

(n=100) who took part in the survey, or 54% of them, chose "pharmacists" as the answer to the question. At the same time, 25 survey participants, or 25% of them, chose the option "pharmaceutical companies" as the answer to the corresponding question. 29 survey participants indicated the option "doctors" as an answer to the corresponding question, which is 29% of the total number of participants.

Conclusions. Based on the data obtained, there is every reason to talk about the importance of further scientific development of issues related to the circulation of counterfeit medicines in order to implement a set of local actions aimed at improving the collection of important information in this category of problems in the field of healthcare.

Key words: falsified medicines, awareness level, doctors, pharmacists, survey.

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**COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF PATHOGENETIC
AND ETIOLOGICAL TREATMENT OF OTOMYCOSIS**

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According to WHO, every fifth inhabitant of the Earth has a fungal disease. Under these conditions, given the constant risk of immunosuppression caused by one reason or another, everyone can become a target for the defeat and subsequent generalization of fungal infection. In this regard, timely treatment and prevention of mycoses is of particular relevance. In 2022, WHO published for the first time a list of the 19 most dangerous fungal pathogens that pose a threat to public health. Most of them are also pathogens of otomycosis. WHO has declared the search for ways to block the spread of these pathogens, as well as to prevent the emergence of resistance to antifungal drugs, to be priority areas of medicine. Most of these pathogens can be pathogens of otomycosis. The purpose of our study was to identify the most common pathogens of otomycosis in Azerbaijan, to study their sensitivity to antifungal to evaluate the effectiveness of pathogenetic treatment of otomycosis with a drug with a keratolytic effect, compared with antifungal drugs that contribute to the development of resistance in fungal pathogens.

Key words: antifungal, otomycoses, susceptibility, salicylic acid.

Connection of the publication with planned research works.

This work is a fragment of a dissertation for the degree of Doctor of Philosophy in medicine.

Introduction.

In 2022, WHO published for the first time a list of the 19 most dangerous fungal pathogens that pose a threat to public health. WHO has declared the search for ways to block the spread of these pathogens, as well as to prevent the emergence of resistance to antifungal drugs, to be priority areas of medicine [1]. At the moment there are only 4 groups of antifungal agents and several candidate drugs under development. In addition, many of these drugs are not available in the pharmacy chain, in addition, most of them are not available

due to the high cost. Considering the above, the spread of diseases such as skin mycoses, thrush, oropharyngeal candidiasis and the lack of rapid methods for diagnosing sensitivity to drugs creates a real threat of an avalanche-like growth of resistance. Therefore, the most important directions in the work of doctors are the revision of the usual methods of treating fungal diseases, the search for more affordable means, while blocking the appearance of more resistant strains.

According to WHO, every fifth inhabitant of the Earth has a fungal disease [2]. Under these conditions, given the constant risk of immunosuppression caused by one reason or another, everyone can become a target for the defeat and subsequent generalization of fungal infection. In this regard, timely treatment and prevention

of mycoses is of particular relevance. The vast majority of these 19 "most dangerous" pathogens can be pathogens of fungal ear damage [3]. In otorhinolaryngology, 6-10% of diseases are caused by fungal infection. Up to 50% of these are otomycoses. Otomycosis refers to a pathological process caused by fungal flora involving the skin of the auricle, the external auditory canal, the eardrum, the middle ear (in the presence of perforation or shunt) and the postoperative cavity of the middle ear [4]. The frequency of the disease is directly related to the climate: it increases in humid and hot climates. Depending on the climate, the incidence of fungal otitis externa among all otitis externa is 26-80%. The disease occurs in all age categories, but the most affected is the age of 30-40 years. There is no statistically significant difference between the involvement of men and women, rural or urban population [5]. Pathogenetic factors play a special role in the occurrence of the disease: frequent contact with water, traumatization of the external auditory canal (cotton buds, earphones), local and systemic antibiotic therapy, the presence of inflammatory chronic ear diseases, etc. In children, the distribution is somewhat different about 13-18%.

