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Clinical Efficacy of Phytopreparation in the Treatment of Acute Rhinosinusitis in Children

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Acute rhinosinusitis is one of the most common diseases of childhood. Difficulties in identifying pathogens increase the importance of pathogenetic therapy. A survey on clinical efficacy of mucolytic agents of plant origin in the treatment of acute rhinosinusitis of not more than 2 days in 95 children aged 4 - 14 years and having respiratory viral infection has been conducted. The dynamics of the disease's symptoms (rhinorrhea, nasal congestion, and smell condition) were estimated based on the diaries that are filled by parents every day. The study demonstrated the feasibility of including phytopreparation in the complex therapy of acute rhinosinusitis in children.

Key words*: acute rhinosinusitis, treatment, mucolytic therapy, herbal remedies, the effectiveness of the children.*

Acute rhinosinusitis (ARS) is one of the most common forms of lymphoma incidence in the structure of frequently ill children [1, 2]. Patients with diseases of the paranasal sinuses (SNPs) are the dominant group for referral to ENT-departments of medical institutions and constitute 62% [3].

In most cases, development of ARS is associated with viral respiratory infection. Epiteliatropic viruses cause mucociliary transport disorder and development of inflammation of nasal mucosa plate, which in turn leads to a blockade of paranasal sinus mouths, to increased production of mucus with altered rheological characteristics, a secondary disorder of local immunity. Under these conditions, bacterial superinfection transform acute catarrhal rhinosinusitis into acute purulent rhinosinusitis. Approximately in half of the cases of acute purulent rhinosinusitis there was detected Streptococcus pneumoniae (48,2%), less often - Haemophilus influenzae (12,4-23%), and even less often Moraxella catarrhalis (15-20%), Streptococcus pyogenes, Staphylococcus aureus, anaerobes, and other pathogens [4]. Long,

torpid rhinosinusitis course in infants may be caused by atypical microbial flora - chlamydia and mycoplasma [5].

Statement of etiologically verified diagnosis of sinusitis in everyday ambulatory practice has certain complexities. This is primarily due to the limited capacity of available tests for the identification of potential pathogens. Even during targeted studies the etiology of rhinosinusitis is not established in almost one third of cases [6]. In addition, in more than half of the observations there is stated a significant difference in species composition and sensitivity to antibiotics of microflora from the nasal cavity and paranasal sinuses, causing critical evaluation of the etiological significance of traditional bacteriological studies in sinusitis [7]. Sowing of etiologically important agents of rhinosinusitis and its sensitivity to commonly used antibiotics is a subject to fluctuations [8].

Studies involving both children and adults show that early administration of antibiotics for acute sinusitis has no advantage compared with placebo neither to relieve the symptoms nor to prevent complications [9]. In 33% of children having acute sinusitis pathogen infection was not detected, and 70% of the positive dynamics was observed without the use of antibiotics [10]. These findings raise the importance of pathogenetic therapy aimed at restoring drainage and ventilation of the paranasal sinuses, which in the early stages of the disease may prevent the development of suppurative inflammation in the paranasal sinuses.

Mucus nature and functional ability of the ciliated epithelium have decisive importance in the drainage of the paranasal sinuses. The nature of the mucus covering the surface of the ciliated epithelium of the sinuses changes during ARS under the influence of an infectious agent (virus first, and then bacterial) change, which leads to disruption of mucociliary transport and stagnation of fluid in the sinus. In these circumstances, mucolytic therapy is required to ensure adequate drainage of the sinuses [11].

Recently, herbal products have proved their efficacy in treatment of ARS in adults and children, as they have a complex effect and high safety profile [12-15]. The original product Sinupret produced by 'Bionorica' company is the classic and most famous member of this group. It was successfully applied in Germany for about 70 years, and in other countries – for about 30 years.

