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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

FEATURES OF THE ETIOPATHOGENESIS OF UPPER RESPIRATORY TRACT INFECTIONS CAUSED BY CONDITIONALLY PATHOGENIC MICROORGANISMS

Specialty: 2414.01- Microbiology

Scientific field: Medicine

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BAKU – 2024

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Dissertation Council FD 2.28 of the Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the Azerbaijan Medical University

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Rəşad Şəmsəddin oğlu Talışınskiy
"12" 12 2024-ü

GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the topic. Currently, respiratory infections with various etiopathogenesis constitute the most widespread group of diseases, affecting a certain contingent of the population. İN many cases, patients purposefully avoid prompt, thorough treatment of the life-threatening complications that such illnesses might induce. Despite affecting the upper respiratory tract, respiratory infectious processes can progress to more serious and recurring disorders such as tonsillitis, pharyngitis, laryngitis, bronchitis, and bronchial asthma. These conditions can have a substantial impact on the patient's quality of life[1,2]. The role of the body's own immune system in tolerance to the causative agents of the infectious process is indisputable in cases, such as the transition of infectious processes of the upper respiratory tract to the chronic diseases listed above, the formation of antibodies against it, the hapten nature of these antibodies, and the spread of the inflammatory process to various parts of the upper respiratory tract[3]. In addition to the pathogenetic mechanisms mentioned above, it is also important to study the characteristic features of microorganisms that constitute the etiological factors of the mentioned diseases. The prompt and targeted investigation of the fight against microorganisms and the administration of effective antimicrobial treatment against them are of crucial importance.

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3. Ujunwa F. A. and C. T. Ezeonu, “Risk factors for acute respiratory tract infections in under-five children in Enugu Southeast Nigeria,” Annals of Medical and Health Sciences Research, vol. 4, no. 1, pp. 95–99, 2014.

Several recent studies have demonstrated that microorganisms play a role in the development of infectious processes in various mucous membrane areas of the body, including the mucous membrane of the upper respiratory tract, not separately, but together, interacting with each other[4,5].

Therefore, research on how pathogenic, opportunistic, and non-pathogenic microorganisms interact with mucosal membranes and which species are important for infectious processes is currently a relevant topic. In addition to providing a topic for further research, these studies could potentially increase the utilization of probiotics and antibiotic therapy intended for the subsequent elimination of respiratory infectious processes[6,7].

Direct identification of the main causative agents and organization of the optimal prophylactic measures are the most effective methods against microorganisms. Infectious processes of the upper respiratory tract can be of bacterial origin, for which specific treatment tactics should be selected. To eliminate infectious processes caused by bacteria, probiotics are successfully used along with antibiotic therapy, and in most cases, positive results are achieved.

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5. Cheung M.K, Lam WY, Fung WYW, Law PTW, Au CH, et al. Sputum Microbiota in Tuberculosis as Revealed by 16S rRNA Pyrosequencing. PLoS One 2013;8(1):e54574.
6. AboElfotoh M. N., E. M. Rasheed, S. M. Sharaf, and N. A. Tohamy, "Evaluation of nutritional status of children with acute lower respiratory tract infection," Egyptian Journal of Hospital Medicine, vol. 79, no. 1, pp. 532–537, 2020.
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The positive effects of probiotic microorganisms on human health are mediated through three main mechanisms of action. First, certain probiotics can directly displace or inhibit the growth of pathogens, either by acting directly or by affecting commensal microorganisms of the human microbiota. Second, some probiotics can enhance epithelial barrier function by modulating signaling mechanisms. Third, most probiotic strains can also modulate the immune responses of the human body, exert specific local and systemic effects and regulate the balance of pro- and anti-inflammatory cytokines[8].

Studies have shown that the use of probiotics and synbiotics reduces infectious complications in patients in intensive care units, and meta-analyses have demonstrated that the use of probiotics is safe and effective for preventing infectious processes in postoperative and mechanically ventilated patients in intensive care. Bacteria of the genera Lactobacillus, Bifidobacterium, Streptococcus, and Bacillus, some E. coli species, and fungi of the genus Saccharomyces are most commonly used as probiotics[9].

Human health is also affected by prebiotics in addition to probiotics. Prebiotics are substances that are not digested by human digestive enzymes but can be fermented by the intestinal microbiota, causing specific changes in the composition or activity of the gastrointestinal microbiota, thereby benefiting the health of the host.

Purpose of the research: Determination of the role of various microorganisms in the etiopathogenesis of upper respiratory tract infections and optimization of treatment and preventive measures.