At the stage of the initial appeal to the otolaryngologist, the complaints characteristic of otomycosis constitute the first link of diagnosis. The clinic of the disease largely depends on age, comorbid status and the causative agent of otomycosis [6]. Pain syndrome, itching, feeling of congestion, characteristic colored discharge, pathological elements on the skin of the external auditory canal and the auricle. In persons with immunosuppression, dangerous and, in recent years, a more frequent fungal disease is malignant otitis externa, occurring with a lesion of the temporal bone. It proceeds fulminantly, often with a fatal outcome. The pathogens can be *Candida albicans*, *Aspergillus niger*, *Scedosporium apiospermum* [7]. In the last decade, cases of fatal cases caused by *Candida auris*, a multidrug resistant causative agent of otitis media and otomastoiditis, not detected by cultural research methods, have been detected on almost all continents [8].

The aim of the study.

To identify the most frequent pathogens of otomycosis in Azerbaijan, to study their sensitivity to antifungal drugs, to evaluate the effectiveness of pathogenetic treatment of otomycosis with a drug with a keratolytic effect, compared with antifungal drugs that contribute to the development of resistance in fungal pathogens.

Object and methods of research.

This was a prospective study of patients with a definitive diagnosis of otomycosis between November 2020 and September 2023. The study was completed in accordance with the Declaration of Helsinki ethical guidelines for human subject research. Written informed consent was acquired from all participants before the study.

Inclusion criteria included: patients with characteristic fungal deposits in EAC, positive fungal culture or fungal smear.

Exclusion criteria included: absence or perforation of the tympanic membrane, pregnant or lactating women, systemic antifungal drug within 2 weeks prior to the study.

A total of 90 patients were recruited and randomly assigned into 3 treatment groups: 1) 2% alcohol solution of salicylic acid, 2) povidone- iodine solution 10%, 3) 1%

alcohol solution of clotrimazole. Before treatment, the fungal deposits in the EAC were cleaned under end otoscope and sent for routine fungal and bacterial cultures for all patients. Next, in each group local drug was applied directly in the EAC. The dose was 3 drops twice daily for 2 weeks. There were 30 people in each treatment group. All cases were followed up over 6 months after the treatment was completed. Additionally the following data of all participants were collected: gender, age, duration, predisposing factors, symptoms, medical history, comorbidities, fungal and bacterial culture results, treatment outcomes and adverse effects of drugs.

Recovery was defined as an asymptomatic patient with clean EAC and negative fungal smear. Relapse was considered cases of recurrence of the disease after a confirmed recovery in the same ear.

Statistical data processing was performed using the IBM SPSS 26.0 computer program. Absolute values and percentage frequencies with standard errors were used in the descriptive statistics of the study results. Pearson's criterion χ^2 was used for intergroup comparisons. The level of statistical significance of the differences was considered $p < 0.05$.

Research results and their discussion.

The study involved 97 patients with suspected otomycosis. Fungal culture results showed that 7 cases were positive, but the exact species was unable to be identified. There were 90 patients who had complete clinical diagnosis, treatment, and follow-up data: 30 patients in each group of treatment. They were aged from 2 months to 86 years, with a mean age 37,2 years. The medical history ranged from 2 days to 2 years. Of these, 49 are women and 41 are men. In 51.7% of patients, the external auditory canal with the eardrum was affected. Isolated tympanic membrane lesion (myringitis) was observed in 3,4% of patients. The most common complaint was ear pain ($75,6 \pm 4,5$) followed by colored discharge ($63,3 \pm 5,1$), itching ($62,2 \pm 5,1$), hearing loss ($53,3 \pm 5,3$). The most frequent predisposing factor in patients was traumatization of the external auditory canal with ear sticks ($57,8 \pm 5,2$). Twenty-one (23,3%) patients had a history of frequent contact with water. In twelve (13,3%) patients, the disease appeared after systemic antibacterial therapy. 22.3% of women constantly wore hijab. Twenty-four (26,7%) cases had comorbidities such as diabetes mellitus, iron deficiency anemia, allergy. Some patients has multiple factors.

