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FEASIBILITY OF USING A PROBIOTIC BACTERIAL COMPLEX IN THE FORM OF A THROAT SPRAY IN THE LOCAL TREATMENT OF ACUTE VIRAL TONSILLITIS

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Summary

The aim of the study was to determine the feasibility of using a probiotic bacterial complex in the form of a throat spray in the local treatment of acute viral tonsillitis based on the analysis of its clinical and microbiological efficacy.

Materials and methods. The randomized controlled trial involved 46 people with acute tonsillitis diagnosed on the basis of clinical and pharyngoscopic signs. According to the treatment received, patients were divided into 2 groups. Patients in the control group (23 people) were treated according to the unified clinical protocol «Tonsillitis». The main group included 23 patients who, in addition to the protocol treatment, received a probiotic agent in the form of a throat spray containing a complex of bacteria of the genus *Bacillus*. To exclude the bacterial etiology of acute tonsillitis, a modified Centor scale (McIsaac scale) was used. Evaluation of the effectiveness of treatment was based on the study of the dynamics of clinical and pharyngoscopic signs of the disease, as well as the establishment of quantitative and qualitative changes in the microbiota of the palatine tonsils during treatment.

Results. The analysis of the dynamics of the main clinical and pharyngoscopic parameters indicates a more significant and rapid normalization in patients of the main group. The results of microbiological studies show that the use of a probiotic bacterial complex in the treatment of acute tonsillitis in patients of the main group contributed to the elimination of dysbiotic changes, restoration of the population level of the main representatives of the palatine tonsils microbiome and colonization resistance of the oropharynx.

Conclusions. It has been established that acute viral inflammation of the palatine tonsils occurs under conditions of quantitative and qualitative changes in the species composition of the microbiota of this biotope and is accompanied by an increase in dysbiotic disorders during the course of the disease. It has been confirmed that the use of a probiotic bacterial complex in the form of a spray in the local treatment of acute viral tonsillitis is appropriate due to its proven clinical and microbiological efficacy, and also makes it possible to refrain from premature administration of antibacterial chemotherapy.

Keywords: acute viral tonsillitis, probiotic bacterial complex, bacteria of the genus *Bacillus*, microbiota of the palatine tonsils

INTRODUCTION

Inflammatory diseases of the lymphadenoid pharyngeal ring are defined by the term «tonsillitis» and today are one of the most pressing problems of clinical otorhinolaryngology due to the growing incidence, frequent episodes, high risk of developing tonsillogenic and metatonsillar complications [3]. The prevalence of this pathology is about 15 % of the total population, with

a particular prevalence among children and young adults. Acute inflammation of the palatine tonsils (sore throat, acute tonsillopharyngitis) is one of the most common reasons for patients to visit otolaryngologists, general practitioners, and pediatricians [12, 16].

Today, views on the etiology, pathogenesis, diagnosis and treatment of inflammatory diseases of the palatine tonsils are changing. The vast majority of researchers

associate the occurrence of inflammation in the palatine tonsils with microorganisms of different taxonomic groups. According to modern scientific data, the etiological factors of acute tonsillitis are most often, in 70-90 % of cases, viruses [16, 18]. The most common viral pathogens causing acute inflammatory diseases of the palatine tonsils are adenoviruses, rhinoviruses, coronaviruses, influenza and parainfluenza viruses, Coxsackie A virus, Epstein-Barr virus, herpes viruses [12, 23]. In addition, these pathogens create the basis for the development of inflammation in this biotope of bacterial and fungal origin, and are capable of interacting with other microorganisms to form polymicrobial associations, which ultimately can affect the clinical course of the disease, lead to a deterioration in the effectiveness of treatment, cause purulent inflammatory local (paratonsillitis and paratonsillar abscess) and general complications (glomerulonephritis, cardiomyopathy, etc.).

Numerous studies have established that under conditions of viral damage to the oropharyngeal mucosa, there is a fluctuation in the quantitative and qualitative indicators of the taxonomic composition of the autochthonous obligate (main, indigenous, resident, dominant) microbiota of this biotope [1, 8, 14, 17]. The main representatives of the palatine tonsils microbiome are diphtheroids, α -hemolytic streptococci, and γ -hemolytic streptococci, *Lactobacterium* spp, *Bifidobacterium* spp., *Actinomyces* spp., *Corynebacterium* spp., *Fusobacterium* spp., *Mycoplasma* spp., *Neisseria* spp., *Peptostreptococcus* spp., *Prevotella* spp., *Treponema* spp., *Veillonella* spp. [10, 22]. The population of these microorganisms makes up 98-99% of the microbiocenosis of the palatine tonsils and is an important component of the nonspecific defense of the macroorganism, which is realized through the mechanisms of colonization resistance to opportunistic and pathogenic infections. Due to the physiological activity of saprophytic and commensal microorganisms, as well as the action of their metabolic products, the mechanism of their antagonistic action is realized: adhesion, reproduction and colonization of foreign pathogens are suppressed, and at the same time, the species diversity of normobiota and the stability of microecology of various biotopes of the macroorganism are maintained [11, 20]. The quantitative loss of these microorganisms, especially in the context of viral infection, leads to an impoverishment of the biodiversity of the oropharyngeal microbiome and creates conditions for the development of secondary infection caused by opportunistic pathogens of different taxonomic groups [2, 19].