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8. Андреев, В.А. Пробиотики: нерешенные вопросы / В.А. Андреев, О.У. Стецюк, И.В. Андреева // - Смоленск: Клиническая микробиология и антимикробная химиотерапия, - 2022. № 4, - с. 345-360.
9. Markowiak, P. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health / P. Markowiak, K. Śliżewska // Nutrients, - 2017. 9 (9), - p. 1021

Tasks of the research

1. Comparative assessment of the occurrence of various bacteria during acute respiratory infection,
2. Comparative assessment of the occurrence of various microorganisms in patients with pharyngitis and tonsillitis,
3. Determination of the sensitivity of K. pneumoniae isolates from patients with acute tonsillitis to various new-generation antibiotic drugs,
4. Comparative microbiological assessment of the effectiveness of treatment for various acute infectious diseases of the respiratory tract,
5. Comparative assessment of quantitative and qualitative indicators of α-hemolytic streptococci in bronchitis and pneumonia, depending on the severity of the disease,
6. Study of the occurrence of various representatives of microflora in materials (smears) obtained from the nasopharyngeal areas of pregnant women.
7. Study of the sensitivity of some microorganisms obtained from patients with acute respiratory infections to various antibiotics.

Scientific novelty:

- The sensitivity of isolates of the K. pneumoniae and H. influenzae species from patients with tonsillitis to various new-generation antibiotic drugs used in treatment was determined,
- A comparative assessment of the quantitative and qualitative indicators of α-hemolytic streptococci and Neisseria (non-pathogenic) species was performed, depending on the severity of the disease during bronchitis and pneumonia,
- The sensitivity of various types of microorganisms isolated from patients with acute respiratory infections to antibiotic drugs was evaluated.

Practical significance of the research:

- Improving probiotic therapy for various respiratory tract infections will increase the effectiveness of treatment measures.

- Extensive study of the microflora of the respiratory tract during infectious processes of various etiologies has created new diagnostic opportunities.
- Studying the sensitivity of opportunistic microorganisms to antibiotics in patients with acute respiratory infections can play an important role in optimizing treatment measures.

Main provisions of the dissertation presented for defense.

1. It is advisable to conduct more extensive microbiological analyses of various infectious diseases of the respiratory tract.
2. The combined use of antibiotics, the associative activity of which to individual respiratory pathogens has been determined, plays an important role in the course and cure of various local infectious processes.
3. It is advisable to assess the sensitivity of antibiotics used to eliminate infectious processes.
4. Identifying the main pathogens in upper respiratory tract diseases provides the basis for organizing optimal treatment and preventive measures.

Publications. The results and fragments of the dissertation work are reflected in 5 theses and 8 articles.

Probation. The results of the research were discussed at the following conferences:

Current Problems of Medicine dedicated to the 100th anniversary of the Azerbaijan Democratic Republic, 2018. L International correspondence scientific and practical conference “International scientific review of the problems and prospects of modern science and education” (Boston. USA. October 22-23, 2018). V International Scientific Congress on "Modern Problems of Pharmacy", dedicated to the 90th anniversary of the establishment of the Azerbaijan Medical University and the 80th anniversary of Higher Pharmaceutical Education in Azerbaijan, 2021. The primary discussion of the dissertation was performed at the 18th meeting of the Department of Medical Microbiology and Immunology and the Department of Epidemiology of AMU on March 16, 2022. It was also discussed at the 14th scientific seminar

of the BED 4.19 One-time Dissertation Council of AMU on May 31, 2024.

Structure and volume of the dissertation. The dissertation is 146 pages (205,804 characters) of computer content and consists of Introduction (6,748 characters), Literature review (62,510 characters), Materials and Methods of the Research (10,901 characters), Results of Personal Research (94,681 characters), Chapter IV (13,752 characters), Results (15,137 characters), Conclusions (1,771 characters), Practical Recommendations (304 characters) and a list of references. The dissertation is illustrated with 16 tables and 17 graphs. The list of references includes 158 sources.

MATERIALS AND METHODS OF THE RESEARCH

The research was conducted in the laboratory of the Bacteriological and Clinical Department of the Republican Clinical Hospital. The material of the work was patients who applied to the Republican Clinical Hospital. The objects of the study were patients who applied to the departments of Allergology, Pulmonology, ENT, and Pathological Pregnancy with acute respiratory infections. Patients with acute respiratory infections (ARI) were taken materials (smears) from the nose, pharynx, and larynx during the early stages of the disease, complications, and recovery. For comparison, materials (smears) were taken from the upper respiratory tract of 45 healthy individuals.

Patients

- 15 persons – ARI (comparative assessment of bacteria)
- 15 persons – ARI (association of bacteria)
- 15 persons – ARI (effect of probiotics)
- 15 persons – Pharyngitis (frequency of occurrence of bacteria)
- 47 persons – Acute tonsillitis (K.pnevmoniae izolates)
- 35 persons - Acute tonsillitis (H. influenzae isolates)

- 12 persons - Acute pharyngitis
- 13 persons – Acute bronchitis
- 12 persons – Typical pneumonia
- 11 persons – Rhinitis
- 12 persons – Sinusitis
- 45 persons - Completely healthy

Comparative evaluation of the effectiveness of treatment

Examination methods

Bacteriological examination of pathological materials

Gram-stained preparations of samples taken from the upper respiratory tract were examined. At the same time, the material (smear) was cultured on various nutrient media. In the examination of fungal elements, the treatment of clinical material with 10% KOH is of great importance.

