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Ultrasound diagnostics of gastroesophageal reflux in the patients with bronchial asthma

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Objective — to assess the efficacy of ultrasound imaging of the esophagus for diagnosing gastroesophageal reflux disease (GERD) in the patients with bronchial asthma (BA).

Materials and methods. 81 patients with bronchial asthma have been examined. Special diagnostic methods, including ultrasound imaging of the esophagus, have been used for the diagnosis of GERD.

Results and discussion. Contrast-enhanced ultrasound imaging of the esophagus allows to diagnose pathological gastroesophageal reflux in 88,8 % of the patients with clinical pattern of GERD. Moreover, ultrasound imaging of the esophagus demonstrates its efficacy for diagnosing a hiatal hernia that has been detected in 43.8 % of the study patients. The comparative analysis of ultrasound findings with the results of other instrumental studies has shown that pathological changes have been revealed in 3 cases during fibroesophagogastroduodenoscopy (FEGDS) and roentgenography of the esophagus and stomach while sonographic findings have been normal. Conversely, the signs of GERD have been defined in 3 out of 4 patients during the additional ultrasound imaging while FEGDS findings have been normal.

Conclusions. US of the esophagus has proved its high efficacy as the additional method for a primary GERD diagnosis. It is necessary to comprehensively examine the upper digestive tract of the patients with BA by means of ultrasound imaging of the esophagus.

Key words:
ultrasound imaging of the esophagus, gastroesophageal reflux disease, bronchial asthma.

КОНТАКТНА ІНФОРМАЦІЯ

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Over the past years the scientists and physicians from all over the world have taken a great deal of interest in the problem of gastroesophageal reflux disease (GERD). It is truly considered the pathology of the 21st century due to the last decade pronounced tendency toward the overall decreased rates seen with peptic ulcer and increased rates of GERD. Statistics confirm that accurate inquiry helps to detect the symptoms of GERD, primarily its cardinal sign — heartburn, in almost 50 % of the adult population of the developed countries as well as the changes in the esophageal mucosa in 10 % of the individuals that have undergone endoscopy [1, 3, 10].

The importance of the problem under investigation is determined by high prevalence of GERD and its medical and social significance. On the one hand, the latter can be explained by the negative effect of the typical symptoms on the patients' quality of life, and, on the other hand, by atypical clinical manifestations making a diagnostic process more complicated and requiring collaborative efforts of the doctors of different specialties. These results in the close attention the investigators pay to the peculiarities of the clinical course of GERD and improvement of the methods of its diagnostics [7, 9].

In the recent years, the number of the clinical studies suggesting the relation between GERD and pathologies of other organs and systems has

increased. A large group of the so-called atypical (extraesophageal, supraesophageal) manifestations of the disease has been identified. The bronchopulmonary manifestations (chronic cough, aspiration pneumonia, bronchiectatic disease, fibrosing alveolitis and etc.) are primarily associated with bronchial asthma (BA) due to the new findings being obtained every year and indicating pathogenetically substantiated interrelation between asthma and GERD.

The interrelation between bronchospasm and GERD was firstly established by W. Osier in 1892. The investigator described the attack of dyspnea the patient had been experiencing after eating. Further observations allowed to identify high prevalence (according to different evaluations from 53 to 87.3 %) of GERD associated symptoms among the patients with BA. The studies suggested the correlation between severity of BA and gastroesophageal reflux manifestations: frequent symptoms of gastroesophageal reflux were observed in 70 % of the patients with severe asthma, 46 % with moderate asthma and 30 % with mild asthma. More frequent and more severe clinical presentations of asthma were related to sleep, the supine position, and eating. Additionally, GERD was diagnosed in 30 % of the patients with no complaints («silent reflux»). It confirms the necessity of a thorough examination of the upper gastrointestinal tract in this category of the patients [3, 8].

Some peculiarities of BA pathogenesis may simultaneously trigger the development of the conditions worsening GERD symptoms and signs. Therefore, a lot of patients with asthma have an increased tonus of the parasympathetic nervous system and, consequently, a hyperallergenic response to the nonspecific stimuli. Moreover, bronchospasm induced by methacholine inhalation intensifies the lower esophageal sphincter relaxation and increases the number of GERD episodes in this category of the patients. The cough, elevating intra-abdominal pressure and aggravating the lower esophageal sphincter incompetence (LESI), concludes a vicious circle in the patients with both bronchopulmonary and gastrointestinal tract pathologies [10]. Additionally, the hyperventilation syndrome and increased intrathoracic pressure typical for broncho-obstructive disorders induce displacement of the pedicle flaps of the diaphragm responsible for the formation of the gastroesophageal barrier. Taking asthma medications, including oral and nebulized β_2-antagonists as well as theophylline, is crucial for the reduction of the lower esophageal sphincter tonus [5].

