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APPLICATION OF COMBINATION THERAPY IN THE TREATMENT OF ACUTE RESPIRATORY DISEASES IN CHILDREN

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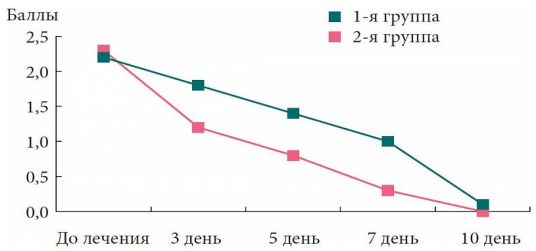
Annotation

Respiratory diseases account for up to 90% of all infectious pathology in childhood. The highest incidence is observed in children during the first years of life, which is explained by their first contacts with respiratory infections and the formation of immunity. The situation often worsens when a child begins attending organized childcare institutions, where the number of contacts increases.

KEY WORDS: acute respiratory diseases in children, respiratory diseases, infections in children, pediatrics, infectious diseases.

Acute respiratory infections are often accompanied by obstructive manifestations in children, especially at an early age . Anatomical and physiological features of the bronchial tree structure (relatively narrow airways, significant development of blood and lymphatic vessels, hyperplasia of mucous glands, low levels of immunoglobulin A, insufficient collateral ventilation, and reduced elasticity of lung tissue) determine the tendency to bronchial obstruction during acute respiratory infections in children of the first years of life and the appearance of unproductive cough . Respiratory viruses damage the ciliated epithelium of the respiratory tract mucosa and increase its permeability to allergens, which leads to increased bronchial hyperreactivity, promotes IgE hyperproduction, and sensitization of the body to non-infectious allergens .

We studied the rationale for using the combined drug **Ascoril Expectorant** (salbutamol, bromhexine, guaifenesin, racementhol) in the treatment of cough in mild to moderate acute respiratory infections caused by laryngitis, rhinopharyngitis, tracheitis, and bronchitis. The study was based on clinical efficacy and safety in 75 children aged 2–10 years (Group 1). The comparison group (Group 2) consisted of 30 children of the same age with similar clinical symptoms who received **Bromhexine** (4 mg bromhexine hydrochloride in 5 ml of syrup). Ascoril Expectorant is a combined drug affecting several pathogenetic mechanisms of bronchopulmonary diseases accompanied by bronchial obstruction and the formation of viscous, difficult-to-expectorate secretions . Ten milliliters of the syrup contain salbutamol (2 mg), bromhexine hydrochloride (4 mg), guaifenesin (100 mg), and racementhol (1 mg).



Bromhexine hydrochloride has mucolytic and expectorant effects due to depolymerization and destruction of mucoproteins and mucopolysaccharides contained in sputum. It also stimulates secretory cells of bronchial mucosa producing surfactant, which ensures alveolar stability during breathing, protects against adverse factors, and improves the rheological

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properties of bronchial mucus . It is prescribed orally three times a day: adults and children over 14 years – 8–16 mg; children under 14 years and patients with body weight less than 50 kg – 8 mg; children under 6 years – 4 mg.

Salbutamol is a selective β2-agonist that produces a bronchodilatory effect. It also influences mucociliary clearance by stimulating mucus secretion and the activity of ciliated epithelium, inhibits mediator release from mast cells and basophils, eliminates antigen-dependent suppression of mucociliary clearance, and reduces the release of neutrophil chemotactic factors . According to the instructions, inhaled salbutamol is prescribed for children older than 18 months at a dose of 2.5 mg (up to 5 mg if necessary) up to four times a day. When administered orally, the dose for children aged 2–6 years is 1–2 mg (0.1 mg/kg) 3–4 times daily, for children 6–12 years – 2 mg 3–4 times daily. The maximum daily dose is 24 mg; for children over 12 years – 2–4 mg 3–4 times daily, with a maximum single dose of 8 mg and a maximum daily dose of 32 mg.