Staphylococcus - At 35-40°C, media with the same composition were preferred, as they grow better in media containing blood or carbohydrates, sugar media (1% glucose), table salt, egg yolk salt, milk salt agar.

Culture preparation.

In the microbiology laboratory, samples taken from the upper respiratory tract were cultured on 5% sheep blood agar, which is the most favorable nutrient medium for the isolation of group A beta-hemolytic streptococci, the most common pathogen. A bacitracin susceptibility test was performed to determine whether the streptococci belonged to group A.

Candida spp.

To identify Candida albincans, it was cultured on Sabro medium. At the same time, the material was natively treated with 10% KOH and microscopic examination was also performed.

Enterococclar spp.

It grows well in ordinary and bile media. Identification parameters: it grows easily in ordinary nutrient media, it is identified as Gram-positive, paired, motile, non-encapsulated diplocates, enterococci. Growth in bile media and hydrolysis of esculin are differential signs.

Neisseria spp.

It forms non-hemolytic colonies resembling dewdrops on serum and blood agar enriched with carbon dioxide, which do not grow in ordinary nutrient media. Under microscopy, it appears bean-shaped.

Escherichia coli

It forms raspberry red colonies in an endo medium and is inoculated into differential media containing lactose. It grows well at 37^0C. It is identified by its biochemical properties. The serotype is determined using polyvalent OK sera.

Klebsiella pnevmoniae

It forms colonies at 37^0C in ordinary nutrient media, breaks down lactose, and forms red raspberry colonies in Endo medium. The pathogen was cultured and identified by inoculation into lactose and ordinary nutrient media.

H.influenzae

It is a facultative anaerobe, growing better in aerobic conditions. Factors X and V are required for their growth. The optimal nutrient medium for cultivation is "chocolate agar". "Chocolate agar" is prepared by heating blood at 80^0 C for 15 minutes. As a result of heating, erythrocytes hemolyze, and factors X and V are released. Since the nutrient medium takes on a brownish color, it is called "chocolate agar". The phenomenon of satellite formation has been observed in cultivation.

Clinical method.

Complete blood count (CBC) hemoglobin (g/L), monocytes (in %), leukocytes (number x 10^9/L), platelets (number x 10^9/L), lymphocytes (in %), erythrocytes (number x 10^{12}/L), erythrocyte sedimentation rate (ESR 1 hour/mm).

Statistical method.

Statistical processing of the results obtained during the research was carried out using the Statistics 7.0 computer application program. All the obtained results were illustrated in tables and diagrams.

The occurrence of various bacteria in the palatine tonsils during acute respiratory infection was comparatively evaluated. For this purpose, out of 202 patients, 15 patients with an acute respiratory infection, aged between 30 and 50, and without other background

diseases, and 15 completely healthy individuals without any diseases were recruited for the comparative microbiological study.

The age range of healthy individuals, as well as patients, was between 30 and 50 years. As biological material, the smear was taken from the palatine tonsils and cultured in a Petri dish with a nutrient medium. Biological materials taken from patients and healthy individuals were analyzed for the genera Enterococcus, Micrococcus, Klebsiella, Neisseria, Staphylococcus, Streptococcus and Escherichia coli species. The patients were individuals with acute respiratory viral infections who applied to the Republican Clinical Hospital named after M.A. Mirgasimov. It should be noted that the biological samples were sent for examination to the central laboratory of the Republican Clinical Hospital named after M.A. Mirgasimov.

In order to comparatively evaluate the occurrence of various bacterial associations in the palatine tonsils during acute respiratory infection, we recruited 15 individuals aged 30-50 with acute respiratory infection and no other background diseases for a microbiological study. As biological material, the smear was taken from the palatine tonsils and cultured in a Petri dish with a nutrient medium. During the microbiological study, the occurrence of associations of microorganisms such as Staphylococcus aureus and Streptococcus pyogenes (1), Staphylococcus aureus and Streptococcus oralis (2), Staphylococcus epidermicus and Streptococcus pyogenes (3), Staphylococcus aureus and Streptococcus milleri (4), and Streptococcus pyogenes and Staphylococcus haemoliticus (5) was studied.

In order to study the effects of probiotics on the microflora of the palatine tonsils during acute respiratory infection, 15 people aged between 30 and 50 with acute respiratory infections of viral origin and without other background diseases were involved in a microbiological study. Smears were taken from the palatine tonsils as biological material and inoculated into a Petri dish with a nutrient medium. Then, along with the main treatment (with the drug Loroben), probiotics (Linex) were administered to the patients, and after the clinical symptoms disappeared, the presence of species such as Enterococcus,

Micrococcus, Klebsiella, Neisseria, Staphylococcus, Streptococcus, and Escherichia coli was examined again in biological materials.