The analysis of the patient's complaints and anamnesis are the initial steps to be taken to diagnose GERD. Heartburn is the most characteristic symptom of this pathology and different investigators report its prevalence between 60—90 % of the patients with GERD. The peculiarity of this sign becomes more distinct if heartburn dominates in the clinical pattern and a comprehensive inquiry can reveal up to 92 % of the patients afflicted by this disease (by comparing with endoscopy findings and pH-monitoring) [1]. Regurgitation (acid burp) is also typical for GERD. Although it occurs less frequently than heartburn, the coexistence of these signs makes the clinical evaluation more sensitive. Different methods are used during instrumental diagnostics of the disease. At present 24-hour pH-metry is the gold standard for the diagnosis of GERD. The drawbacks of the diagnostic procedure include significant labor inputs, invasiveness, high cost and sometimes poor tolerance accompanied by adverse effects. The endoscopic investigation (FEGDS) is used to detect and classify reflux esophagitis, perform biopsy, and carry out monitoring of the therapy. However, it should be taken into account that 50—60 % of the patients with clinical manifestations of GERD do not have any visible signs of the esophageal damage [7, 10]. In this case it is recognized as endoscopy-negative (nonerosive) gastroesophageal reflux disease. Additionally, the doctors should keep in mind invasiveness of FEGDS that is, consequently, hindering its wide use for the examination of the individuals with bronchoobstructive disorders as well as the elderly. By means of roentgenography gastroesophageal reflux (GER) is diagnosed in 10—50 % of the study patients because it is rather difficult to detect retrograde flow of the barium suspension from the stomach as it lasts over three minutes and is of low volume. Moreover, the time necessary to complete the observation is limited by increased radiation exposure. This method demonstrates its rather low efficacy for the early diagnosis of GERD [10]. Over the past years ultrasound imaging of the esophagus (US) has been introduced as the method of diagnosing GERD [2].

The study has confirmed a challenging character of the factors leading to mutual worsening of the diseases and the prospects in the diagnosis of the combined pathology. It provides evidence of the necessity for the development of the diagnostic algorithm and determination of the predictors on the efficacy of therapy for combined pathologies.

Objective — to assess the efficacy of ultrasound imaging (US) of the esophagus for diagnosing gastroesophageal reflux disease in the patients with bronchial asthma.

Materials and methods

The research was performed according to the GCP requirements. All patients were informed about the

conditions before the start of the research. An informed agreement was signed after receiving consent to participate in the study from the patient, a copy of which was left with the patient.

Eighty-one patients have been enrolled into the study based on the previous diagnosis of BA in Kyiv City Clinical Hospital N 3. The subjects consisted of the individuals with endogenous form of the disease. The diagnostic criteria have included typical complaints, anamnesis and presence of reversible bronchial obstruction revealed by functional examination of the lungs (an increase in the values for forced expiratory volume at the end of the first second by > 15 % against the initial values following the inhalation of the bronchodilator — 200 mcg of salbutamol). The mean age of the patients was (68.1 ± 10.2) years. During the diagnostic process of GERD in the patients with BA widely recognized methods have been used: clinical (analysis of the patient's complaints, taking anamnesis, physical examination), laboratory (clinical and biochemical blood tests, clinical urinalysis) and instrumental studies (ECG, US of the organs of the abdominal cavity, roentgenoscopy and roentgenography of the lungs). The special diagnostic methods for the evaluation of the esophagus, stomach and duodenum (FEGDS accompanied by the morphologic studies, ultrasound imaging of the esophagus, in some cases roentgenoscopy of the esophagus and stomach, short-term pH monitoring of the esophagus and stomach) have been additionally used.

