Respiratory tract pathology is most common in adults [13] in the developed world. Despite last year’s success in diagnoses and treatment of respiratory diseases, the whole world is facing an increase in pulmonary diseases [12].

The number of patients with bronchial asthma suffered from concomitant extrapulmonary pathology, including subjects with bronchial asthma associated with gastroesophageal reflux disease, is also increasing. Combination of these diseases, from multiple sources [2, 3, 9], is observed in 34–89% of patients, however, in 24% of patients, reflux could not be recognized by clinical observation. The rate of severe asthma episodes occurring after eating the food has been estimated to be notably higher in patients suffered from bronchial asthma with concomitant gastroesophageal reflux disease rather than in patients with bronchial asthma without gastroesophageal reflux disease [1, 4].

Multiple studies have shown that asthma attacks can be triggered by hypersensitivity of respiratory tract to different irritants, which act to cause and aggravate swelling of bronchial mucus, mucus distention and bronchospasm [4,9]. Asthma attacks may occur at any time of day, but people reported nocturnal attacks more common; it appears to be due to an increase (prevalence) in the parasympathetic tone of the vegetative nervous system as well as due to a reduction in the regulation effect of the cerebral cortex on subcortical vegetative centers. These changes appear to be caused by association of asthma attacks with gastroesophageal reflux [5]. In daily therapeutic practice, the following factors indicate a probable role of gastroesophageal reflux disease in the development and aggravation of asthma symptoms: late clinical stages of asthma, aggravation of asthma symptoms occurring after eating the food, especially after overeating, in supine position, angular position, after exercise, worsening of asthma symptoms at night, concordance of cough attack, rales, dyspnoea with symptoms of gastroesophageal reflux disease (heartburn).

Several pathogenic mechanisms have been proposed to explain the etiology of asthma attacks with concomitant gastroesophageal reflux disease. They are induced: 1) by activation of vagal pathways of gastroesophageal reflux-induced broncho-obstruction by esophageal contents [14]; 2) by direct activation of esophageal contents which leads to exudative inflammation of bronchial mucus [15]. Other investigators believe that bronchial asthma [1, 10] initiates a “vicious cycle” leading to development and maintenance of gastroesophageal reflux probably by increasing the pressure gradient between the thorax and abdomen. Progression of bronchial asthma usually leads to manifestation and further development of extensive bronchial tree obstruction of varying severity [4].

Data on the intensity of effects of bronchoconstriction in patients with reflux esophagitis reveal about the possibility of using vagal receptors in the pathogenesis in the presence of esophageal inflammation. A number of authors suggest that there are specific esophageal mucosal damage receptors, so called nociceptors [9].
Selection of medicinal products used in the treatment of bronchial asthma and gastroesophageal reflux disease in these patients requires an ad hoc approach. A complex pathology – bronchial asthma and gastroesophageal reflux disease – is accompanied by an increase in the need for short-acting bronchodilators up to 1.5 times compared to patients without symptoms of gastroesophageal reflux disease. Treatment of bronchial asthma and gastroesophageal reflux disease should be rational (where possible, polypharmacy should be avoided) and sparing considering underlying diseases, usually requiring administration of additional medicinal products. Inhaled corticosteroids and bronchial spasmolytics are widely used in the treatment of patients with bronchial asthma.

It is known that Berodual N is a combination broncholytic containing fenoterol and ipratropium bromide, rendering positive effect on the smooth muscles of the bronchi. It is quite clear that a lower esophageal sphincter, smooth muscle, is the main component of the antireflux mechanism. A reduced LOS tone is observed in 20-80 % of patients with gastroesophageal reflux disease [2], with the reduction rate correlated with the severity of disease. The positive effect of Berodual N on the smooth muscle of LOS in patients suffered from bronchial asthma with concomitant gastroesophageal reflux disease cannot be excluded.

**Purpose of this study:** to study the efficiency of Berodual N in the background therapy of patients with bronchial asthma with concomitant gastroesophageal reflux disease.

**Materials and methods**

32 patients were involved in the study. The diagnosis of bronchial asthma is established according to GINA criteria based on specific complaints, history, presence of reversible bronchial obstruction according to External Respiratory Function (increase in forced expiratory volume in first second by 13 % and after intake of bronchodilator – 200 µg salbutamol). In survey and study of the history among patients with bronchial asthma, we allocated a group of patients with symptoms of gastroesophageal reflux disease (particularly, heartburn, acid regurgitation) and/or documentary evidence for a past history of gastroesophageal reflux disease. The subjects were assigned into two groups. These groups included 72.1 % of patients with moderate bronchial asthma. All subjects with bronchial asthma received pathogenic treatment according to the Order No. 128 of the Ministry of Health of Ukraine “On Approval of Clinical Protocols of Medical Care in the Specialty “Pulmonology” [8] of March 19, 2007. Statistical treatment was carried out using mathematical and statistical software including MS Excel and consists in further comparison [6].

Analysis of examination results for 32 patients revealed the following features. The diagnosis of bronchial asthma index, in particular, night symptoms (dyspnoea, cough), revealed the prevalence in group 1 of 21 patients (91.3 %). In group 2, the total number of patients who experienced nocturnal asthma was 8 (88.8 %) patients. Thus, these findings compare favorably to those reported by other authors, who tended to regard gastroesophageal reflux disease as a potential trigger of nocturnal asthma.

