

M. M. Ostrovskiy, O. I. Varunkiv
Ivano-Frankivsk National Medical University

Selection of the optimal scheme for obstructive syndrome management in virus-induced acute bronchitis

Key words: *acute bronchitis, acute respiratory viral infection, bronchial obstruction.*

Prevention and proper treatment of respiratory pathologies that occur against the backdrop of acute respiratory viral infections (ARVI) and influenza remain extremely important issues for health care systems in most countries of the world (Y. I. Feshchenko, 2009, 2013; I.V. Dziublyk et al., 2011). Currently, according to the various statistical reports, the incidence of acute bronchitis ranges from 13.2 to 34 % of respiratory diseases. The actual scale of prevalence of acute bronchitis in adults can be estimated by the findings of R. Gonzales et al., 2000, in the United States: about 5% of Americans aged over 18 years have from acute bronchitis at least once a year, and in 1997 it became the cause of more than 10 million visits to physicians. The incidence is influenced by epidemic outbreaks of influenza and other ARVI, weather factors, and coverage of the population with preventive vaccinations.

Among the etiologic factors of primary importance is infection, namely two types of respiratory viruses: those affecting mainly the lower respiratory tract (influenza viruses A and B, parainfluenza, respiratory syncytial virus, human metapneumovirus) or those affecting mainly the upper respiratory tract (coronaviruses, adenoviruses, rhinoviruses) [7]. It is known that acute respiratory viral infections rank first in the structure of incidence of viral infections. According to the Ukrainian Center of influenza and acute respiratory infections, during the period from 1994 till 2010 approximately 8.5 million people have influenza and ARVI annually, which is 18% of the population of Ukraine. As regards influenza only, in our country each year some 700 million people suffer from it annually. According to the World Health Organization (WHO), every year, during outbreaks of influ-

enza epidemics in the world, 500 million people get ill, of which 2 million people die. Apart from seasonal outbreaks of ARVI, in 5–10 % of cases of acute bronchitis pathogens are *Bordetella pertussis* and *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*. We would like to emphasize especially that the concept of «acute bacterial bronchitis» is recognized false (except for some cases of diseases in patients with tracheostoma or endotracheal intubation).

ARVI and influenza often lead to exacerbation and chronic pathologies: asthma, COPD, cardiovascular diseases and kidney diseases. Epidemiological studies indicate that SARS is the cause of 80–85 % of asthma exacerbations in children and 75 % of cases in adults. Moreover, ARVI and influenza often cause the occurrence of pneumonia - both primary viral (fulminant fatal hemorrhagic pneumonia), and secondary bacterial. Despite the large number of effective drugs, therapy does not always provide an opportunity to achieve the desired result. Treatment of respiratory diseases complicated with development of the obstructive syndrome requires a special approach, which greatly affects the quality of life of patients and is usually the cause of formation and progression of irreversible changes in the human body.

According to various sources, the broncho-obstructive syndrome caused by acute bronchitis is present in 45–70 % of patients. In particular, the works of G. L. Yurenev (2012) [2] state that in acute bronchitis signs of bronchial obstruction are present in 60.8 % of patients (Figure).

It should be noted that the development of bronchial obstruction is usually associated with identification of viral pathogens:

- respiratory syncytial virus (up to 50 % of cases, especially in children);
- parainfluenza virus;
- influenza virus and adenoviruses.

Among the bacterial pathogens, *Mycoplasma pneumoniae* should be singled out.

The broncho-obstructive syndrome is a pathological condition characterized by restricted air flow during breathing and characterized by patients as shortness of breath. In addition to the subjective signs (shortness of breath, feeling of tightness in the chest), bronchial obstruction is measured by spirometry data, characterized by decreased rate parameters (forced expiratory volume in the first second (FEV_1) and peak expiratory flow rate (PEF)). However, the earliest manifestation of bronchial obstruction, even at high FEV_1 , is a decline in $FEV_1/FVC < 70\%$. It is known that bronchial obstruction during a chronic pathology of the respiratory system includes functional (reversible) and organic (irreversible) components [6]. While the former may regress spontaneously or under the influence of treatment, the latter are characterized by marked changes in tissue structure and do not resolve spontaneously or as a result of therapy. In the event of obstructive syndrome, the reversible component of airway obstruction prevails in acute pathologies.

The reversible component consists of edema of bronchial mucosa, spasm of smooth muscle and hypersecretion of mucus, resulting from a large range of proinflammatory mediators (interleukin-8, $TNF-\alpha$, neutrophil proteases, free radicals). Proinflammatory mediators stimulate the vagus nerve and cause the release of acetylcholine from cholinergic nerves with subsequent activation of muscarinic cholinergic receptors. According to P. Barnes (2011), leukotrienes play a major role in cholinergic bronchospasm, being 1000 times more active than histamine and causing 2.6 times longer bronchoconstriction, as well as inhibiting the function of cilia of the ciliated bronchial epithelium. Thus, by acting on these receptors, biologically active substances (histamine, prostaglandins, bradykinin, etc.) released during viral replication can cause reflex bronchoconstriction.