Guaifenesin is an effective expectorant with secretolytic and secretomotor effects. It suppresses the urge to cough and reduces the frequency of coughing attacks, alleviates anxiety, restlessness, and autonomic disorders such as neurocirculatory asthenia, palpitations, dyspnea, headaches, and sleep disturbances . It is administered orally after meals 3–4 times daily: children over 12 years – 200–400 mg; 6–12 years – 100–200 mg; 2–6 years – 50–100 mg.

Menthol (racementhol) acts mainly through reflex reactions associated with irritation of sensitive nerve endings. It produces mild reflex vasodilation, a mild antispasmodic effect, slight diuretic and diaphoretic actions, and has a mild sedative effect in cases of increased excitability and sleep disturbances. It stimulates bronchial gland secretion and has weak antiseptic properties due to its nonspecific action on microbial cells. It also helps reduce colic during flatulence.

Patients received Ascoril Expectorant three times daily in age-appropriate doses: children aged 2–6 years received 5 ml (1 teaspoon), and children aged 6–10 years received 5–10 ml (1–2 teaspoons). Treatment was started on the first day of the disease and continued for 7–10 days depending on the clinical dynamics. Children in the second group received Bromhexine for the same period. The children in both groups were comparable in age and sex. The mean age was 4 ± 2 years in Group 1 (51 boys – 68%, 24 girls – 32%) and 4.1 ± 1.9 years in Group 2 (20 boys – 66.7%, 10 girls – 33.3%). Allergic background was noted in 55.4% of children in Group 1 and 53.3% in Group 2. The study did not include patients who had taken bronchodilators, mucolytics, antihistamines, inhaled or systemic glucocorticosteroids, other antitussive drugs, or antibiotics within the previous 10 days.

Each child was examined by a physician at least four to five times (days 1, 3, 5, and 7–10 of therapy). Parents recorded the severity of ARI symptoms (cough, dyspnea, sputum production) daily in diaries. Each symptom was scored on a scale from 0 to 3: 0 – absent; 1 – mild, short-term, not affecting the child's well-being; 2 – moderately expressed during the day and at night; 3 – pronounced during the day and night, significantly affecting well-being, appetite, and sleep. A total symptom score was then calculated.

All children underwent respiratory function testing using bronchophonography (BPG) before drug administration and one hour afterward. In children older than 6 years, spirometry parameters were also assessed. BPG was performed using the computer acoustic diagnostic complex "Pattern-01." The method is based on recording respiratory sounds using highly sensitive microphones capable of detecting a wide frequency range, including frequencies not detected during auscultation but having diagnostic significance. The respiratory cycle is scanned

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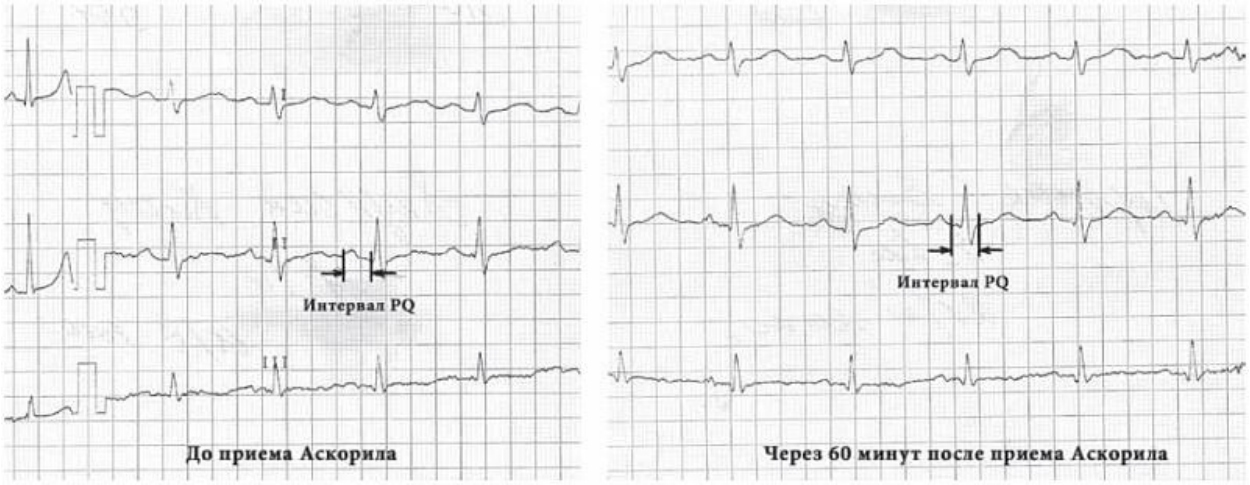
within a frequency range of 200–12,600 Hz, divided into low (200–1200 Hz), medium (>1200–5000 Hz), and high (>5000–12,600 Hz) frequency zones. The high-frequency zone (>5000 Hz) reflects obstructive changes in the airways .