Four fungal taxa namely *Aspergillus*, *Candida*, *Penicillium*, and *Mucor* were identified. *Aspergillus niger* was identified in $50,0 \pm 5,2$. *Candida albicans* in $25,5 \pm 4,5$ cases, *Penicillium natatum* – $18,1 \pm 4,0$. *Mucorales* were detected in $4,3 \pm 2,1$ percent of cases. One patient suffered from mixed infection of *Aspergillus niger* and *Candida glabrata*. The most frequently obtained flora was sensitive to ketokonazole ($47,9 \pm 5,2$), the majority showed resistance to fluconazole ($91,7 \pm 2,8$). The rate of regression of complaints in each of the three treatment groups was taken into account (**table 1**).

The best results were shown by the treatment regimen in group 1 (**table 2**). Already on the 3rd day of treatment, patients noted a significant reduction in pain and itching. In groups 1 and 3, patients often complained of a burning sensation during instillation of the drug ($53,3 \pm 9,1$) and ($40,0 \pm 8,9$), respectively. In group 2, these complaints were rare ($6,7 \pm 4,6$).

Table 1 – Distribution of complaints

Complaints	Salicylic acid	Povidon-iodine	Clotrimazole
Earache	21	24	20
Pruritus	22	16	21
Ear fullness	24	20	17
Tinnitus	13	15	9
All	30	30	30

Table 2 – Disappearance of complaints on the 3rd day

Complaints	Salicylic acid	Povidon-iodine	Clotrimazole
Earache	18(85,7%)	17(70,7%)	15(75%)
Pruritus	15(77,3%)	12(75%)	13(61,9%)
Ear fullness	20(83,3%)	16(80%)	14(82,4%)
Tinnitus	10(76,9%)	11(73,3%)	6(66,7%)

Otomycosis is a disease that is a problem not only for the patient but also for the doctor. In some cases, it can affect the middle and inner ear, sometimes it can be fatal. In otomycosis, the identification of predisposing factors plays a decisive role for the treatment and subsequent prevention of relapses of the disease. In particular, otomycosis was most often found in persons abusing cotton swabs for ear cleaning. Also, a high percentage of patients were women wearing hijab and persons performing religious ablution before namaz. Due to the increase in temperature and humidity in the external auditory canal, a favorable climate was created for the development of the fungal process. In most cases, treatment failures and relapses of the disease occurred in cases of continuation of the predisposing factor, even if the treatment was adequate. The most common side effect was burning. This complaint was mainly in patients with severe fungal myringitis and was absent in patients without myringitis. Over the past 10 years, there have been many studies on the effectiveness of various topical treatments of otomycosis. Mofatteh notes that on the 20th day of treatment with betadine solution and clotrimazole cream, complete recovery occurred in 69.6% and 66.7%, respectively [9]. In the work of Qinqquo, when filling the external auditory canal with a TAEC (triamcinolon acetone, isoconazole cream), compared with a suspension of nystatin, the effectiveness reached 97.6% and 73.5%, respectively [10]. In our study, the sensitivity of flora isolated from otomycosis in patients in Azerbaijan to clotrimazole and nystatin was 36% and 32%, respectively.

Most of these studies confirm the high effectiveness of antifungal agents, especially with the azole group [11]. In our study, the sensitivity of flora isolated from otomycosis in patients in Azerbaijan to clotrimazole and nystatin was 36% and 32%, respectively. There are very few studies studying the effectiveness of drugs with a non-specific effect. Among the available ones, we see their low effectiveness compared to antifungal agents [12].

An indicator of the effectiveness of the drug is the absence of the need to visit the doctor again (**table 3**). In group 1, 23.3% of patients needed cleaning on 7th day. In the 2nd and 3rd groups – 33.3% and 40%, respectively.

Table 3 – The need to clean fungal masses

Need for cleaning	Salicylic acid			Betadin			Clotrimazole		
	N=	%	±m	N=	%	±m	N=	%	±m
7 th day	7	23,3	7,7	10	33,3	8,6	12	40,0	8,9
14 th day	3	10	5,5	6	20	7,3	5	16,7	6,8
	30			30			30		

Conclusions.