These changes in the quantitative and qualitative indicators of the main representatives of the autochthonous microbiota are defined as dysbiosis. Disruption of the oropharyngeal microbiocenosis is also noted with prolonged use of antibiotics and other drugs, such as steroid hormones, cytostatics, immunosuppressants, etc. The consequence of dysbiotic disorders is the suppression of mucosal immunity and an increase in the microbial

load of a given biotope. Thus, a violation of the taxonomic composition, as well as the population level of the main representatives of the normobiota of the biotope can contribute to the development of secondary, auto- or mix-infections, which certainly affects the clinical course of the disease and treatment outcomes [7, 22].

Therefore, the need to prescribe antibacterial agents in the treatment regimens for acute tonsillitis remains a controversial issue today. After all, unreasonable use of antibiotics not only suppresses normal human microbiota, but also leads to increased resistance of pathogenic microorganisms to their action and can have a toxic effect on the internal organs of the macroorganism, increase the risk of allergic reactions, etc. [9]. In the context of viral damage to the palatine tonsils, in order to restore the reference indicators of the species composition of the microbiocenosis and its functional activity, as well as to prevent the development of secondary bacterial and fungal infection, the use of bacterial treatments, namely probiotics, deserves special attention. Probiotic preparations, represented by non-pathogenic living microorganisms and their metabolites, have a positive effect on the health of the macroorganism when consumed in adequate amounts [4, 6, 21, 24].

The aim of the study was to determine the feasibility of using a probiotic bacterial complex in the form of a throat spray in the local treatment of acute viral tonsillitis based on the analysis of its clinical and microbiological efficacy.

MATERIALS AND METHODS

The randomized controlled trial involved 46 people aged 18 to 50 years with a diagnosis of acute tonsillitis of I-II severity, including 29 women and 15 men. Inclusion criteria: patients with acute tonsillitis diagnosed on the basis of clinical and pharyngoscopic signs, age from 18 to 50 years, the presence of voluntary informed consent of the patient to be included in the study. Exclusion criteria: patients with follicular and lacunar forms of acute tonsillitis, existing pregnancy or lactation, inflammatory diseases of the oral mucosa, severe patient's condition due to somatic or mental pathology, history of acute tonsillitis or acute respiratory viral infection (ARVI) within the last 2 weeks, use of systemic or topical antiseptics/antibiotics within the last month, immunocompromised patients. The study protocol complied with the basic principles of the World Medical Association's Declaration of Helsinki for the Ethics of Research Involving Human Subjects. Each patient provided voluntary informed consent for inclusion in the study.

The study was conducted at the otolaryngology department of the 2nd City Clinical Hospital of Poltava City Council. The diagnosis was made on the basis of patients' complaints (sore throat, aggravated by swallowing, fever ≥ 37 °C, general weakness, headache),