Parameters evaluated included frequency-amplitude characteristics of respiratory sounds, duration of the respiratory cycle, ratio of inspiratory and expiratory phases, presence of high-frequency oscillations, and the acoustic component of respiratory work (ACRW), an integral parameter calculated as the area under the curve in the frequency-time domain.

Spirography was performed using the **Spirosift-3000** device (Fukuda Denchi, Japan). Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), peak expiratory flow (PEF), and minimal expiratory flow rates at 25%, 50%, and 75% of vital capacity were recorded.

Children receiving Ascoril Expectorant demonstrated faster positive dynamics of clinical symptoms compared with the comparison group. A significant reduction in daytime cough severity (from 2.3 ± 0.6 to 1.0 ± 0.3 points) was observed by the 4th day in Group 1, while in Group 2 it occurred only by the 7th day of treatment ($p < 0.05$). Complete disappearance of daytime cough symptoms in 93% of patients in Group 1 occurred by days 6–7, whereas in Group 2 the same result was achieved by days 9–10 ($p < 0.05$).



Nighttime cough severity before therapy was 2.7 ± 0.7 points in Group 1 and 2.5 ± 0.5 in Group 2. A significant reduction to about 1.0 point occurred by the 4th day in Group 1 and by the 7th day in Group 2 ($p < 0.05$). Complete disappearance of nighttime cough symptoms in 93% of children occurred by days 5–6 in Group 1 and days 8–10 in Group 2 ($p < 0.05$). Overall, cough symptoms disappeared 3–4 days earlier in children receiving Ascoril Expectorant.

Before treatment all children experienced difficulty expectorating sputum. After therapy, cough became productive and sputum expectoration improved by days 2–3 in Group 1 and by days 4–5 in Group 2 ($p < 0.05$). Recovery occurred by days 6–7 in Group 1 compared with days 9–10 in Group 2 ($p < 0.05$).

Three children in Group 1 (4%) required the addition of antibacterial therapy due to insufficient response, which was lower than in Group 2 (3 children – 10%). Bronchophonographic analysis showed that clinical improvement in Group 1 was accompanied by a significant reduction in ACRW in the high-frequency range, indicating improved bronchial patency. Spirometric data in children older than six years confirmed these results: FEV1

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increased from 85.7% ± 4.9% before treatment to 92.3% ± 3.8% after drug administration ($p < 0.05$), while no significant changes were observed in the comparison group.

The tolerability of Ascoril Expectorant was good. Ninety-six percent of parents rated the treatment effectiveness as high. Only one child developed an allergic reaction in the form of a rash; no other significant adverse effects were reported. No clinically significant changes in heart rate, blood pressure, or electrocardiographic parameters were observed.

Thus, the use of a combined drug is effective in treating cough associated with acute respiratory infections in children. Administration of Ascoril Expectorant reduces disease duration, decreases manifestations of bronchial hyperreactivity, and promotes faster clinical recovery, thereby reducing the risk of inappropriate systemic antibiotic use. In recommended doses, the combination of **β2-agonist + guaifenesin + bromhexine + racementhol** is safe for the treatment of cough in children.

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