the authors.

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Відомості про авторів:
Карпушенко Юлія Валентинівна — к.мед.н., доц. каф. пропедевтики педіатрії ХНМУ. Адреса: м. Харків, проспект Науки, 4.
https://orcid.org/0000-0002-2196-8817.
Фролова Тетяна Володимирівна — д.мед.н., проф., зав. каф. пропедевтики педіатрії ХНМУ. Адреса: м. Харків, проспект Науки, 4.
https://orcid.org/0000-0002-6861-8902.
ДробоваНадіяМиколаївна — к.мед.н., асистент каф. пропедевтики педіатрії ХНМУ. Адреса: м. Харків, проспект Науки, 4.
https://orcid.org/0000-0002-7493-5701.
Ащеулов Олександр Михайлович — к.мед.н., доц. каф. пропедевтики педіатрії ХНМУ. Адреса: м. Харків, проспект Науки, 4.
https://orcid.org/0000-0001-7454-288X.
Стаття надійшла до редакції 04.03.2024 р., прийнята до друку 14.05.2024 р.