To compare the occurrence of various microorganisms in smears taken from different anatomical areas of patients with pharyngitis and tonsillitis, we studied the analysis results and medical histories of 15 patients with pharyngitis and 16 patients with tonsillitis who applied to the Central Laboratory of the Republican Clinical Hospital for analysis. We studied the microbiological composition of smears taken from the oropharynx, nasopharynx, and nasal cavity areas of the patients. Patients with pharyngitis and tonsillitis were conditionally considered as separate groups. The presence of Staphylococcus aureus, Streptococcus pyogenes, Enterococcus faecalis, Klebsiella pneumoniae and Candida albicans microorganisms in the smear samples was studied in number and percentage.

To determine the sensitivity of K. pneumoniae isolates from patients with acute tonsillitis to various antibiotic drugs, we took swears from the oropharynx of 47 people with acute tonsillitis, aged 30-50. Among them, 16 samples were selected in cultures in which the microorganism K.pneumoniae was detected, and pure isolates of the mentioned species were obtained. The sensitivity of the obtained 16 pure K. pneumoniae isolates to antibacterial drugs such as penicillin, amoxicillin, ampicillin, and cefotaxime was studied by applying appropriate antibiotic discs. The sensitivity and resistance of the corresponding microorganism strains to the analogous antibacterial agent were evaluated according to the rings formed around the antibiotic discs. The susceptibility response, sensitivity, and resistance of the respective microorganism strains to the corresponding antibacterial agent were assessed based on the rings formed around the antibiotic discs.

The obtained numerical data were processed using statistical methods and taking into account modern requirements. The mean values (M) for group indicators, their standard error (m), the minimum (min) and maximum (max) values of the series, as well as the frequency of occurrence of quality indicators in groups, were determined.

The parametric Student's t-test method was used for the primary assessment of differences in the variational series. For pairwise related options, the average difference between the selected indicators and the difference between the parts were used to estimate the difference. Then, for checking and refining the obtained quantitative indicators, one of the non-parametric criteria - Wilcoxon (Mann-Whitney) U-criterion was applied. Pearson's $\chi 2$ criterion was used for frequency analysis. Correlation analysis was carried out in order to determine the strength of the relationship between the studied indicators.

It should be noted that the statistical processing of the results obtained during the research was carried out using the Statistica 7.0 computer application program.

The obtained results are displayed in tables and diagrams.

RESULTS OF PERSONAL RESEARCH

Our study, conducted to comparatively evaluate the occurrence of various bacteria in the palatine tonsils during acute respiratory infection, found Enterococcus spp. in the samples of only 1 patient from a group of 15 patients with acute respiratory infection, which accounted for 6.67±6.44% of the group. However, in biological samples obtained from a group of healthy individuals consisting of the same number of healthy persons, no species of the corresponding genus of microorganisms were found. It should be noted that although viruses are the main causative agents of acute respiratory infections of viral origin, due to the pathological condition they cause and the failure of local immune factors, various opportunistic bacterial genera and species also increase, crowding out microorganisms characteristic of other normal microflora.

During the research examinations on the occurrence of species belonging to the Micrococcus genus, the corresponding microorganism species were found in 2 biological samples in the group of patients with acute respiratory infections, which accounted for 13.33±8.78% of the group. However, in the group of healthy persons, this indicator was 6.67±6.44%, with 1 person.

Klebsiella spp. species were found in only 1 sample in biological samples taken from patients, which was 6.67±6.44% in the group. In biological samples taken from the palatine tonsils of healthy individuals, this indicator was almost equal to 0.

Species of the Neisseria spp. genus was detected in one of the biological samples taken from the palatine tonsils of 15 individuals with acute respiratory infections, which was 6.67±6.44% in the group.

Staphylococcus spp. species were detected in 9 of the 15 biological samples taken from the tonsils of individuals with acute respiratory infections, which accounted for 60.0±12.65% of the patient group, while in the group of healthy individuals, these species were found in 6 individuals, which accounted for 40.00±12.65% of the control group.

Streptococcus spp. was found in 5 of the biological samples taken from the tonsils of patients in the group of 15 patients with acute respiratory infection, which represented 33.33±12.17% of the total samples. However, unlike other types of microorganisms, streptococcal species were found in 7 samples taken from healthy individuals, which constituted 46.67±12.88% of the group of healthy persons. The main reason for the higher prevalence of streptococcal species in healthy persons compared to sick individuals is that many representatives of the normal microflora of the upper respiratory tract of humans belong to this group. As a result of our study conducted to comparatively evaluate the occurrence of various bacterial associations in the tonsils during acute respiratory infection, in biological materials taken from the tonsils of 15 patients with acute respiratory infection, associations of Staphylococcus aureus and Streptococcus pyogenes microorganisms were found in 8 samples, which accounted for 53.33% of the total number of patients suffering from acute respiratory infection.

As a result of the study, in biological samples obtained from the tonsils of 15 patients with clinical signs of acute respiratory infection, the association of Staphylococcus aureus microorganisms was observed in 5 samples, which represented 33.33% of the total patients. Association of Staphylococcus epidermicus and Streptococcus pyogenes was observed in 4 of the patients with acute respiratory

infections (n=15) included in the examinations, which is 26.67% of the total patients.

