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EXPERIENCE WITH THE USE OF ORAL PROBIOTIC STREPTOCOCCUS SALIVARIUS K12 FOR THE PREVENTION OF RECURRENCE OF PHARYNGOTONSILLAR EPISODES

Puhlik, S.M.[1]; Andreev, A.V.[1]; Gushcha, S.G.[2]; Tagunova, I.K.[1]; Volyanska, V.S.[1]; Balashova, I.V.[1]; Badiuk, N.S.[3]*

[1]Odessa National Medical University, Odessa, Ukraine

[2]State Institution "Ukrainian Research Institute of Medical Rehabilitation Therapy of Ministry of Health of Ukraine", Odessa, Ukraine

[3]State Enterprise "Ukrainian Scientific Research Institute of Transport Medicine of Health of Ukraine", Odessa, Ukraine

*badiuk_ns@ukr.net

Abstract

Relevance. Pharyngotonsillitis (PhT) is one of the most common recurrent upper respiratory tract diseases. Viruses are the most common cause of disease (Respiratory viruses, Enteroviruses, Herpesviruses), 30% are of bacterial origin. The most serious types of PhT are associated with group of β-hemolytic streptococcus (GAS) - Streptococcus pyogenes, in which antibiotic therapy is the first choice of therapy. In order to reduce the use of antibiotics, to prevent relapses of pharyngotonsillar episodes, a specific probiotic therapy was carried out using Streptococcuss alivarius K12 (SsK12). K12 (SsK12) is a probiotic strain that inhibits the growth of Streptococcus pyogenes, Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis *in vitro*.

Materials and methods. A study was conducted in 90 patients with recurrent pharyngotonsillitis (PhT) of bacterial origin, in whom Streptococcus pyogenes was isolated during bacteriological examination. The course of treatment for patients of all groups was 30 days. Patients of group 1 (30 people) were treated with standard methods. In 30 patients of group 2 (30 people), in addition to standard therapy, the respiratory probiotic "Bactoblis" was used for a course of 30 days. In 30 patients of group 3, standard therapy was carried out with the use of the respiratory probiotic drug "Bactoblis" and additional sanitation of the lacunae of the palatine tonsils by vacuum extraction.

As a result, in patients of groups 2 and 3, the frequency of PhT episodes significantly decreased, and the use of antibiotics decreased too. The most persistent effect of treatment was in patients of group 3 - the quality of treatment and prevention increased, the number of exacerbations decreased, the severity of clinical manifestations, and the drug load decreased. Individual intolerance to the components of the drug has not been identified. However, 6 months after the observation was started, the clinical and laboratory parameters of the main groups began to deteriorate, approaching those of the control group, and more stable therapeutic effect was observed in patients of group 3.

Conclusions. The authors consider it expedient to perform tonsil sanitation twice a year, with further use of the drug "Bactoblis" in patients suffering from PhT.

All human studies were conducted in compliance with the rules of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study". Informed consent was obtained from all participants.

Keywords: *pharyngotonsillitis (PhT), Streptococcus pyogenes, Streptococcus salivarius K12.*

Introduction

Among the most common recurrent diseases of the upper respiratory tract, acute pharyngotonsillitis is one of the most common causes of ambulatory patient referral. This condition is more often caused by viruses (Respiratoryviruses, Enteroviruses, Herpesvirus); only 30% are of bacterial origin.

The most serious types of pharyngotonsillitis are associated with bacterial etiology, such agent as β-hemolytic Streptococcus pyogenes (GAS) group, which are known to be responsible for most pharyngotonsillar infections of bacterial etiology and a significant proportion of mediaacute otitis (1, 2). In such cases, antibiotic therapy is the first choice of therapy. With frequent episodes of pharyngotonsillitis, the pharmacological approach is no longer effective; in such cases surgical removal of the tonsils is considered.

In order to reduce the prescriptions of antibiotic therapy and surgical interventions, the use of a specific probiotic oral therapy was proposed, based on the research of the Australian microbiologist Dr. J. Tagg and his colleagues, who isolated Streptococcus salivarius, named Blis K12 from the oral cavity of a child, and suggested that in the presence of Streptococcus salivarius K12, development of Streptococcus pyogenes is impossible (3).

Research goals. The aim of the research was to evaluate the effectiveness of prophylactic use of the respiratory probiotic "Bactoblis" in patients with recurrent pharyngotonsillitis.