anamnesis data objective examination (enlargement and tenderness of regional lymph nodes near the angle of the mandible along the anterior margin of the upper third of the masseter muscle) and pharyngoscopic signs of acute tonsillitis (hyperemia of the palatine tonsils, enlargement of the palatine tonsils) [13]. For the differential diagnosis of acute tonsillitis of viral origin from bacterial tonsillitis caused by group A β -hemolytic streptococcus, the modified Centor scale (McIsaac scale) recommended by the unified clinical protocol for primary, secondary (specialized) and tertiary (highly specialized) medical care «Tonsillitis» and the evidence-based guideline «Tonsillitis» was used. [12, 13, 15]. The probability of the bacterial nature of acute tonsillitis caused by group A β -hemolytic streptococcus was assessed depending on the patient's age and the number of symptoms (criteria) of the disease indicated in this scale, each of which was evaluated at 1 point. According to the total score, the probability of detecting group A β -hemolytic streptococcus was determined. Thus, if the total score was ≤ 2 , this probability was 11-17 % and was assessed as low. In contrast, with the same number of points obtained, the probability of viral etiology of acute tonsillitis was defined as high [9, 13, 15]. The study included patients with a total score of 0 to 2 points in the assessment of subjective and objective symptoms of the disease. According to the treatment received, patients were divided into 2 groups. Both groups of patients had no significant differences in age, gender, clinical and objective signs of the disease. The control group consisted of 23 patients whose treatment regimen according to the unified clinical protocol «Tonsillitis» included ibuprofen 400 mg twice a day, benzidamine in the form of a spray, 2-3 sprays 3 times a day. The main group included 23 patients who, in addition to the protocol treatment, received an additional probiotic bacterial agent «Bioplasmix throat spray» containing a bacterial component: *Bacillus subtilis*, *Bacillus licheniformis*, *Bacillus amyloliquefaciens*, *Bacillus pumilus*, *Bacillus megaterium* at least 1×10^6 CFU / ml and a complex of enzymes of the *Bacillus* genus (manufactured by Gellingham GmbH & Co. KG, Germany). The duration of treatment in both groups was 7 days.

To evaluate the effectiveness of treatment, the dynamics of clinical and pharyngoscopic parameters before treatment, on days 2, 3, 5 and 7 of the study were determined. The severity of clinical and pharyngoscopic symptoms was assessed on a 4-point scale (from 0 to 3 points), where 0 is their absence, and 3 is the maximum severity. Thus, sore throat was scored accordingly: 0 points – no pain, 1 point – slight sore throat, aggravated by swallowing, 2 – moderately severe pain, making swallowing difficult, 3 – significantly severe pain, swallowing is significantly difficult. Body temperature was assessed as follows: 0 points – from 36°C to 37°C, 1 point – from 37°C to 38°C, 2 points – from 38°C to 39°C,

3 points – above 39°C. In turn, the severity of hyperemia and enlargement of the palatine tonsils was determined as follows: 0 points – the mucous membrane of the palatine tonsils is pink, the palatine tonsils are not enlarged, 1 point – slight hyperemia of the mucous membrane of the palatine tonsils, the palatine tonsils do not extend beyond the palatal arches, 2 points – moderate mucous hyperemia, palatine tonsils slightly extend beyond the palatal arches, 3 points – severe hyperemia of the palatine mucosa with spread to the palatal arches, palatine tonsils extend beyond the palatal arches. The degree of enlargement and tenderness of regional lymph nodes was determined as follows: 0 points – regional lymph nodes are not enlarged, painless, 1 point – slightly enlarged regional lymph nodes, slight tenderness on palpation, 2 points – moderately enlarged regional lymph nodes, moderate tenderness on palpation, 3 points – significant enlargement of regional lymph nodes, tenderness on superficial palpation.

A microbiological study was used to determine the microbial landscape of the palatine tonsils and its changes during treatment. The biomaterial was taken with a sterile swab applicator using a spatula on an empty stomach before treatment and on the 7th day after its start. After collecting the material, the swab was placed in a tube with Ames agar gel transport medium and delivered to the bacteriological laboratory within 2 hours under isothermal conditions. Pure cultures of microorganisms were isolated according to the methodological recommendations. Identification of the isolated cultures of facultative anaerobic and aerobic autochthonous, allochthonous bacteria and yeast-like fungi of the genus *Candida* was carried out according to their biological characteristics: morphological, tinctorial, cultural, biochemical and antigenic. The number of bacteria and yeast-like fungi of the genus *Candida* (population level) was determined by counting colony-forming units in 1 ml (CFU /ml) [5].

The peripheral blood picture was studied according to generally accepted hematological methods. The hemoglobin concentration, absolute number of red blood cells, leukocytes, relative number of lymphocytes and neutrophils, monocytes, eosinophils were determined, the color index and erythrocyte sedimentation rate were calculated.

Descriptive statistics included the calculation of mean values, error bars, and normality of distributions using the Shapiro-Wilk test. Comparison of the main and control groups was performed by the Student's method and the Mann-Whitney method for indicators that did not have a normal distribution. Comparison of related indicators (pretreatment and different periods after treatment) was performed by the Student's method for paired indicators and the Wilcoxon method for indicators that did not have a normal distribution. The threshold of statistical significance was considered to be $p < 0.05$. The JASP 0.16.0.0 program was used to analyze the data.

RESEARCH RESULTS AND DISCUSSION

The main subjective and objective signs of acute viral tonsillitis, such as sore throat, fever, hyperemia and enlargement of the palatine tonsils, and enlargement and tenderness of the regional lymph nodes were observed in 100 % of patients.