Enterococcus faecalis species were identified in 4 out of 16 biological samples taken from patients with tonsillitis, which accounted for 25% of the group. The occurrence of Staphylococcus aureus species in patients with pharyngitis and tonsillitis was almost identical. The occurrence of Streptococcus pyogenes species was higher in patients with tonsillitis. This is further evidence of the special place of streptococci among the main causative agents of tonsillitis. The same situation was recorded in the occurrence indicators of Enterococcus faecalis species. Klebsiella pneumoniae was found in 3 of the biological samples obtained from patients with pharyngitis, which constituted 20% of the group with 15 persons that we conventionally considered as the pharyngitis patient group. However, this species was found in 2 of the biological samples obtained from the tonsillitis patient group, which comprised 12.5% of the group with 16 persons that we conventionally considered as the tonsillitis patient group. During our studies on the occurrence of Candida albicans, it was detected in only 1 of the biological samples we obtained from the pharyngitis group, which constituted 6.7% of the group. In the group of patients with tonsillitis, the occurrence of this microorganism was in 2 samples, covering 12.5% of the group. The occurrence of the Klebsiella pneumoniae microorganism was higher in the group of patients with pharyngitis than in patients with tonsillitis, and the occurrence of the Candida albicans species was higher in the group of patients with tonsillitis. As a result of our study on the occurrence of various microflora in smears taken from the nasopharynx of patients with pharyngitis and tonsillitis, the occurrence of S. aureus species was recorded in 8 samples in the relevant biological materials obtained from a group of 15 patients with pharyngitis, which accounted for 53.3% of the group. In the respective biological materials obtained from a group of 16 patients with tonsillitis, S. aureus was found in 10 nasopharyngeal smear samples, which is 62.5% of the group. Of the nasopharyngeal samples obtained from 15 patients with pharyngitis, representatives of the S. pyogenes species were found in 5, which included 33.3% of patients in the group. S.

pyogenes was isolated from 6 of the 16 patients with tonsillitis who underwent an anatomic biopsy, which represented 37.5% of the group. The occurrence of E. faecalis in nasopharyngeal smear samples obtained from the group of patients with pharyngitis was recorded in 4 samples, accounting for 26.7% of the samples in this group. The presence of the corresponding species in the biological materials obtained from the group of patients with tonsillitis was observed in 3 biological materials, which represented 18.8% of the group of patients with tonsillitis (n=16) (Table 1).

Table 1.

Occurrence of various microorganisms in the nasopharyngeal areas of patients with pharyngitis and tonsillitis

Microorganisms	Patients with pharyngitis (n=15)		Patients with tonsillitis (n=16)	
	n	%	n	%
Staphylococcus aureus	8	53.3*	10	62.5*
Streptococcus pyogenes	5	33.3	6	37.5
Enterococcus faecalis	4	26.7	3	18.8
Klebsiella pneumonie	2	13.3	2	12.5
Candida albicans	1	6.7	2	12.5

Note: *- The average difference between the selected intergroup indicators was significant ($p<0.05$).

The K. pneumoniae species were isolated from only 2 of the nasopharyngeal smears taken from a group of 16 patients with tonsillitis, and it accounted for 12.5% of the total samples taken from patients with tonsillitis. The number of K. pneumoniae species found in the biological materials we collected from the group of patients with pharyngitis was similar to that found in patients with pharyngitis, but these samples accounted for 13.3% of patients with pharyngitis. Candida albicans was isolated from only 1 of the nasopharyngeal samples obtained from a group of 15 patients with pharyngitis, and this was 6.7% of the group. Candida albicans was isolated from 2 of the nasopharyngeal smear samples obtained from a

group of 16 patients with tonsillitis, which represented 12.5% of the corresponding group.

The occurrence of various microflora in smears taken from the nasal cavity of patients with pharyngitis and tonsillitis was determined. S.auresi species was isolated from 5 analogical smears out of 16 taken in the group of patients with tonsilitis, which represented 31.3% of the group. S. aureus was isolated in 4 of the nasal mucosa smears obtained from the group of patients with pharyngitis (n=15), accounting for 26.7% of these patients.

In 3 samples taken from a group of 15 patients with pharyngitis, representatives of the S. pyogenes species were isolated, which was 20% of the analogous samples taken from the corresponding group. This species was found in 4 of the analogous biological samples obtained from 16 patients with tonsillitis, accounting for 25% of the total samples taken from the corresponding group.

E. faecalis was isolated from 2 nasal smears taken from a group of 15 patients with pharyngitis, which represented 13.3% of the corresponding group. E. faecalis was also observed in 2 nasal smears taken from a group of tonsillitis patients (n=16), which represented 12.5% of the corresponding group. Representatives of the E. faecalis species were also observed in 2 of the nasal smears obtained from the group of patients with tonsillitis (n=16), which accounted for 12.5% of the corresponding group.