Sonographic evaluation of the esophagus has been performed on empty stomach in the morning with the patient lying on his back (in the supine position) or on his left side. Scanning has been carried out in the transverse, sagittal and oblique plane through the area relative to the projection of the esophageal lumen of the diaphragm. The procedure enables us to visualize the left lobe of the liver, abdominal part of the esophagus, gastroesophageal junction, diaphragm, and heart. The abdominal part of the esophagus has been visualized below the left lobe of the liver in front of the aorta and has been described as the tube-like structure formed by two hypoechoic rims (front and rear parts of the esophageal walls) and hyperechoic zone (esophageal mucosa and lumen) located between them. The esophageal diameter has been determined by calculating the outside diameter of the esophagus from the front to the rear wall along the perpendicular axis. Normally, the length of the abdominal part of the esophagus ranges between 2.5—3.0 cm, diameter — 1.1—1.5 cm, wall thickness — 0.3—0.5 cm [10].

The study has included two stages: on empty stomach (I) and after drinking 500 ml of the boiled water (II) at the end of 1, 2, 3, 5, 10, 15 minutes. We have been measuring the length of the abdominal part of the esophagus (from the cardioesophageal angle to the projection of the diaphragm), diameter of the esophagus at the esophageal lumen of the diaphragm (outside-outside size), thickness of the esophageal wall, and width of the esophageal lumen.

GER has been diagnosed based on the retrograde flow of the fluid in the esophagus and extension of the abdominal part of the esophagus during contrast-enhanced investigation following filling up the stomach with water. Normally, the extension of the abdominal part of the esophagus does not occur. The widely recognized verifiable signs of GER are retrograde flow of the fluid, extension of the abdominal part of the esophagus within (9.0 ± 3.6) minutes after a start of the examination, an increase in the values for a diameter of the esophagus at the end of the third minute of the contrast-enhanced investigation by (0.35 ± 0.06) cm.

Results and discussion

While questioning the patients with BA and taking their anamnesis we have formed the group of 40 patients (I group) with the symptoms of GER and/or with the confirmed history of GERD. The clinical presentations of reflux have been related to heartburn (burning sensation in the retrosternal area radiating from xiphoid process to the pharynx), regurgitation of food, acid burps, bitter and gaseous eructation, odynophagia, globus sensation (the feeling of the lump in the throat), substernal distress arrested by drinking water or taking antacids. GERD has been clinically diagnosed on the basis of the indicated symptoms, primarily heartburn, and if they have been observed two or more times per week. The mean age of the patients — (69.4 ± 8.9) years, including 15 (34.9 %) men and 25 (65.1 %) women. The leading share has been allotted to the individuals with moderate BA and amounted to 72.1 %, the duration of the disease has ranged between 1 and 46 years, at average (17.4 ± 10.8) years. 41 patients with bronchial asthma without any signs of GERD (BA without GERD) have been enrolled in the control group (II group). Their mean age — (65.6 ± 11.8) years, 16 (38.2 %) men and 25 (61.8 %) women. This group has predominantly included the individuals with moderate asthma (67.1 %) and with average disease duration — (14.8 ± 9.3) years.

As to the accompanying pathologies that have been diagnosed in the representatives of both groups it should be noted that the groups have been homogeneous. Hypertension (I—II stages) has been diagnosed in 23 (54.6 %) patients of the first group and in 24 (53.9 %) patients of the second group; ischemic heart disease (IHD), in 33 (76.7 %) and

35 (76.3 %) patients respectively; diabetes mellitus of Type 2 — in 10 (23.3 %) and 12 (28.9 %) cases; glaucoma — in 3 (6.9 %) and 4 (10.5 %) study patients, gastric ulcer and / or duodenal ulcer in remission — in 7 (13.9 %) and 5 (13.2 %) patients, accordingly.

The mean value for forced expiratory volume (FEV_1) in the patients of group I has been (68.5 ± 16.9) % against the normal values, in group II — (70.7 ± 18.8) % ($p > 0.05$). However, statistically significant difference has been established in the values for maximal expiratory flow at 25 % of forced vital capacity in (43.0 ± 17.7) % of the study patients of group I against (56.6 ± 24.6) % of the individuals of group II. It is an evidence of more severe distal obstruction in the patients suffering from both BA and GERD. In addition, statistically significant difference has been stated in the mean values for vital capacity of the patients of both groups: in group I this value has been (79.5 ± 17.1) %, in group II — (87.1 ± 17.8) % ($p = 0.006$).

The analysis of the patients' complaints has been carried out by evaluating some factors including:

– an amount of the attacks caused by expiratory daytime and nocturnal dyspnea;
– the need for short-acting bronchodilators in the daytime and at night;
– the characteristics of the prescribed basic therapy for bronchial asthma (daily inhalation dose of glucocorticosteroids, long-acting β-antagonists);
– pronounced heartburn, belching, retrosternal distress;
– daily need for antacids.