During treatment, patients in both the main and control groups showed a gradual positive dynamics of clinical and pharyngoscopic signs of the disease with their maximum regression by day 7. Data on changes in the severity of the main symptom of the disease – sore throat in patients of the main and control groups are shown in figure 1.

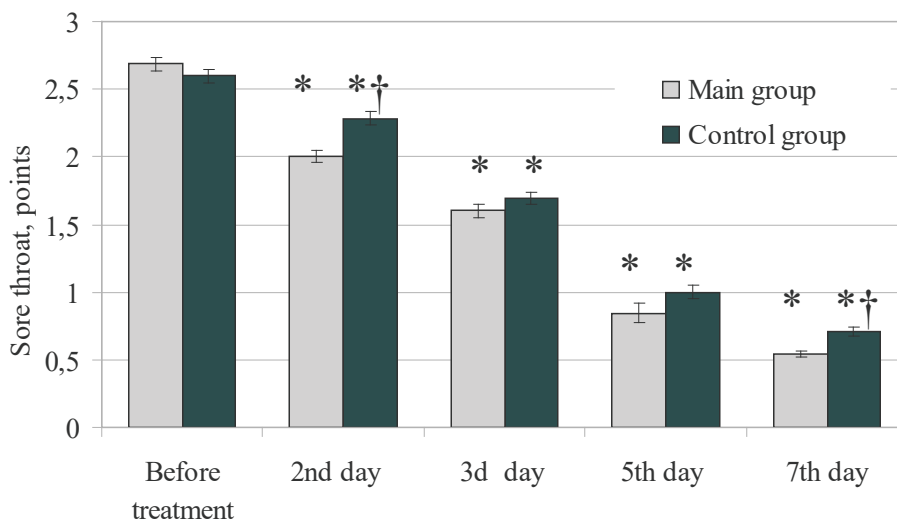


Figure 1. Dynamics of sore throat in patients of the main and control group during treatment. * – statistical significance of the difference with the indicators before treatment; † – statistical significance of the difference with the corresponding indicators of the main group

According to the results of the studies, a gradual daily regression of sore throat pain was found in patients of both groups. In 96 % of patients (22 patients) in the main group, the maximum reduction in sore throat intensity was noted by day 5 of treatment. At the same time, 22 % of patients (5 patients) in the control group still had sore throat during this period.

The dynamics of body temperature indicates a more significant and rapid normalization in patients of the main group. Thus, on the 3rd day of treatment, 78.3 % of

patients (18 patients) in the main group had thermometry data that corresponded to the normative values, and by the 5th day of treatment – in all patients of the group. However, in 34.8 % of patients (8 patients) in the control group on day 3 of treatment, an elevated body temperature was noted, followed by its decrease in accordance with the physiological norm on day 5 of the study.

Analysis of the results of pharyngoscopic examination (fig. 3) revealed positive changes in local symptoms in patients of both study groups.

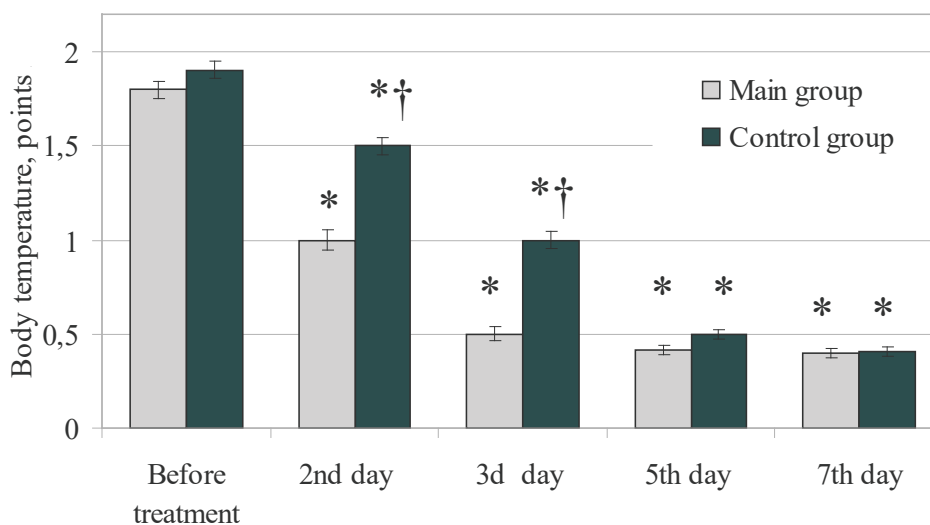


Figure 2. Dynamics of thermometry in patients of the main and control groups during treatment; * – statistical significance of the difference with the pre-treatment values; † – statistical significance of the difference with the corresponding values of the main group