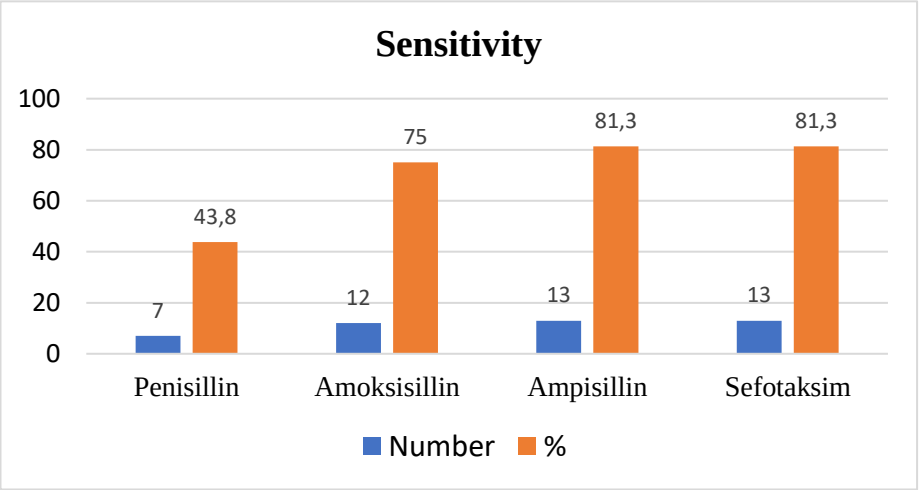
The occurrence of K. pneumoniae in nasal smears obtained from the group of patients with pharyngitis was 6.7%, observed in only 1 sample. The occurrence of the corresponding species in analogous biological material samples obtained from patients with tonsillitis was 6.3%, which corresponded to 1 smear sample in this group.

The occurrence of the C. albicans species was 0. It was not found in any sample in both the tonsillitis and pharyngitis groups.

We determined the occurrence of various representatives of the microflora in nasopharyngeal smears obtained from pregnant women. S. aureus was isolated in 9 of the nasopharyngeal smear

cultures obtained from 50 pregnant women, which accounted for 18% of the total cases. Of the studied smear cultures, S. haemolyticus was recorded in only 1, or 2% of them. S. epidermidis was isolated in 4, or 8% of the nasopharyngeal smears obtained from pregnant women. Among the streptococci, the S. mitis species was found in 5 of the mentioned biological materials, which was 10% of the total materials. In the mentioned biological materials, Candida was found in only 3 samples, which represented 6% of the total nasopharyngeal smears. A similar result was recorded when studying the occurrence of E. coli in cultures of smears taken from the nasopharyngeal areas of pregnant women. The primary reason why studying the microflora of pregnant women is important is that, even though the female body is in a healthy state, changes in hormonal status and, as a result, the local immune system of anatomical and physiological areas can lead to the development of conditionally pathogenic microorganisms. During the study of biological material obtained from a group of 12 women in the last trimester of pregnancy, this indicator was detected in 3 cases, which is 25% in the corresponding group. According to the corresponding biological materials obtained from this group, S. pneumoniae dominated the inflammatory process in the pharynx in 1 sample, which represented 8.3% of the corresponding group. However, in a group of 20 pregnant women in the first trimester, no study object showed dominance of the relevant microorganism in the process. The same results were recorded for the E. auruginosa species. In immunological examinations, 5 patients had high IgE, which accounted for 10% of the total cases.

We determined the sensitivity of K. pneumoniae isolates from patients with acute tonsillitis to various new-generation antibiotic drugs. Seven out of ten pure K. pneumoniae isolates from patients with acute tonsillitis were observed to be highly sensitive to penicillin, which was 43.8% of the total isolates. Resistance to the relevant antibacterial drug was observed in only 1 isolate, which represented 6.3% of the total isolates (Graph 1).



Graph 1. Quantitative indicators of susceptibility of K. pneumoniae isolated from patients with acute tonsillitis to various antibiotics

To study the sensitivity of the isolates to various antibacterial drugs, we took smears from the oropharynx of patients aged 30-50 years. K.pneumoniae was detected in 35 patients among them. 16 colonies were selected in which the K. pneumoniae microorganism was detected, and pure isolates of the mentioned species were obtained.

High sensitivity to Cefotaxime was recorded in the isolate of K. pneumoniae. During the study of the sensitivity of K. pneumoniae colonies isolated from the respective patients to Cefotaxime, high sensitivity to the mentioned drug was recorded in 15 cases, which constituted 93.8% of the total cases. No resistance to Cefotaxime was recorded in any of the isolate samples.

The susceptibility of pure K. pneumoniae isolates to amoxicillin was recorded in 12 isolates, which was 75% of the total isolates, and resistance to amoxicillin was recorded in only 1 case, which represented 6.3% of the total samples.

Microbiological examinations are also considered mandatory during clinical and laboratory examinations of patients suspected of having an upper respiratory tract infection. Microbiological examination

of biological material taken from the nasopharynx is of great importance in the timely detection of bacteria, fungi or viruses that cause the disease and in the implementation of targeted treatment measures.