The main symptoms of gastroesophageal reflux disease in the examined patients were heartburn (89.3 %), acid regurgitation (54.2 %), and regurgitation (15.1 %). However, only 4 patients (12.5 %) reported severe heartburn (3-4 points on a Likert scale), the majority of patients reported mild-to-moderate heartburn, respectively, in 14 (43.8 %) and 12 (37.5 %) patients. All the patients underwent esophagogastroduodenoscopy. X-rays of the esophagus and stomach were taken with 24 patients in accordance with standard practice. Patients were monitored for a month. Patients of both groups received routine background therapy (short-acting inhaled corticosteroids and β2-agonists, where necessary), proton pump inhibitors (PPI), antisecretory treatment, if required. The second group of patients additionally received Berodual N in the form of a freon-free metered dose inhaler taken as 1 puff in the morning and in the evening. 1 dose of the metered dose inhaler Berodual N contains ipratropium bromide (20 µg) and fenoterol hydrobromide (50 µg).

According to the severity of gastroesophageal reflux disease (the intensity of heartburn, esophageal affection according to the Los Angeles classification), anti-secretory treatment with omeprazole was performed at a dose of 40 mg (32 patients) and antacids (Maalox) as needed. The efficiency of therapy was assessed on the change in clinical progression of gastroesophageal reflux disease, heartburn relief during treatment, improvement of erosive ulcerous defects according to ECG findings. The effect of the therapy on bronchial asthma was assessed based on symptom scores during the day and night, the use of bronchodilators for 24 hours, changes in FEV1 and VC values.

**Results**

Accumulation of data and their mathematical treatment were carried out using licensed software of Microsoft Office 2007. Statistical treatment was carried out using mathematical and statistical software including MS Excel and consists in the determination of parts (percent) and mean error with further comparison [6].

The main symptoms of gastroesophageal reflux disease in the examined patients were heartburn (89.3 %), acid regurgitation (54.2 %), and regurgitation (15.1 %). However, only 4 patients (12.5 %) reported severe heartburn (3-4 points on a Likert scale), the majority of patients reported mild-to-moderate heartburn, respectively, in 14 (43.8 %) and 12 (37.5 %) patients. All the patients underwent complete instrumental examination. According to the Los Angeles classification, 28 patients (87.5 %) reported mild esophagitis (“A”) in two study groups; esophagitis of B and C stages was diagnosed in 3 (9.3 %) and 1 (3.2 %), respectively.
The examined patients completed a daily diary assessing frequency and intensity of symptoms. A Likert scale was used to measure severity of individual symptom.

Analysis of examination results for patients before treatment highlighted the following changes. There was also no statistically significant difference between FEV₁, PFR25% mean values in patients of group 1 and group 2 (table 1). During the analysis of asthma symptoms throughout the day and night (dyspnea, cough), there was also no statistically significant difference.

The response to the performed treatment was assessed based on diurnal and nocturnal asthma attacks, use of bronchodilators for 24 hours, changes in FEV₁ and VC values. The outcome analysis of both groups demonstrated a positive effect of the management of GERD in patients with bronchial asthma on the aforementioned criteria (table 1). The most pronounced effect was observed with respect to nocturnal asthma attacks. The treatment effect on diurnal asthma attacks was noted to a lesser extent; a reduction in bronchodilator use was observed in both groups. The differences in dynamics of diurnal and nocturnal dyspnoea attacks, the need for bronchodilators in patients of group 2 were statistically significant. Statistically significant improvement in parameters of external respiration was noted in this group.

Conclusion

The data obtained demonstrated that combination therapy of patients with bronchial asthma associated with gastroesophageal reflux disease (including co-administration of proton pump inhibitors with basic antasthmatic therapy) decreased clinical symptoms of both disorders, improved quality of life for patients and improved lung function parameters (FEV₁, VC). The response to the performed treatment was noted to a lesser extent; a reduction in bronchodilator use was observed in both groups. The differences in dynamics of diurnal and nocturnal dyspnoea attacks, the need for bronchodilators in patients of group 2 were statistically significant. Statistically significant improvement in parameters of external respiration function was noted in this group.

References


КЛІНИЧНИЙ ДОСВІД ЗАСТОСУВАННЯ КОМБІНОВАНОГО ПРЕПАРАТУ НА ОСНОВІ ФЕНОТЕРОЛУ І ІПРАТРОПІЮ БРОМІДУ В КОМПЛЕКСНІЙ ТЕРАПІЇ БРОНХІАЛЬНОЇ АСТМИ У ПОЄДНАННІ З ГАСТРОЕЗОФАГЕАЛЬНОЮ РЕФЛЮКСНОЮ ХВОРОБОЮ

Т. В. Бездітко, Л. А. Овчаренко, Л. О. Бойко, Г. В. Єрьоменко

Резюме. Обстежено 32 хворих на бронхіальну астму (БА), поєднану з гастроезофагеальною рефлюксною хворобою (ГЕРХ). Хворих було розподілено на дві групи. Обидві групи приймали базисну антиастматичну терапію, інгібітори протонної помпи, антисекреторну терапію за потреби. Пациєнти другої групи додатково щоденно вранці та ввечері приймали препарат Беродуал Н. Отримані дані свідчать про позитивний вплив Беродуалу Н на перебіг ГЕРХ у хворих на БА.

Ключові слова: астма, гастроезофагеальна рефлюксна хвороба, якість життя.

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CLINICAL EXPERIENCE WITH THE COMBINED DRUG BASED ON FENOTEROL AND IPRATROPIUM BROMIDE IN THE TREATMENT OF BRONCHIAL ASThma IN COMBINATION WITH GASTROESOPHAGEAL REFLUX DISEASE

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Summary. Thirty two patients having bronchial asthma (BA) complicated by gastroesophageal reflux disease (GERD) have been examined. The patients have been divided into two groups, each one receiving comprehensive anti-asthmatic therapy, proton pump inhibitors and, if required, antiserective treatment. The second group was addionally taking Berodual N every day in the morning and evening. The data testifying a positive effect of Berodual N upon GERD clinical course in patients with BA, have been obtained.

Key words: asthma, gastroesophageal reflux disease, quality of life.

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