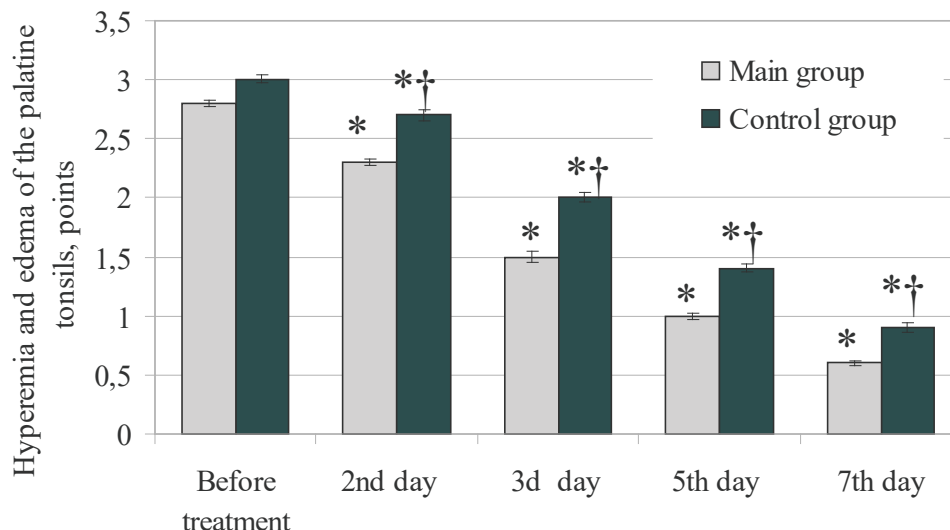


Figure 3. Dynamics of hyperemia and edema of the palatine tonsils in patients of the main and control groups during treatment; * – statistical significance of the difference with the pretreatment values; † – statistical significance of the difference with the corresponding values of the main group

In 82.6 % of patients (19 patients) in the study group, the degree of inflammation of the palatine tonsils decreased almost twice on the 3rd day after the start of treatment, and by the 5th day of treatment, 96 % of patients (22 patients) had normal palatine tonsils. At the same time, the subjects of the control group also

had a regression of objective signs of the disease, but normalization of the pharyngoscopic picture was observed only on the 7th study day.

Along with this, there was a slow positive dynamics in inflammatory changes in the regional lymph nodes (fig. 4).

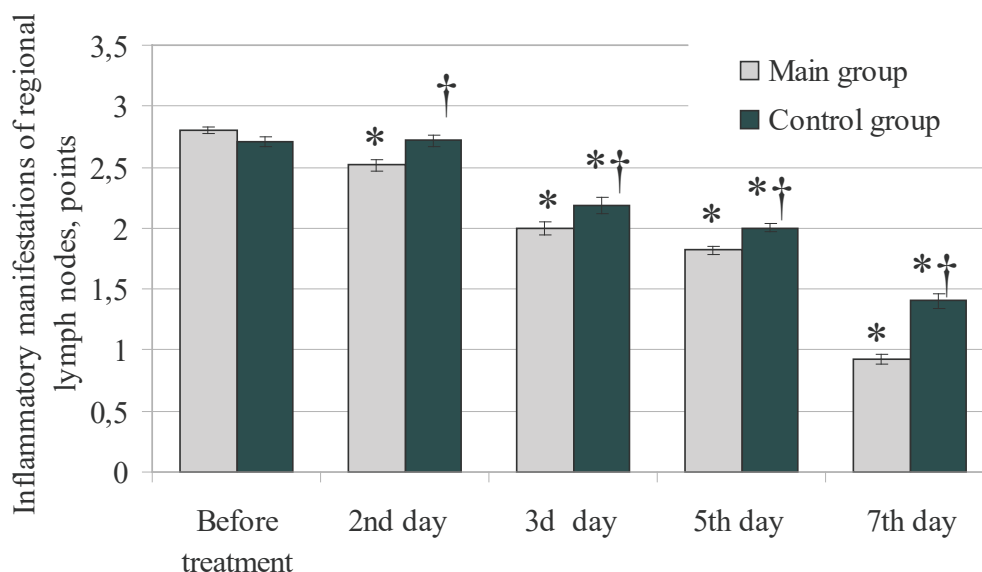


Figure 4. Dynamics of inflammatory manifestations in the regional lymph nodes in patients of the main and control groups during treatment; * – statistical significance of the difference with the pretreatment values; † – statistical significance of the difference with the corresponding values of the main group

Regional lymphadenitis in patients of the main group was absent in all cases on day 7 of treatment, while in 13 % of subjects (3 patients) from the control group this symptom was still present at the specified time. It should be noted that the reduction in the severity of subjective clinical symptoms and thermometry was faster and more

pronounced in both study groups than the subsidence of inflammatory manifestations of the palatine tonsils and regional lymph nodes.