To conduct a comparative microbiological assessment of the effectiveness of treatment for various acute infectious diseases of the respiratory tract, we recruited 12 patients with acute pharyngitis, 11 with acute tonsillitis, 13 with acute bronchitis, 12 with typical pneumonia, 11 with rhinitis, and 10 with acute sinusitis, from all patients aged 30-50. Microbiological examinations were performed on the patients twice, before and after treatment.

In biological materials obtained from a group of 11 patients with acute tonsillitis, the colonization ability of Streptococcus spp. representatives, which is a qualitative indicator, was 6.73±0.26 CFU/mg before treatment procedures, but after treatment this indicator increased slightly and was found to be 6.95±0.14 CFU/mg. Nevertheless, the occurrence of representatives of the corresponding genus in biological materials was 81.8% in the group, being found in 9 samples before and after treatment.

As a result of the study, the colonization ability of Neisseria spp. in biological materials obtained from a group of 12 patients with acute pharyngitis was found to be 6.13±0.22 CFU/mg before treatment, while after treatment this indicator increased to 6.98±0.19 CFU/mg. The occurrence of the relevant microorganism group was 50%, in 6 out of 12 oropharyngeal smears before treatment, and 91.7% of the group, which was in 11 samples after treatment. In biological materials obtained from a group of 11 patients with acute tonsillitis, the colonization ability of Neisseria spp. was 6.39±0.21 CFU/mg before treatment, but after treatment and the disappearance of clinical symptoms, this indicator decreased slightly and was calculated to be 6.22±0.13 CFU/mg. The occurrence of the corresponding species in this group remained unchanged before and after treatment Thus, it occurred in 6 of the samples, which was 54.5% of the group (Table 2).

Before treatment, lactobacilli were found in only 1 of the biological materials taken from 12 patients with acute pharyngitis, or

8.3% of the total group. The colonization ability of representatives of the corresponding genus in this sample was 4.03 CFU/mg.

Table 2

Evaluation of treatment measures in acute respiratory infections by microbiological parameters

	Patients with acute pharyngitis (n=12)		Patients with acute tonsillitis (n=11)	
Microorganisms	Occurrence Number and %	Colonization ability (CFU/mg)	Occurrence Number and %	Colonization ability (CFU/mg)
Streptococcus spp.				
Before treatment	10 (83.3)	6.45±0.20	9 (81.8)	6.73±0.26
After treatment	12 (100)	6.96±0.13 #	9 (81.8)	6.95±0.14
Neisseria spp.				
Before treatment	6 (50.0)	6.13±0.22	6 (54.5)	6.39±0.21
After treatment	11 (91.7) *	6.98±0.19 #	6 (54.5)	6.22±0.13
Staphylococcus spp.				
Before treatment	7 (58.3)	4.17±0.23	6 (54.5)	4.12±0.25
After treatment	5 (41.7)	3.62±0.15	7 (63.6)	4.23±0.31
S. Aureus				
Before treatment	6 (50.0)	4.08±0.26	5 (45.4)	4.06±0.21
After treatment	4 (33.3)	3.56±0.18	4 (36.4)	4.23±0.25
Enterococcus spp.				
Before treatment	4 (33.3)	6.04±0.28	4 (36.4)	5.77±0.30
After treatment	2 (16.7)	4.83±0.13 #	3 (27.3)	5.41±0.17
Candida spp.				
Before treatment	3 (25.0)	3.98±0.21	2 (18.2)	4.00±0.15
After treatment	2 (16.7)	3.42±0.17	3 (27.3)	4.24±0.20

*Note: *- $p<0.05$, when comparing the frequency indicators before and after treatment; # - $p<0.05$, when comparing quality indicators before and after treatment.*

After treatment, the occurrence of the Lactobacillus species among the relevant materials was recorded in 2 samples, which amounted to 16.7% of the group. The average colonization ability of the

lactobacilli observed in the 2 samples was found to be 3.10±0.26 CFU/mg.

In the biological materials obtained from a group of 11 patients with acute tonsillitis before treatment, the presence of lactobacilli was observed in 2 samples, which was 18.2% of this group. In these 2 samples, the colonization potential of the corresponding microorganisms was calculated to be 4.14±0.18 CFU/mg on average. In the biological materials obtained after treatment, the mentioned species were found in only 1, which was 9.1% of this group. In the mentioned sample, the colonization potential of the corresponding species was found to be 3.34 CFU/mg. Microbiological examination of oropharyngeal smears taken from a group of 12 patients with acute pharyngitis before treatment, revealed Staphylococci in 7 samples, which was 58.3% of the group. After treatment, this indicator was recorded in 5 samples, representing 41.7% of the group. Although the colonization ability of total staphylococci was calculated to be 4.17±0.23 CFU/mg in the group of patients with acute pharyngitis before treatment, this indicator decreased significantly after treatment and was found to be 3.62±0.15 CFU/mg.