While analyzing the course of bronchial asthma, the nocturnal symptoms and signs of the disease (difficulty breathing, cough) have prevailed in group I — in 19 (47.7 %) patients against only 30.7 % (13 patients) in group II, wherein the difference has been statistically significant.

A special attention has been paid to revealing reflux associated symptoms of bronchial asthma among the patients of group I. The temporal link between the attacks of difficulty breathing or wheezing, cough, chest congestion and clinical presentations of GERD (heartburn, regurgitation, retrosternal disturbances) as well as simultaneous worsening of bronchial asthma and GERD have been detected in 27 (31.4 %) patients. Notably, in the majority of cases it has been done only after our deliberate focus on those issues.

Asking a patient about his/her complaints and taking anamnesis may allow a doctor to find out the factors associated with likely contribution of GERD to the development and aggravation of asthma symptoms: late onset of asthma; worsening of asthma symptoms after eating, in the supine position, after physical overexertion; worsening of nocturnal asthma symptoms; cough accompanied with rales, dyspnea and reflux-related signs.

Ultrasound imaging of the esophagus has been performed in group I consisting of 40 patients. According to the findings pathological GER has been diagnosed in 20 (50.0 %) individuals, GER accompanied by a hiatal hernia — in 15 (38.8 %) patients, and a hiatal hernia in 2 (5.0 %) patients. In 3 (6.3 %) study patients with clinical signs of GERD ultrasound results have shown no pathologies.

Taking into account the ultrasound criteria of pathological GERD, the latter has been diagnosed due to an increase in the values for a diameter of the esophagus at the end of the third minute of the contrast-enhanced investigation by 0.35 cm, at the end of the fifth minute — by 0.42 cm, as well as extension of the esophageal diameter within 9 minutes or more after drinking water.

Meanwhile, in some cases even at the end of 15 minutes of the examination the esophageal diameter has not got back to its initial values being 1.45 cm against 1.32 cm prior to the examination.

To sum up, the contrast-enhanced ultrasound imaging of the esophagus and stomach allows us to detect pathological gastroesophageal reflux in 88.8 % of the patients with clinical presentations of GERD. In fact, US of the esophagus is a non-invasive method, easily tolerated and accessible in the general medicine and gastroenterology. The signs of reflux have been detected by neither endoscopy nor roentgenography (except the case when the pathology has been complicated by reflux-esophagitis).

Moreover, US of the esophagus has shown its high efficacy for the diagnosis of a hiatal hernia, that has been detected in 43.8 % of the study cases.

The inquiry of the patients has demonstrated that none of them was experiencing any discomfort during the examination and all 40 patients (100 %) were expressing their readiness to undergo the procedure again. The same cannot be said about other instrumental methods GI tract examination.

The comparative analysis of ultrasound findings with the results of other instrumental studies has shown that pathological changes have been revealed in 3 cases during FEGDS (1 patient with incompetence of cardia) and roentgenography of the esophagus and stomach (2 patients with a hiatal hernia) while sonographic findings have been normal. Conversely, during the additional ultrasound imaging the signs of GERD have been defined in 2 out of 4 patients and GER accompanied by a hiatal hernia — in 1 patient, while EGDS findings have been normal.

Only comprehensive examination of the patients increases the chances to diagnose gastroesophageal reflux and the conditions contributing to its development.

The findings of ultrasound examination of 25 patients of group II do not indicate any signs of GER. A hiatal hernia revealed during endoscopy and roentgenography has been confirmed in 15 (60.0 %) individuals during US.

To sum up, the patients with BA without a clinical picture of GERD are more rarely diagnosed with the conditions leading to the development of reflux (a hiatal hernia, incompetence of cardiac sphincter), and contrast-enhanced ultrasound is still highly efficient diagnostic method of esophageal pathologies.