Methods

The material was the data of examination of 90 patients with recurrent pharyngotonsillitis (RPhT) of bacterial etiology, the treatment of which was carried out in a standard way. The age of the subjects ranged from 15 to 40 years. 30 patients were considered as a control group, 60 patients were treated with the drug "Bactoblis". Clinical efficacy was assessed by the frequency of relapses, the severity of the clinical course, changes in the bacterial flora of the nasopharynx and oropharynx.

Results

To find out the nature of the disease - viral or bacterial, a diagnostic scoring system was used - a modified Centor/McIsaac scale, which underlies adequate etiopathogenetic treatment (4).

For traditional treatment, all patients with recurrent pharyngotonsillitis, in accordance with the clinical picture during exacerbation, were prescribed non-steroidal anti-inflammatory drugs, symptomatic drugs, if 4-5 Centor criteria were met, empiric antibiotics were used.

For the treatment of infections caused by group A β-hemolytic streptococcus (ABHS) agents, penicillin and amoxicillin were used as first-line drugs. However, the presence of resistance in 30% of the strains isolated from patients with pharyngotonsillitis does not allow the eradication of ABHS. In some patients, data on the presence of allergy to penicillins were obtained from the anamnesis. Therefore, the drugs used were azithromycin or first generation of cephalosporins.

The study was supposed to compare the prophylactic efficacy of the drug "Bactoblis", to assess the tolerability of the drug in patients with recurrent pharyngotonsillitis caused by a large number of various bacterial pathogens (Haemophilus influenza, Streptococcus pneumonia, Moraxella catarrhalis, Micrococcus luteus, Streptococcus anginosus, Eubacterium saburreum, Micromonas micros and others), among which β-hemolytic Streptococcus pyogenes (GABHS) was detected during bacteriological research.

The drug "Bactoblis". The main constituent of the drug is Streptococcus salivarius BLIS K12, which is capable of producing bacteriocins (Salivaricina A2 and B) -antibiotics that inhibit the growth of most types of pathogenic bacteria: Streptococcus pyogenes, Haemophilus influenza, Streptococcus pneumonia, Moraxella catarrhalis, Micrococcus luteus, Streptococcus anginosus, Eubacterium saburreum, Micromonas micros and others (5,6).

All patients with exacerbation of the disease received standard treatment. 30 patients were considered as a control group, 60 patients of the main group were treated with the drug "Bactoblis".

- 1st control group (30 patients) did not receive prophylactic treatment with Streptococcuss alivarius K12; the average age was 28.1 years.
- The main group (60 patients) was divided into 2 and 3 groups:

2nd group - 30 patients (average age 28.8 years), received prophylactic treatment with Streptococcuss alivarius K12.

3rd group - 30 patients (average age 28.6 years), received prophylactic treatment with Streptococcuss alivarius K12 and sanitization of the tonsils lacuna

For 30 days, patients of group 2 as preventive therapy after the end of the course of antibiotic therapy received the drug "Bactoblis" - a respiratory probiotic in the form of tablets for absorption in the oral cavity, 1 tablet per day, until the tablet is completely dissolved, in the evening before bedtime.

Patients of group 3, after the end of the course of antibiotic therapy, underwent vacuum sanitation of the tonsils' lacunae using the Tonsillor apparatus, in a course of three to five procedures for each patient, followed by prophylactic administration of the Bactoblis drug for 30 days.

In our work, the lacunae of the tonsils were sanitized using the Tonsillor apparatus, which made it possible not only mechanically remove the contents with an antiseptic solution, but also to act on the tonsil tissue with ultrasound through the solution used, which created an additional therapeutic effect, providing a bactericidal effect, improving microcirculation and metabolic processes.

The use of the Tonsillor apparatus for sanitizing of the tonsils' lacunae unlike rinsing the mouth with an antiseptic solution increased essentially the probability of complete removal of caseous masses from the tonsils' lacunae. For manipulation, an applicator with a nozzle is installed on the amygdala, which the doctor selects so that the amygdala fits inside. Further, the nozzle is slightly pressed against the pharyngeal wall and sanitation takes place using the vacuum extraction mode. The sanitization takes 30-60 secondsoneachside.

Outpatient monitoring of the patient's condition was carried out either at an appointment with the attending physician, or using a mobile connection. The duration of the studies was 9 months. Each trimester, the number of pharyngotonsillar exacerbations episodes was recorded, their duration was recorded, a clinical assessment of the severity of the course of the disease, drug load was carried out, a bacteriological study was carried out (taking smears from the pharynx).

