

ASSESSMENT OF THE CLINICAL EFFECTIVENESS OF COMBINED BRONCHOLATIC DRUGS (JOSET) IN THE TREATMENT OF ACUTE OBSTRUCTIVE BRONCHITIS IN CHILDREN

**Makhmudov I.,
Aliyeva U.,
Mustafaeva S.,
Huseynova A.,
Valiyeva K.**

Department of Children's Diseases of Azerbaijan medical university
<https://doi.org/10.5281/zenodo.10815202>

Abstract

Actuality. Acute infectious diseases of the upper respiratory tract (URI) accompanied by cough occupy an important place among children's respiratory pathologies. Thus, the incidence of acute respiratory infections (ARIs) among children is 4-5 times higher than that of adults and accounts for more than 90% of all infectious and parasitic diseases. In this regard, the highest indicators are recorded before school, especially in the first 3 years. Acute bronchitis (AB), which is caused by infectious damage to the lower respiratory tract, is considered one of the most common diseases in children. The incidence of KB in the pediatric population is 75-250 per 1000 children. Acute obstructive bronchitis (COB) means an inflammatory disease of the bronchial tree with symptoms of obstruction, in other words, symptoms of bronchial permeability disturbance. The course of COPD in children is accompanied by weak productive cough, increased vocal whistling, tachypnea and distant dry rales. Presented in this article, in addition to interpreting the modern ideas about the etiopathogenesis, classification and clinical-diagnostic features of acute bronchitis in children, as well as the results of our research in the direction of studying the therapeutic effectiveness of JOSET as a combined broncholytic drug used in the treatment of acute obstructive bronchitis. described.

Keywords: Children, acute respiratory tract infections, acute bronchitis, acute obstructive bronchitis, mucocactive preparations, combined broncholytics, treatment.

Introduction. Acute bronchitis (AB) means acute infectious inflammation of the bronchial mucosa of various etiologies. KB with infectious damage of the lower respiratory tract is more common in children. This is also reflected in statistical data. Thus, the incidence of KB in the pediatric population is 75-250 per 1000 children [1,2]. In the International Classification of Diseases (ICD-10), acute respiratory infections of the lower respiratory tract are coded as AB J20.0–J20.9 [5]. Bronchospasm, fibrinosis, membranous, purulent and septic variants of AB, as well as acute tracheitis and tracheobronchitis are also included in this block. In accordance with the recommendations of ICD-10, the etiology of the disease should be taken into account in the diagnosis of "acute bronchitis". It has been determined that in children, AB is of viral etiology and is mostly caused by rhinosyncytial, corona and adenoviruses, as well as parainfluenza, type A and B influenza viruses. About 17-33% of cases, AB can be of mixed ("virus-virus", ("virus-bacterial") etiology [2]. Due to the impossibility of determining the etiology in many cases, AB is classified as «acute bronchitis of unknown etiology» and coded with J20.9. It should be noted that currently in pediatric practice, the working classification of AB is used, reflecting the clinical variants of broncho-pulmonary diseases. According to this classification, two forms of AB are distinguished: acute simple bronchitis (ASB) and acute obstructive bronchitis (AOB) [5-10]. Acute uncomplicated bronchitis (AOB), the main clinical symptom of which is cough, is accompanied by mild intoxication symptoms and subfebrile body temperature usually lasts for 2-3 days. There are no percussive changes on the lungs. On auscultation,

dry and wet crackles of different calibers are heard on both sides. ASB usually has a benign course and does not require specific treatment.

Acute obstructive bronchitis (AOB) is characterized by diffuse bronchial obstruction syndrome, which develops as a result of infectious inflammation of the bronchial mucosa. The basis of bronchial obstruction is edema of the mucous membrane, hyperproduction of bronchial secretion, which acquires pathological features [4-7]. In most cases, obstructive bronchitis, caused by viruses and coded CA20.Y ("Other specified bronchitis") in the new International Classification of Diseases (ICD-11), is observed more often in early-aged children due to the anatomical and physiological characteristics of the respiratory organs, as well as caused by the failure of the immune system. The first clinical signs of AOB are non-productive cough. In most cases, the child's condition is not disturbed, but prolonged breathing and distended wheezes attract attention. A «box-like» sound is heard as a percussion over the lungs, and dry crackles are heard on the background of prolonged breathing during auscultation. In some cases, it is possible to hear wet crackles of various calibers, as well as small bubbles. After the obstruction syndrome disappears, the cough becomes productive, and the auscultation is dominated by transmission rales. It should be noted that the symptoms such as the child's anxious compulsive state, tachypnea and shortness of breath are characteristic only for severe bronchial obstruction [7]. Etiopathogenetic treatment of KOB combines complex therapy consisting of antiviral, broncholytic and mucolytic drugs. Mucoactive drugs (mucolytic, mucokinetic, expectorant agents, as well as