High prevalence of GER, including its silent form, among the patients with BA necessitates more accurate examination of the upper GI tract in this category of the patients. A required in-patient hospital stay restricts application of highly efficient 24-hour pH-metry. Moreover, pronounced bronchial obstruction often results in poor tolerance of the invasive instrumental studies due to accompanying respiratory insufficiency, allergic response to anesthetics, ENT diseases (allergic and/or rhinosinusitis polyposa) while the additional roentgenography causes increased radiation exposure. Taking into account the economic aspects of the treatment, it may be agreed that it is necessary to limit the number of complex and costly diagnostic procedures. The above-mentioned requires a search for alternative diagnostic methods for the examination of the patients with GERD and BA, to which contrast-enhanced ultrasound imaging of the esophagus and stomach can be referred. In addition, there is evidence that this diagnostic procedure is well tolerated by patients, and this characteristic may be considered while controlling GERD in the course of treatment.

Conclusions

We have assessed the efficacy of ultrasound diagnostics of gastroesophageal refluxes and a hiatal hernia as an accompanying pathology in the patients with BA. There is evidence of high efficacy of this additional non-invasive method of primary diagnostics. It is necessary to carry out a comprehensive examination of the upper GI tract in the patients with BA, especially with its severe forms making diagnosis of GERD more difficult, by means of ultrasound imaging of the esophagus as a primary diagnostic method.

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Ультразвукова діагностика гастроезофагеальних рефлюксів у хворих на бронхіальну астму

Мета роботи — визначити можливості ультразвукової діагностики (УЗД) стравоходу в діагностиці гастроезофагеальної рефлюксної хвороби (ГЕРХ) у хворих на бронхіальну астму (БА).

Матеріали та методи. Обстежили 81 хворого на БА. Для діагностики ГЕРХ у хворих на БА застосовували спеціальні методи, в тому числі УЗД стравоходу.

Результати та обговорення. Контрастне УЗД стравоходу в 88,8 % випадків дозволяє виявити патологічний гастроезофагеальний рефлюкс у пацієнтів з клінічними ознаками ГЕРХ. УЗД стравоходу виступає інформатив-

ним також для діагностики грижі стравохідного отвору діафрагми, яка була виявлена в 43,8 % досліджених. Порівняння даних УЗД з результатами інших методів інструментальної діагностики показало, що в 3 випадках нормальних показників ехографічного дослідження зміни були виявлені при фіброезофагогастродуоденоскопії та рентгенографії стравоходу і шлунка. І навпаки, з 4 пацієнтів з нормальними показниками фіброезофагогастродуоденоскопії при додатковому УЗД у 3 виявлено ознаки ГЕРХ.

Висновки. Виявлено високу інформативність УЗД стравоходу як додаткового методу первинної діагностики ГЕРХ. У осіб з БА, особливо з тяжкими формами, для виявлення ГЕРХ доцільно проводити комплексне обстеження верхніх відділів травного тракту з використанням УЗД стравоходу.

Ключові слова: ультразвукова діагностика стравоходу, гастроезофагеальна рефлюксна хвороба, бронхіальна астма.

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Ультразвуковая диагностика гастроэзофагеальных рефлюксов у больных бронхиальной астмой

Цель работы — определить возможности ультразвуковой диагностики (УЗИ) пищевода в диагностике гастроэзофагеальной рефлюксной болезни (ГЭРБ) у больных бронхиальной астмой (БА).

Материалы и методы. Обследовали 81 больного БА. Для диагностики ГЭРБ у больных БА применяли специальные методы, в том числе УЗИ пищевода.

Результаты и обсуждение. Контрастное УЗИ пищевода в 88,8 % случаев позволяет выявить патологический гастроэзофагеальный рефлюкс у пациентов с клиническими признаками ГЭРБ. УЗИ пищевода выступает информативным также для диагностики грыжи пищеводного отверстия диафрагмы, которая была обнаружена в 43,8 % исследованных. Сопоставление данных УЗИ с результатами других методов инструментальной диагностики показало, что в 3 случаях нормальных показателей эхографического исследования изменения были обнаружены при фиброэзофагогастродуоденоскопии и рентгенографии пищевода и желудка. И наоборот, из 4 пациентов с нормальными показателями фиброэзофагогастродуоденоскопии при дополнительном УЗИ у 3 выявлены признаки ГЭРБ.

Выводы. Выявлена высокая информативность УЗИ пищевода в качестве дополнительного метода первичной диагностики ГЭРБ. У лиц с БА, особенно с тяжелыми формами, для выявления ГЭРБ целесообразно проводить комплексное обследование верхних отделов пищеварительного тракта с использованием УЗИ пищевода.

Ключевые слова: ультразвуковая диагностика пищевода, гастроэзофагеальная рефлюксная болезнь, бронхиальная астма.