The results of hematologic examination of patients in the main and control groups are shown in table 1.

Table 1

Hemogram parameters in patients with acute tonsillitis

Indicator	Main group			Control group		
	n=13	n=6	n=4	n=10	n=8	n=5
Absolute red blood cell count ($\times 10^{12}/l$)	3,9 \pm 0,04	4,2 \pm 0,09	3,8 \pm 0,08	4,1 \pm 0,07	4,3 \pm 0,08	3,9 \pm 0,14
Absolute leukocyte count ($\times 10^9/l$)	3,7 \pm 0,03	6,8 \pm 0,03	9,5 \pm 0,07	3,6 \pm 0,09	7,2 \pm 0,09	10,3 \pm 0,07
Relative number of lymphocytes (%)	42,1 \pm 0,43	35,7 \pm 0,35	41,8 \pm 0,56	42,1 \pm 0,33	34,1 \pm 0,16	42,5 \pm 0,28
Relative number of monocytes (%)	10,8 \pm 0,13	8,5 \pm 0,12	10,5 \pm 0,20	10,5 \pm 0,13	8,4 \pm 0,12	10,2 \pm 0,19
Relative number of s/y (%)	44,6 \pm 0,21	52,4 \pm 0,31	45,1 \pm 0,27	45,1 \pm 0,30	53,1 \pm 0,31	44,4 \pm 0,25
Relative number of p/y (%)	2,4 \pm 0,09	3,2 \pm 0,11	2,6 \pm 0,08	2,3 \pm 0,09	4,4 \pm 0,13	2,9 \pm 0,13
ESR (mm/h)	17,4 \pm 0,12	14,3 \pm 0,17	18,2 \pm 0,13	18,02 \pm 0,09	13,6 \pm 0,21	19,0 \pm 0,12

The general blood counts of patients in the main and control groups had the following changes. Thus, in 52.2 % of patients (12 patients) of the main group and in 43.5 % of patients (10 patients) of the control group, peripheral blood showed typical changes characteristic of a viral infection: mild leukopenia and neutropenia with simultaneous lymphocytosis. The results of hematologic examination in 30.4 % of patients (7 patients) in the main and 34.7 % of patients (8 patients) in the control groups were within the age-related norm. In 17.4 % of patients (4 patients) of the main group and 21.7 % (5 patients) of the control group, the hemogram analysis revealed a slight leukocytosis, along with relative lymphocytosis and monocytosis. The number of erythrocytes and hemoglobin concentration in all patients of both the main

and control groups corresponded to the reference values. Acceleration of ESR up to 20 mm/h occurred in 73.9 % of patients (17 patients) of the main and 65.2 % of patients (15 patients) of the control groups.

Since viral damage to the palatine tonsils can lead to changes in the population level, as well as the species composition of the main representatives of the indigenous microbiota of this biotope, a cultural study of the microbial landscape of the palatine tonsils of patients in the main and control groups was performed. The results of the study of the microbiota of the palatine tonsils of patients in the main group are presented in table 2.

Representatives of the microbiota of the palatine tonsils of patients in the control group are presented in table 3.

Table 2

Number of strains of the main representatives of the normobiota, isolated from patients in the main group

The main representatives of the normobiota of the palatine tonsils	Number of strains	
	Before treatment	On the 7th day of treatment
Alpha and gamma hemolytic streptococci	18	21
Neisseria spp.	16	20
Coagulase-negative staphylococci	13	18
Diphtheroids	12	18
Candida albicans	10	9

Table 3

Number of strains of the main representatives of the normobiota, isolated from patients in the control group

The main representatives of the normobiota of the palatine tonsils	Number of strains	
	Before treatment	On the 7th day of treatment
Alpha and gamma hemolytic streptococci	19	17
Neisseria spp.	16	14
Coagulase-negative staphylococci	12	10
Diphtheroids	12	10
Candida albicans	9	9