combined broncholytics) are prescribed to the patient in order to dilute the sputum and reduce its stickiness (viscosity) during a low-productive cough that does not perform its protective function, in other words, does not have the ability to clean the respiratory tract. In severe cases, antiinflammatory drugs can be added to the treatment regimen. In the case of obvious obstruction, additional oxygenation of the inhaled air is indicated, and in the case of severe respiratory failure, even artificial ventilation of the lungs is indicated. In recent years, the use of broncholytic drugs by inhalation is more preferred in children with relapsing broncho-obstruction, as well as bronchial asthma, which developed against the background of CVD. It has been determined that the maximum effect of such therapy in early-aged children is obtained when using drugs containing a short-acting selective agonist of β_2 -adrenoreceptors and a blocker of M-cholinoreceptors, especially when administered using a nebulizer [4-7]. However, it is not possible to administer broncholytics by inhalation during the first episode of bronchial obstruction caused by CVD, as

well as when the family's financial resources are low. In such cases, special importance is attached to the use of combined oral drugs that affect various links of the pathogenetic chain of respiratory diseases accompanied by weak cough and broncho-obstruction. In recent years, the oral use of theophylline and its analogues has been abandoned due to the very short range between therapeutic and toxic doses in the treatment of COPD in children, and selective β_2 -adrenomimetics (salbutamol and its analogues), which are better tolerated by children, are preferred [7]. From this point of view, «JOSET», which is approved for use in children as a combined broncholytic drug, attracts special attention. The effectiveness of this drug, which contains active components such as broncholytic (salbutamol), mucolytic (bromhexine) and expectorant (guaifenesin), is conditioned by its broncholytic, expectorant and mucolytic effects. The composition of the preparation and the mechanism of pharmacological action of the active components are given in the following table (table-1).

Table-1

The amount of active components in JOSET and their pharmacological effect

Name of the preparation and active components	Composition (mg)	Mechanism of action
<u>Salbutamolsulfate (syrup)</u> Salbutamol (Broncholytic agent)	1,205 mg 1 mg	• Stimulates mucociliary clearance, stimulates regeneration and mitotic activity of ciliated epithelium • Inhibits the release of inflammatory mediators, stimulates sputum secretion • Expands bronchi, stimulates β_2-adrenoreceptors, prevents bronchospasm
Bromhexine hydrochloride (Mucolytic agent)	2 mg	• It has a mucolytic and expectorant effect due to the depolymerization of mucoproteins and mucopolysaccharides. • Has a mild antitussive effect • Enables the secretion of sputum by activating the mucus epithelium • Along with the spasmolytic effect, it stimulates the glandular secretion of the bronchi, reduces the irritation of the mucous membrane of the respiratory tract.
Guaifenesin	50 mg	• Stimulates the secretion of the liquid part of bronchial mucus, • Increases the volume of sputum and reduces its stickiness. • Increases the ciliary activity of the bronchus and trachea • Enables the transition of dry cough to wet productive cough
Menthol	500 mg	• Has spasmolytic and antiseptic effect • Lightly stimulates bronchial gland secretion • Has a soothing effect and reduces mucous membrane irritation
Excipients: Na methylparahydroxybenzoate; Na propylparahydroxybenzoate; sucrose; propylene glycol; Na saccharinate; sorbic acid; glycerol; citric acid monohydrate; clear sorbitol (non-crystallized); coloring (sunset yellow) substance; distilled water		

The therapeutic effectiveness of this drug is determined by the pharmacological effect of its active components on pathogenetic changes involved in the development of bronchial obstruction, in other words, on various links of pathogenesis. Despite the widespread use of combined bronchodilators in pediatric practice, there is little information about their effectiveness and safety in the literature [3]. The interest and need to conduct this research that we have presented comes from these reasons.

Goal of the work: was to study the effectiveness of combined broncholytic drugs (JOSET) in early-aged children with acute obstructive bronchitis.