Besides, in addition to parasympathetic (M_1 - and M_2 -cholinoreceptors) part of the nervous system, the occurrence of broncho-obstructive syndrome in the presence of a viral

infection is also influenced by sympathetic (β_2 -adrenoreceptors). Respiratory infections can block the β_2 -adrenoreceptors, which results in the development or strengthening of bronchial obstruction [2]. These pleiotropic effects cause impaired microcirculation, activation of lipid peroxidation, hypoxia.

It should be noted that the number of β_2 -adrenoceptors and M-cholinergic receptors localized in the bronchial tree is different. Thus, β_2 -adrenoreceptors are located predominantly in the distal airways, whereas recent studies show that effector cholinergic receptors are located both in the distal (small) and bronchial submucosal glands, and in the airway epithelium. These are so-called abneuronal cholinoreceptors. Interestingly, these cholinoreceptors are not associated with the branches of the parasympathetic nervous system. In addition, the sensitivity of M-cholinergic receptors of the bronchi does not decrease with age, which allows using M-cholinoblocking agents in elderly and senile patients with COPD.

In order to relief bronchial obstruction, the most effective route of administration is inhalation, because the medication directly enters the bronchi and quickly takes effect. High concentrations of drugs develop in the airways, while the drug concentration in the blood is negligible. Despite the differences in the mechanism of action of various bronchodilators, their most important feature is the ability to eliminate spasm of bronchial muscles and facilitate the passage of air into the lungs.

The first line of treatment for preventing the symptoms of bronchial obstruction of any etiology is inhaled short-acting β_2 -agonists. The bronchodilatory effect of short-acting β_2 -agonists occurs within 4–5 min, reaching its maximum within 40–60 minutes, and the duration of effect is 4–5 hours [5]. However, the foregoing implies that vagus-dependent bronchoconstriction that occurs in patients with acute respiratory tract pathology (laryngitis, tracheitis, bronchitis) against viral infections cannot be treated effectively by administering only β_2 -agonists, so there is a need to use drug combinations [1]. In some cases, a combination therapy with β_2 -agonists and anticholinergics has advantages over monotherapy with either of them. The effectiveness of their combination is due to different mechanisms of action [5]:

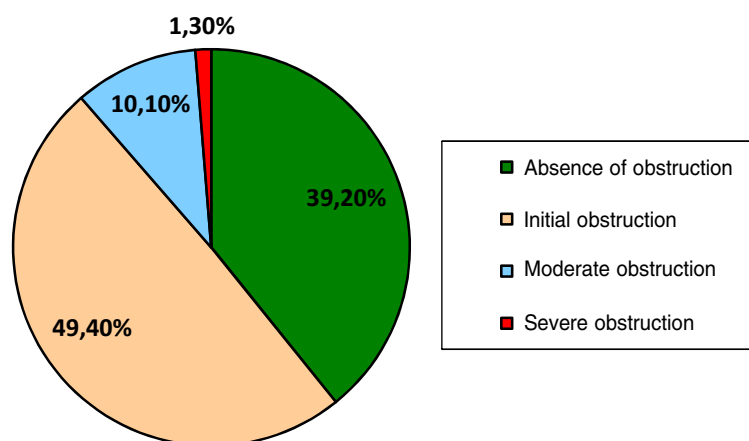


Figure 1. Obstructive disorders in acute bronchitis.

- β_2 -agonists act through the sympathetic nervous system, anticholinergics - through the parasympathetic nervous system;

- additional (synergistic) effect;

- different onset and duration of action (quicker effect of β_2 -agonists, and more prolonged action of anticholinergic drugs);

- dose reduction (smaller dose of each of the drugs compared with monotherapy doses to achieve the same effect), and thus fewer side effects

- two active ingredients are contained in a single carrier that simplifies their use, improves compliance, reduces costs and saves materials.

Berodual N fully complies with these criteria, as it consists of a β_2 -agonist (fenoterol hydrobromide) and M-anticholinergic (ipratropium bromide), which counteracts both points of application of the virus. Berodual N is able to provide dual control of bronchial obstruction symptoms in virus-induced acute bronchitis. The combination of substances results in potentiation of the bronchodilatory action without increasing adverse effects due to a reduced dose of each of them. In addition to the broncholytic effect, the presence of an anticholinergic reduces the sensitivity of cough receptors, decreases oxygen consumption by the respiratory muscles, reduced the mucus secretion. Besides, one should remember the phenomenon of polymorphism of homozygous β_2 -adrenergic receptors that occurs in the Caucasian population in 15 % of cases, the Mongoloid and Negroid population in 30 % of cases, and causes distorted sensitivity to β_2 -agonists. The combination therapy makes it possible to achieve the desired bronchodilatory effect in these patients [3].

At the onset of a virus-induced bronchial obstruction it is recommended to use Berodual solution for nebulation, and then proceed to using (if necessary) a metered inhalation device.