According to the results of the microbiological study of the normobiota of the palatine tonsils of patients of both study groups, 137 bacterial and fungal clinical strains were isolated. The microbial profile of the resident microorganisms of the palatine tonsils under conditions of viral inflammation was characterized by quantitative and qualitative impoverishment compared to that in their physiological state. In order to determine the microecological state in this biotope, the population level of each microorganism species was also determined. Thus,

during the culture study, in 59 % of cases (27 people), before treatment, the dominant position belonged to alpha and gamma hemolytic streptococci (*Streptococcus viridans*, *Streptococcus mitis*, *Streptococcus mutans*, *Streptococcus salivarius*), the population level of which was determined in the range of 10^3 - 10^5 CFU/ml. The next place in terms of frequency of sowing belonged to non-pathogenic representatives of the genus *Neisseria* with a microbial contamination rate of 10^2 - 10^4 CFU/ml. Strains of coagulase-negative staphylococci (*Staphylococcus*

epidermidis, *Staphylococcus saprophyticus*) were isolated in 45.6% of cases (21 patients). The quantitative index of these isolates ranged from 10^4 to 10^6 CFU/ml. In 41 % of patients (19 people), diphtheroids with a microbial load range of 10^3 - 10^5 CFU/ml were determined in the structure of the automicrobiota. The density of colonization of the main representatives of the microbiota differed from the normative indicators by 2-3 orders of magnitude [5, 10]. Thus, the results of the microbiological examination of the palatine tonsils before treatment indicate a violation of colonization resistance and the presence of dysbiotic changes in the oropharyngeal biotope.

The data of repeated microbiological examination on the 7th day of treatment revealed the isolation of alpha- and gamma-hemolytic streptococci in 91% of cases (21 patients) of the main group. At the same time, there was an improvement in the quantitative indicators of these microorganisms to the level of 10^6 - 10^7 CFU/ml. The same trend was observed in relation to other representatives of the microbiocenosis of the palatine tonsils: *Neisseria spp.* were isolated in 87% of patients of the main group, coagulase-negative staphylococci in 78%, diphtheroids also in 78%. The number of *C. albicans* strains tended to decrease, and their population level decreased to 10^3 CFU/ml. Thus, the analysis of the results of the microbiological study in patients of the main group shows that the use of the probiotic complex contributed to the normalization of the population level of the main representatives of the taxonomic composition of the palatine tonsils microbiome, the elimination of dysbiotic changes and the restoration of oropharyngeal colonization resistance.

A culture study of the microbial profile of the palatine tonsils of patients in the control group on day 7 of treatment revealed a quantitative decrease in the strains and population level of alpha- and gamma-hemolytic streptococci, which were isolated in only 74% of patients (17 patients) in the control group. The number of strains of other resident oropharyngeal microorganisms also decreased: *Neisseria spp.* were isolated only in 60.9% of patients of the main group, coagulase-negative staphylococci in 52.1%, diphtheroids in 43.5%. The number of patients with *C. albicans* remained unchanged with a correspondingly high population level. Thus, in the context of viral damage to the palatine tonsils in patients of the control group, destabilization of the quantitative and qualitative composition of the indigenous microbiota was observed, the phenomena of dysbiosis increased, which led to deeper disruption of the microecology of this biotope and created conditions for the development of bacterial complications.

The noted positive dynamics of the main clinical symptoms, restoration of the physiological state of the palatine tonsils and the quantitative composition of the microbiota in patients of the main group in a shorter

time are associated with the antiviral activity of probiotic bacteria *Bacillus spp.* and their ability to implement immune-mediated mechanisms due to the modulation of innate and adaptive immunity [21, 24]. Numerous experimental studies have shown that the antiviral effect of *Bacillus* microorganisms is associated with the peptides they produce. These compounds reduce the viral load and inhibit viral replication in biological samples. [7, 21]. In addition, under the influence of probiotic bacteria of the genus *Bacillus*, there is an increase in the production of endogenous interferon, an increase in IL-12, transforming growth factor (TGF- β), and IL-10. Along with this, there is also an activation of the cellular and humoral link of adaptive immunity mediated by type 1 T-helper (Th1) with a simultaneous decrease in the activity of type 2 T-helper (Th2) and the release of IgG and IgA [7, 21].

Thus, the presence of such significant and beneficial effects for the macroorganism from the use of a probiotic bacterial preparation is ensured by the physiological properties of bacteria of the genus *Bacillus*, namely: high immunological activity, antiviral action, powerful antagonistic effect against pathogenic and opportunistic microbiota, as well as fungi of the genus *Candida*. These characteristics of the drug make it possible to refrain from premature and inappropriate prescription of antibacterial drugs or to postpone their use, which is especially important in the context of rapid growth of microbial resistance to antimicrobial agents.

CONCLUSIONS

1. Acute viral inflammation of the palatine tonsils occurs under conditions of quantitative and qualitative changes in the species composition of the microbiota of this biotope and is accompanied by increased dysbiotic disorders during the course of the disease.