In the study of the microbial landscape of the upper respiratory tract in 100% of patients included in the study there were isolated Strertococcus pyogenes, 65.3% - an association of various bacteria, of which: 29.2% - Streptococcus viridans, 17.2% - Staphylococcus aureus, 15, 8% - Staphylococcus epidermidis, 1.8% - Klebsiella pneumonia, 1.2% - Escherichia coli, 1% - Pseudomonas aeruginosa. Bacteriological examination in patients was carried out at the time of patient referral after exacerbation, before the use of antibacterial drugs and symptomatic agents.

In patients assigned to the control group, the number of inflammatory pharyngotonsillar episodes over 9 months of observation was 127 cases. In patients belonging to the 2ndgroup, the number of inflammatory pharyngotonsillar episodes was 86 cases for 9 months of observation, and 60 cases were found in patients of the 3rdgroup.

The results in terms of morbidity showed significant reduction in pharyngotonsillar inflammatory episodes compared to the previous year and the control group. In the main groups, there was the drug load decrease and the antibacterial drugs dose decrease. The most persistent improvement was in patients of the 3rdgroup, who received the drug "Bactoblis" after sanitation of the tonsils. Relapses of pharyngotonsillitis were short-lived, the clinical picture was smoother, antibiotic therapy was used in 5 cases.

Analyzing the number of exacerbations by trimesters, we noted an enough stable and long-term effect in the main group of patients during the first and second trimesters, but already in the third trimester, i.e. 60 days after the start of observation, the number of episodes of illness began to increase and approached the values of the control group.

If in the first trimester the number of exacerbations in the 2ndgroup, who took the probiotic without sanitation of the tonsils' lacunae, was 51.1% of the indicators in the control group, and with sanitation - 34.3%, then in the third trimester, respectively, 83.7% and 55.8%.

When examining the microbial landscape after 90 days, the bacterial flora in the control group of patients changed insignificantly. In 42.3% of patients,

Streptococcus pyogenes was isolated both in monoculture and in associations. The association of various bacteria was found in 49.5% of studies: 21.1% - Staphylococcus epidermidis, 12.1% - Streptococcus viridians, 7.3% - Staphylococcus aureus, 7.9% - Candida albicans, 1.1% - Klebsiella pneumonia.

Thus, as a result of the treatment carried out in all observation groups, the dissemination of the mucous membrane of the oropharynx by representatives of the pathogenic flora, in particular β-hemolytic Streptococci, decreased. Higher efficiency was achieved in the 3rd group, where, in order to establish and maintain the functional state of the oral microflora after the end of antibiotic therapy, vacuum sanitation of tonsil lacunae and subsequent prophylactic treatment with a respiratory probiotic was carried out. In the third trimester, i.e. 6 months after the start of observation, clinical and laboratory parameters in the main groups began to deteriorate, approaching those of the control group, which indicates the need for a repeated course of preventive therapy.

Considering that in none of the studies conducted with the participation of 60 people who took "Bactoblis" there were no adverse reactions associated with the use of the drug, individual intolerance to the components of the drug was not identified, and was generally assessed as good. This result indicates the possibility of more frequent and more prolonged use of the probiotic for prophylactic purposes, especially in patients with long-term and frequent illnesses.

Conclusions

Thus, the use of the drug "Bactoblis" as part of basic therapy in patients with acute pharyngotonsillitis in the 2nd group increases the effectiveness of treatment compared to the control group, as evidenced by a decrease in the severity of clinical manifestation, a decrease in the number of exacerbations and drug load. The use of vacuum sanitation of tonsil lacunae followed by the use of a respiratory probiotic drug "Bactoblis" significantly increases the effectiveness of treatment.

On the basis of the data obtained, in order to increase the efficiency of treatment of patients suffering from relapses of pharyngotonsillitis, the authors proposed to carry out sanitation of the tonsils with the subsequent use of the drug "Bactoblis" twice a year.

Acknowledgments

The authors declare that there are no conflicts of interest.

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Table 1. The number of inflammatory pharyngotonsillar episodes in the observation groups during 9 months

Observation period	I trimester	II trimester	III trimester
Exacerbation rate	Number of cases	Number of cases	Number of cases
Control group - 30 people	41	39	43
The main group without sanitation of the tonsils - 30 persons	21	28	36
Main group with tonsilsanitation - 30 people	14	16	24