Material and methods. The researches were conducted on 38 children aged 1-4 years old, with mild and moderate forms of AOB that do not require intensive therapy (no pathology noted by other organs and systems). In the treatment process, no anti-inflammatory drugs or other preparations were used except for JOSET. Composition for all patients involved in the study: selective agonist of β_2 -adrenoreceptors - salbutamol; mucolytic - bromhexine; and an expectorant - the

Indian-made combined preparation JOSET (Uniks pharmaceutical Laboratory, registration number LSP-001953/07), consisting of active components such as guaifenesin, was prescribed. It should be noted that the drug was easily and well accepted by all patients, and no additional or unwanted effects were recorded. Dosing of the drug was carried out by strictly following the doses appropriate for this age group (50 ml each time x 3 times a day) [4-6]. In order to investigate the effectiveness of the drug, the dynamics of the disease (the nature of the changes), the intensity of the cough, the rate of transformation of dry cough into a productive cough, and the rate of elimination of bronchial obstruction were monitored regularly once every 3 days. The received indicators were evaluated with a 4-point system. A higher score indicates a more severe symptom. Thus, «maximum noticeable» sign-3 points; «mild» - 2 points; «minimal» - 1 point; «absence of symptoms» corresponds to- 0 points. At this time, special attention was paid to how the drug is accepted by children, fixing all additional and unwanted effects.

Results. In 35 (92.1%) of the children included in the examination, bronchial obstruction was manifested by mild expiratory dyspnea (1.48 ± 0.3 points). 28 (73.7%) children had distended wheezing, 32 (87.2%) patient had a non-productive intense cough (2.4 ± 0.2 points). Although the rest of the children had a wet cough, the sputum was difficult to expel because it was very sticky. In 16 (42.1%) patients, seizure-like cough was the main disturbance of sleep and appetite. The use of JOSET as a combined broncholytic in the treatment of all children with AOB was accompanied by a short-term reduction of pathological symptoms. Thus, against the background of the therapy, 34 (89.5%) children began to observe positive dynamics with the reduction of bronchial obstruction syndrome to a minimal level from the 3rd day of treatment. It should also be noted that none of these patients had progression of obstruction or respiratory failure and did not require the use of additional drugs. At the same time, starting from the 3rd day, 24 (63.2%) patients had a decrease in the frequency and intensity of cough, which was clinically accompanied by an improvement in the general condition, normalization of sleep, and a tendency to increase appetite. During this period, the intensity of cough was not higher than 1.3 points. On the 5th day of treatment, 37 (97.4%) patients had an almost complete disappearance of the obstruction syndrome, and a decrease in the intensity of cough up to 47.4%. Starting from the 7th day of therapy, despite the occasional cough in some patients, the cough completely disappeared in 33 (86.8%) patients. However, it should be remembered that, taking into account the presence of salbutamol as an active component, issues such as sensitivity to adrenomimetics or contraindications to taking the drug should be specified when prescribing the drug, and the dosing regimen of the drug should be strictly observed, especially in children under 1 year of age. Thus, in children with a body mass (BW) of <10 kg, a single dose of salbutamol should not exceed 0.1 mg/kg [4-7]. 5 ml of JOSET syrup contains 1 mg of salbutamol. For this reason, it is not recommended to give the drug at a dose

higher than 0.5 ml per 1 kg of body weight in children with a body weight of <10 kg.

Conclusion. Thus, it was determined that during the treatment of AOB in children with JOSET, on the 5th day of therapy, symptoms of obstruction disappear in 97.4% of patients, and the intensity of cough decreases by 47.4% compared to the initial level. On the 7th day of therapy, despite the occasional cough in some patients, the cough in 86.8% of patients completely disappears. At the same time, it was found that when the recommended dosage regimen is followed, the drug is well tolerated by children and no unwanted side effects are observed. Taking into account all that has been said, it can be concluded that the use of JOSET, which has high clinical effectiveness as a combined bronchial preparation, is considered appropriate for early-aged children with AOB.