2. The use of a probiotic bacterial preparation in the form of a spray in the local treatment of acute viral tonsillitis has established its clinical efficacy based on a faster regression of the main symptoms of the disease and normalization of pharyngoscopic signs.

3. The microbiological effectiveness of the probiotic bacterial complex in the conditions of viral damage to the palatine tonsils was manifested in the elimination of dysbiosis and the restoration of the quantitative and qualitative composition of the microbiota of this biotope.

4. The study of the clinical and microbiological efficacy of the probiotic bacterial agent determined the feasibility of its use in the local treatment of patients with acute viral tonsillitis.

5. The clinical and microbiological effects of a probiotic bacterial preparation in the topical treatment of patients with acute viral tonsillitis allow us to refrain from

premature administration of antibacterial chemotherapy, which is an important measure to prevent the development of antibiotic resistance.

Perspectives of subsequent scientific research.

The results obtained during the study provide the basis for a more detailed study of the effect of probiotic agents based on bacteria of the genus *Bacillus* on the development and course of both acute and chronic inflammatory diseases of the oropharynx in order to improve the effectiveness of their treatment, minimize the risks of possible complications, and correct the microbiome of this biotope. It is promising to further study the antimicrobial activity of probiotic preparations containing bacteria of the genus *Bacillus* on biofilm forms of the main pathogens of inflammatory diseases of the oropharynx.

FUNDING AND CONFLICT OF INTEREST

The study has no external sources of financing. The authors declare no conflict of interest.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The study protocol complies with the basic principles of the World Medical Association Declaration of Helsinki «Ethical Principles for Medical Research Involving Human Subjects» and the current regulations of Ukraine, and was approved by the Biomedical Ethics Commission of Poltava State Medical University. Each patient provided voluntary informed consent for inclusion and participation in the study.

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Резюме

ДОЦІЛЬНІСТЬ ЗАСТОСУВАННЯ ПРОБІОТИЧНОГО БАКТЕРІЙНОГО КОМПЛЕКСУ В ФОРМІ СПРЕЯ ДЛЯ ГОРЛА В МІСЦЕВОМУ ЛІКУВАННІ ГОСТРОГО ВІРУСНОГО ТОНЗИЛІТУ

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Мета: визначити доцільність застосування пробіотичного бактерійного комплексу в формі спрею для горла в місцевому лікуванні гострого вірусного тонзиліту на основі аналізу даних його клінічної та мікробіологічної ефективності.

Матеріали та методи. В рандомізованому контрольованому дослідженні прийняли участь 46 осіб з діагностованим на підставі клінічних і фарингоскопічних ознак гострим тонзилітом. Відповідно до отриманого лікування хворі були розподілені на 2 групи. Пацієнти контрольної групи (23 особи) приймали лікування згідно з уніфікованим клінічним протоколом «Тонзиліт». До складу основної групи увійшли 23 хворих, які, окрім протокольного лікування, отримували пробіотичний засіб у формі спрею для горла, що містить комплекс бактерій роду *Bacillus*. Для виключення бактеріальної етіології гострого тонзиліту, використовували модифіковану шкалу Centor (шкала McIsaac). Оцінювання ефективності лікування проводилося на підставі вивчення динаміки клінічних та фарингоскопічних ознак захворювання, а також встановлення кількісних та якісних змін мікробіоти піднебінних мигдаликів в процесі лікування.

Результати. Аналіз динаміки основних клінічних та фарингоскопічних показників свідчить про більш суттєву та швидку їхню нормалізацію у хворих основної групи. Результати мікробіологічних досліджень доводять, що застосування пробіотичного бактерійного комплексу в лікуванні гострого тонзиліту у пацієнтів основної групи сприяло усуненню дисбіотичних змін, відновленню популяційного рівня основних представників мікробіому піднебінних мигдаликів та колонізаційної резистентності ротоглотки.

Висновки. Встановлено, що гостре вірусне запалення піднебінних мигдаликів виникає в умовах кількісних та якісних змін видового складу мікробіоти даного біотопу та супроводжується посиленням дисбіотичних порушень в процесі перебігу захворювання. Підтверджено, що застосування пробіотичного бактерійного комплексу в формі спрею в місцевому лікуванні гострого вірусного тонзиліту є доцільним через доведену його клінічну та мікробіологічну ефективність, а також надає можливість утриматися від передчасного призначення антибактеріальних хіміопрепаратів.

Ключові слова: гострий вірусний тонзиліт, пробіотичний бактерійний комплекс, бактерії роду *Bacillus*, мікробіота піднебінних мигдаликів