In the biological materials taken from 11 patients in the group of patients with acute tonsillitis, the occurrence of total staphylococci was recorded in 6 samples before treatment, which was 54.5% for the respective group. After treatment, the occurrence of total staphylococci was recorded in 7 samples, which was 63.6% for the group. The colonization index of total staphylococci in the mentioned biological material samples was calculated to be 4.12±0.25 CFU/mg before treatment but increased to an average of 4.23±0.31 CFU/mg after treatment.

The S. aureus species was found in 6 out of 12 oropharyngeal smear samples obtained before treatment from a group of patients with acute pharyngitis, or 50% of the samples in the total group. The colonization ability of the corresponding microorganism in the mentioned samples was calculated as 4.08±0.26 CFU/mg. After treatment, the occurrence of S.aureus in the group of patients with acute pharyngitis was recorded in 4 samples, accounting for 33.3% of the

group. The average colonization ability of S.aureus samples observed in the mentioned 4 samples was found to be 3.56±0.18 CFU/mg.

Thus, in recent years, the study of some important aspects of the immune system and microflora disorders, as one of the main problems of infectious diseases and pediatric practice, is of particular importance in the diagnosis, treatment and prevention of acute respiratory diseases. In this regard, the basis of most clinical laboratory examinations is the study of the ratio of immune cell populations, qualitative and quantitative indicators of normal and conditionally pathogenic microflora. Thus, the basis of most clinical laboratory examinations is the study of the ratio of immune cell populations, and the qualitative and quantitative indicators of normal and conditionally pathogenic microflora. Classical bacteriological methods require extensive study of diagnostics, which allows us to judge the functional activity and clinical significance of the number of certain bacteria and the violation of the ratio of their various populations. Practitioners recommend the use of oral penicillin or erythromycin to treat streptococcal pharyngitis.

CONCLUSIONS

1. Staphylococcus spp. was detected in 60.0±12.65% of biological samples taken from 15 individuals with acute respiratory infections, while in the group of healthy individuals, this number was 40.00±12.65%.
2. In biological samples obtained from the tonsils of 15 patients with clinical signs of acute respiratory infection, the association of Staphylococcus aureus and Streptococcus oralis microorganisms was observed in 5 samples, which accounted for 33.33% of the total patients.
3. Although K. pneumoniae was observed in 6.67±6.44% of cases before treatment, the occurrence of respective microorganisms was 0 after treatment.
4. Enterococcus faecalis species were identified in 4 out of 16 biological samples taken from tonsillitis patients, which represented

25% of the group. The occurrence of the Staphylococcus aureus species in pharyngitis and tonsillitis patients was almost identical.

5. S. pyogenes was isolated from 20% of the biological samples taken from a group of 15 patients with pharyngitis.
6. The main importance of changes in the microflora of pregnant women and their study is that, despite the healthy state of the female body, during pregnancy, conditionally pathogenic microorganisms can develop due to changes in the hormonal status and, consequently, the local immune system of anatomical and physiological areas.
7. The study of susceptibility of 16 K. pneumoniae isolates from patients with acute tonsillitis to cefotaxime revealed high susceptibility in 13 samples.

PRACTICAL RECOMMENDATIONS

1. The results of relevant research have created conditions for the activities of practicing physicians and the improvement of treatment tactics in appropriate patients.
2. Selective selection and combined use of antibiotics during treatment, as shown in the study, may allow for faster clinical outcomes.
3. Microbiological examination of biological material taken from the nasopharynx is of great importance in the timely detection of disease-causing bacteria, fungi, or viruses and in the implementation of targeted treatment measures.

Publications

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2. Kəskin virus mənşəli resipirator infeksiya zamanı damaq badamcıqlarında mikrobiosinozun qiymətləndirilməsi (Saglamlıq jurnalı 4 səh.122-127. 2018, Əliyev M.H., İbayeva Ş.Ə.)

3. Bronxit və pnevmaniya zamani xəstəliyin agırlıq dərəcəsindən asılı olaraq müxtəlifMikroorqanizm növlərinin kəmiyyət və keyfiyyət göstəriciləri (Azərbaycan təbabətininMüasir naliyyətləri 4 səh.144-148.2018.Əliyev M.H., İbayeva Ş.Ə.)
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5. Faringitli və tonzilitli xəstələrdə müxtəlif mikroorqanizmlərin rast gəlməsinin müqayisəsi (AzərbaycanTəbabətinin müasir naliyyətləri 2. səh. 136-139. 2018, Əliyev M.H. İbayeva Ş.Ə.)
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The defense of the dissertation will be held at the FD 2.28 Dissertation Council meeting on "15" January 2025 at "16⁰⁰".

Address: 14 A. Gasimzade St., (conference hall), AZ 1022, Baku city.

The dissertation is accessible at the library of the Azerbaijan Medical University.

Electronic versions of the dissertation and abstract are available on the official website of the Azerbaijan Medical University (amu.edu.az).

The abstract was sent to the required addresses on 12 december 2024.

Signed for print: 06.12.2024
Paper format: 60x84 1/16
Volume: 36,322 characters
Order: 100
Number of hard copies: 30
"Tabib" Publishing House