The active ingredients of plants included into the drug product supplement each other with their pharmacological properties and clinical effects:

• gentian root has a reflex action, stimulating increase of bronchial secretion; it does not contain tannin, therefore, its tonic effect is not accompanied by a stimulating effect;

• primrose flowers have an expressed secretolytic, anti-inflammatory and expectorant action, as

well as antimicrobial effects; Primin, which is the main allergen, contained in primula and provoking allergy, is not contained in that part of the plant, which is used in the manufacture of the drug;

• sorrel has anti-inflammatory, antimicrobial, secretolytic, immunomodulatory and antioxidant effects;

• elder flowers have antispasmodic and secretolytic action;

• vervain has expectorant, secretolytic, antiviral and immunomodulatory effects.

Sinupret has quite an expressed antiviral effect: primrose flowers and verbena herb prevents the replication of influenza A viruses, of parainfluenza type I, as well as respiratory syncytial virus that are the most common infections of the paranasal sinuses, especially in children [16]. This herbal drug has mucolytic action, improving the rheological properties of the fluid, which helps it further escape from the paranasal sinuses. Primrose flowers stimulate ciliary activity of the upper respiratory tract mucosa, that is they have mucokynetik influence [17, 18]. All drug components (primrose and elderberry flowers, sorrel, and vervain) have anti-inflammatory effect on the mucous membrane of the respiratory tract. The combination of the drug effects leads to the restoration of drainage and ventilation of the paranasal sinuses. The individual components have immunopotentiating, antioxidant activity [19, 20].

The aim of this study was to investigate the clinical effectiveness of mucolytic therapy for ARS in children. Sinupret was used as a mucolytic drug.

The objectives of the study included:

- Determining the feasibility of the test in children having ARS on a background of respiratory viral infection, to prevent negative rhinosinusitis courseflow;
- Studying the effectiveness of phytopreparation in children of different age groups;
- Studying the incidence of bacterial purulent rhinosinusitis in children of different age groups.

The study was conducted on the basis of six major child health clinics and daily care unit of child ENT-department of City Hospital of. N. Semashko, in Rostov-na-Donu. The study included 95 children aged 4 to 14 years (mean age is 7.4 years) having ARS not longer than 2 days and who did not receive antibiotic treatment, secretolytic and mucolytic agents and antihistamines within two previous weeks.

To achieve the aim of research there were formed two groups: primary group (75 patients) and control group (20 patients). More than half of children (56, 58.9%) were diagnosed with light course flow of ARS, and 41.1% of patients had moderate flow. The degree of severity was determined on the basis of complaints, medical history, examination data and the standard general clinical research methods.

As a primary treatment, all patients received topical decongestants, nasal shower with saline, and anti-viral drugs. In addition, the primary children group was prescribed herbal products as mucolytic drugs: children aged 2 - 6 years - 15 drops 3 times a day, those aged 6 - 14 years - 25 drops or 1 tablet 3 times a day.

At the first visit, all parents were given diary forms of observation, where they had to note the dynamics of the main symptoms: general condition, nasal congestion, nasal discharge, smell. Here are the fragments of diaries (Tables 1 and 2).

The dynamics of the disease was assessed by parents using four quality characteristics: worse, unchanged, improved, recovery.

Degree of decrease in general health and the severity of the main symptoms of ARS (nasal congestion, nasal discharge, breach of smell) was assessed by a 4-point system.

This diary included the list of designated medical drugs, a daily report of their reception, which characterized the adherence and the need for other medications (including both by doctor's prescription and self-medication).

During further ENT-examinations (on the 4th, 8th, and 12th day if necessary) there were performed anterior and posterior rhinoscopy, otoscopy, pharyngoscope; there were analyzed diaries data, which was daily filled with parents; there was evaluated the clinical picture of the disease, the efficacy and safety of the studied phytopreparation; anf finally there was determined further tactics of patients care:

- If ARS sympthoms relieved (the disappearance of secretions from the nose, the restoration of nasal breathing and sense of smell to the premorbid level, normalization of body temperature), then therapy was considered successful and the study was completed;
- If there appeared symptoms of acute purulent rhinosinusitis (headache, pain in the projection of the paranasal sinuses, unilateral purulent nasal discharge), antibiotic therapy was prescribed.