References:

1. Geppe N.A., Kozlova L.V., Gorelov A.V., Kondyurina E.G., Malakhov A.B., Ilienikova N.A. Acute respiratory tract infections in children. Diagnostics, treatment, prevention: clinical guidelines. Moscow: MedCom-Pro; 2018. 200 p. (In Russ.)// Геппе Н.А., Козлова Л.В., Горелов А.В., Кондюрина Е.Г., Малахов А.Б., Ильенкова Н.А. Острые инфекции дыхательных путей у детей. Диагностика, лечение, профилактика: клиническое руководство. М.: МедКом-Про; 2018. 200 с.
2. Baranov A.A., Namazova-Baranova L.S., Tatochenko V.K., Bakradze M.D., Polyakova A.S., Kulichenko T.V. et al. Acute Bronchitis in Children (KP381). 2018. (In Russ.) Available at: https://library.mededtech.ru/rest/documents/cr_239/ //Баранов А.А., Намазова-Баранова Л.С., Таточенко В.К., Бакрадзе М.Д., Полякова А.С., Куличенко Т.В. и др. Острый бронхит у детей (KP381). 2018.
3. Vakhitov Kh.M., Pikuza O.I., Ibragimova Zh.R. Study of the clinical effectiveness and safety of combination therapy for cough in acute bronchitis in children. Practical medicine. 2013; 74 (5): 174–177.3.//Вахитов Х.М., Пикуза О.И., Ибрагимова Ж.Р. Изучение клинической эффективности и безопасности комбинированной терапии кашля при остром бронхите у детей. Практическая медицина. 2013; 74 (5): 174–177.
4. Malakhov A.B., Dronov I.A., Shakhnazarova M.D. Efficacy and safety of using combined medication (bromhexine + guaifenesin + salbutamol) for treating the acute respiratory infections in children. Pediatriya. Prilozhenie k zhurnalu Consilium Medicum = Pediatrics. Appendix to the journal Consilium Medicum. 2016;(01):65–69. (In Russ.) Available at: //Малахов А.Б., Дронов И.А., Шахназарова М.Д. Эффективность и безопасность комбинированного препарата (бромгексин + гвайфенезин + сальбутамол) для лечения острых респираторных инфекций у детей. Педиатрия. Приложение к журналу Consilium Medicum. 2016;(01):65–69. Режим доступа: <https://elibrary.ru/item.asp?id=27379796>.
5. Geppe N.A., Rozinova N.N., Mizernitsky Yu.L. and others. Working classification of the main

clinical forms of bronchopulmonary diseases in children. Medical newspaper. 2009; 9 (11) (2): 7–9. // Геппе Н.А., Розина Н.Н., Мизерницкий Ю.Л. и др. Рабочая классификация основных клинических форм бронхолегочных заболеваний у детей. Медицинская газета. 2009; 9 (11) (2): 7–9.

6. Zaitseva S.V., Snitko S.Yu., Zaitseva O.V., Lokshina E.E. Treatment of acute obstructive syndrome in children with acute respiratory diseases. Attending doctor. 2013; 11:50–55.// Зайцева С.В., Снитко С.Ю., Зайцева О.В., Локшина Э.Э. Терапия острого обструктивного синдрома у детей с острыми респираторными заболеваниями. Лечащий врач. 2013; 11: 50–55.

7. Meshcheryakov V.V., Pavlinova E.B., Safonova T.I. and others. Comparative effectiveness of oral and inhaled forms of salbutamol in the treatment of bronchial asthma in children. 13th National Congress on Respiratory Diseases. S.-Pb., 2003: 56. //

Мещеряков В.В., Павлинова Е.Б., Сафонова Т.И. и др. Сравнительная эффективность оральной и ингаляционной форм сальбутамола при лечении бронхиальной астмы у детей. 13-й Национальный конгресс по болезням органов дыхания. С.-Пб., 2003: 56.

8. O'Grady K.F., Grimwood K., Sloots T.P., Whitley D.M., Acworth J. P., Phillips N. et al. Upper airway viruses and bacteria and clinical outcomes in children with cough. *Pediatr Pulmonol.* 2017;52(3):373–381. doi: 10.1002/ppul.23527 .

9. Jurca M., Ramette A., Dogaru C.M., Goutaki M., Spycher B.D., Latzin Ph. et al. Prevalence of cough throughout childhood: A cohort study. *PLoS One.* 2017;12(5):e0177485. doi: 10.1371/journal.pone.0177485.

10. Stokes D.C., Dozor A.J. *Pediatric Pulmonology, Asthma, and Sleep Medicine.* Elk Grove Village, United States: American Academy of Pediatrics; 2018.