Thus, the combined use of a bronchodilator drug Berodual N containing a β_2 -agonist and a M-anticholinergic helps to overcome the existing broncho-obstructive syndrome in virus-induced acute bronchitis, tracheitis, laryngitis and thus prevent more devastating (and sometimes life-threatening complications) of influenza and ARVI.

References

1. Блохин, Б. М. Современные подходы к терапии обострений бронхиальной астмы у детей [Текст] / Б. М. Блохин // Трудный пациент. — 2011. — Т. 9, № 8–9. — С. 36–39.
2. Цветкова, О. А. Ингаляционная терапия бронхообструктивного синдрома [Текст] / О. А. Цветкова // Трудный пациент. — 2011. — Т. 9, № 2–3. — С. 26–30.
3. Юдина, Л. В. Бронхообструктивный синдром: возможности современной терапии [Текст] / Л. В. Юдина // Здоров'я України. — 2007. — № 20. — С. 54–55.
4. Юрнев, Г. Л. Преимущества комбинированных бронхолитических препаратов в лечении острого бронхообструктивного синдрома [Текст] / Г. Л. Юрнев // Пульмонология и аллергология. — 2012. — № 3. — С. 13–18.

5. Яшина, Л. А. Сравнительная характеристика эффективности и безопасности комбинированных бронхолитиков: ипратропия бромид + фенотерол и ипратропия бромид + сальбутамол [Текст] / Л. А. Яшина // Здоров'я України. — 2006. — № 21 (154). — С. 1–7.

6. Bousquet, J. Asthma: from bronchoconstriction to airways inflammation and remodeling [Text] / J. Bousquet, P. K. Jeffery, W. W. Busse, M. Johnson, A. M. Vignola // Am. J. Respir. Crit. Care. Med. — 2000. — Vol. 161. — P. 1720–1745.

7. Gonzales, R. G. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis [Text] / Gonzales R. G. et al. // Annals of Internal Medicine. — 2001. — № 134 (6). — P. 521–529.

ВЫБОР ОПТИМАЛЬНОЙ СХЕМЫ ПРЕОДОЛЕНИЯ ОБСТРУКТИВНОГО СИНДРОМА ПРИ ВИРУС-ИНДУЦИРОВАННЫХ ОСТРЫХ БРОНХИТАХ

Н. Н. Островский, А. И. Варункив

Резюме

Согласно данным различных статистических отчетов показатели заболеваемости острым бронхитом колеблются от 13,2 до 34 % среди болезней органов дыхания. На уровень заболеваемости влияют эпидемические вспышки гриппа и других острых респираторных вирусных инфекций, вне сезона эпидемических вспышек на первом месте выступают бактериальные возбудители. По разным данным бронхообструктивный синдром вследствие перенесенного острого бронхита выявляется у 45–70 % пациентов. Для купирования бронхообструкции наиболее эффективным путем введения лекарственных средств является ингаляционный по причине непосредственного поступления препарата в бронхи и быстрого начала его действия. Комбинированная терапия β_2 -агонистами и холинолитиками имеет преимущества перед монотерапией каждым из них, поскольку вагус-зависимый бронхоспазм, возникающий у больных с острой патологией дыхательных путей на фоне вирусной инфекции, невозможно эффективно лечить, принимая только β_2 -агонисты.

Ключевые слова: острый бронхит, острая респираторная вирусная инфекция, бронхообструктивный синдром.

Научно-практический журнал «Астма и аллергия», 2014, №1
М. М. Островский

Профессор, д. мед. наук, заведующий кафедрой фтизиатрии и пульмонологии с курсом проф. заболеваний
ГВУЗ «Ивано-Франковский медицинский университет»

SELECTION OF THE OPTIMAL SCHEME OF BRONCHOCONSTRICTION MANAGEMENT IN VIRAL-INDUCED ACUTE BRONCHITIS M. M. Ostrovskiy, O. I. Varunkiv

Abstract

According to various statistical reports, the incidence of acute bronchitis range from 13.2 to 34 % of all respiratory diseases. The influence on the incidence have as outbreaks of influenza so acute respiratory viral infection, but between seasonal epidemic outbreaks the bacterial pathogens are on the first place. According to various sources bronchial obstruction occurs in 45–70 % of patients with acute bronchitis. The inhalation technique is the most effective way for the treatment of bronchial obstruction, because the drug enters directly into the bronchi. Combination therapy with β_2 -agonists and anticholinergic agents have an advantage compared to monotherapy with each of them, because vagus-dependent bronchospasm, which occurs in patients with viral acute airway pathology cannot be effectively treated by taking only β_2 -agonists.

Key words: acute bronchitis, acute respiratory viral infection, bronchial obstruction.

Theoretical and practical J. «Asthma and Allergy»

M. M. Ostrovskiy, MD, professor
Chief of the department of phthisiology and pulmonology
of Ivano-Frankovsk National Medical University