Before treatment, the assessment score of symptoms, used to assess the severity of the disease, was similar in both groups of patients (mean is 11.6 and 11.8, respectively). Comparison of the dynamics of disease symptoms was carried out on the 8th day of treatment. In all cases, prescriptions of the physician were followed accurately, and there were discovered no side effects of medication.

Integral assessment of symptoms and signs of the disease (recovery, improvement, no change, deterioration), that was conducted using questionnaire, revealed the differences in two groups (Table 3).

As it can be seen from Table 3, the most notable differences are identified in terms of absence of any symptom changes: only in 4% of the primary group patients, symptoms remained

virtually unchanged, whereas in the comparison group the symptoms remained at 20% of patients ($p < 0.05$). Primary group and comparison group results were statistically significantly different in terms of the number of patients with full recovery (24 and 15%, respectively, $p < 0.05$)

Comparable results were obtained when comparing the scoring of symptoms: during the second visit (8th day from the treatment start), the mean score of symptoms in the primary group was 5.4, and in the control group - 6.9.

The average duration of illness in children of the primary group was lower than in the control group: 7.6 days vs 9.6 days in the comparison group.

During further observation, one patient (1.3%) from the primary group and one patient (5%) from the control group were appointed antibiotic therapy due to the development of acute bacterial rhinosinusitis.

Our study confirms the results of published reports on clinical efficacy of Sinupret in the treatment of ARS [21-24]. All patients received the same pathogenetic therapy (decongestants, antihistamines, nasal showers) aimed to eliminate swelling of the mucous membrane of the nasal cavity and to improve evacuation of the contents of paranasal sinuses. However, the primary children group who received additional herbal product as a mucolytic and mucokynetik drug, had a more significant therapeutic effect after 6 days of treatment start.

It is confirmed now, that swelling of the mucous membrane of ostiomeatal complex and reduced mucociliary clearance in the paranasal sinuses are the main pathogenetic factors of acute bacterial rhinosinusitis accession along with ARS. Therefore it can be concluded thatherbal drugs provided an additional therapeutic success in the primary group in comparison with the control group.

Therefore, the clinical research demonstrated the feasibility of using Sinupret for treatment of acute rhinosinusitis in children.

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Table 1. A fragment of a diary for symptoms assessment

1-й day of treatment Date ⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋	**2-й day of treatment** Date ⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋	**3-й day of treatment** Date ⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋	**4-й day of treatment** Date ⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋⌊⌋
Compared to the last day **before the start of the research**, runny nose:			
☐ Cured ☐ Improvement ☐ No change ☐ Impairment	☐ Cured ☐ Improvement ☐ No change ☐ Impairment	☐ Cured ☐ Improvement ☐ No change ☐ Impairment	☐ Cured ☐ Improvement ☐ No change ☐ Impairment

Table 2. Dynamics of intensity of the major disease symptoms

Dynamics of intensity of the major disease symptoms	**1 day**	**2 day**	**3 day**	**4 day**	**5 day**
Date:					
General health:					
good (1)					
inertia (2)					
ailment (3)					
temperature rise >37^0c (4)					

Nasal congestion:					
Free nasal breathing (1)					
Periodical congestion (2)					
Partial congestion of one or two sides (3)					
Complete congestion of both sides (4)					
Nasal diacharge:					
None or minimal (1)					
Little discharge (2)					
Plethorical (3)					
Extremely plethorical (4)					
Smell:					
normal (1)					
decreased (2)					
no smell (3)					
Drug intake: mark "+" if prescriptions of physician were followed					
1.					
2.					
If you used other drugs, please state their name and dose:					
1.					
2.					

Table 3. Assessment of the dynamics of disease symptoms on the 8th day of treatment

Integral assessment of main disease symptoms	**Primary group (n = 75)**		**Control group (n = 20)**	
	Total number	**%**	**Total number**	**%**
Recovery	18	24	3	15
Improvement	54	72	13	65
No change	3	4	4	20