The effect of salicylic acid solution in group 1 patients was based on the keratolytic effect on the upper layers of the keratinizing epithelium of the auricle, external auditory canal and eardrum affected by fungal mycelium. In immunocompetent patients, the fungal lesion usually does not spread beyond the epidermis. Therefore, the detachment and elimination of the epidermis involved in the process together with the fungal mycelium leads to the healing of the patient. Due to the keratoplastic properties of salicylic acid, rapid and high-quality epithelization of the surface occurs. Thus, bypassing the lengthy process of diagnosis and determination of sensitivity to antifungal agents, in uncomplicated cases, a 2% alcohol solution of salicylic acid is more effective in the treatment of otomycosis compared with a betadine solution and a 1% alcohol solution of clotrimazole. Systemic antifungal drugs, as a rule, are presented in pharmacies in small quantities and besides, the price for them is quite high. Therefore, a comparative evaluation of drugs with low cost, given the high frequency of relapses in otomycosis, is very relevant.

Prospects for further research.

It is planned to further study effective methods of treatment of otomycosis.

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ПОРІВНЯЛЬНА ОЦІНКА ЕФЕКТИВНОСТІ ПАТОГЕНЕТИЧНОГО ТА ЕТІОЛОГІЧНОГО ЛІКУВАННЯ ОТОМІКОЗУ

Поладова Л. Р.

Резюме. Мета – порівняти ефективність лікування препаратом саліцилової кислоти та двох лікарських засобів з прямою протигрибковою дією. Визначити спектр найчастіших збудників отомікозу в Азербайджані та їх чутливість до найчастіше використовуваних протигрибкових препаратів.

Об'єкт і методи дослідження. Контрольоване рандомізоване дослідження, що включало пацієнтів з діагнозом зовнішній грибовий отит, розділених на три групи, що отримували різне лікування: 1) 2% спиртовий розчин саліцилової кислоти, 2) розчин бетадину, 3) 1% спиртовий розчин клотримазолу. Діагноз було встановлено на основі отоендоскопії та лабораторних даних. Критеріями включення пацієнтів у дослідження було виявлення елементів активної грибової флори при мікроскопії мазку патологічного матеріалу, взятого з хворого вуха, а також виявлення грибових культур при посіві на пластинки з декстрозним агаром Сабуро. У кожній групі було по 30 пацієнтів. Курс лікування тривав 14 днів. Критеріями ефективності лікування було зменшення та зникнення скарг у пацієнтів, покращення отоскопічної картини та відсутність елементів активної грибової флори у мазку.

Оцінку результатів лікування було проведено через 3 дні, 7 днів, 14 днів, 6 місяців. Були зареєстровані ускладнення та рецидиви. Результати порівнювалися між групами.

Результати дослідження. У дослідження було включено 90 пацієнтів, віком від 2 місяців до 86 років. З них 49 жінок та 41 чоловік. У 51,7% пацієнтів було ураження зовнішнього слухового ходу та барабанної перетинки. Ізольоване ураження барабанної перетинки (мірингіт) спостерігалось у 3,4% пацієнтів. *Aspergillus niger* було виявлено у 50,0%±5,2. *Candida albicans* у 25,5%±4,5 випадків, *Penicillium natatum* – 18,1%±4,0. *Mucorales* були виявлені у 4,3%±2,1% випадків. Найпоширенішими симптомами були біль у вусі (75,6±4,5) та кольорові виділення (63,3±5,1). Найчастішим провокуючим фактором у пацієнтів було травмування зовнішнього слухового ходу вушними паличками (57,8±5,2). Найчастіше встановлена флора була чутлива до кетоконазолу (47,9±5,2), у більшості визначено резистентність до флуконазолу (91,7±2,8). Найкращі результати показала схема лікування у першій групі. Вже на третій день лікування пацієнти відмічали значне зниження болю та свербіж. У першій та третій групах пацієнти часто скаржилися на відчуття печії при закапуванні препарату (53,3±9,1) та (40,0±8,9) відповідно. У другій групі ці скарги були поодинокими (6,7±4,6).

Висновки. Минаючи тривалий процес діагностики та визначення чутливості до протигрибкових препаратів, у неускладнених випадках 2%-й спиртовий розчин саліцилової кислоти більш ефективний при лікуванні отомікозу у порівнянні з розчином бетадину та 1%-м спиртовим розчином клотримазолу.

Ключові слова: протигрибкові препарати, отомікоз, чутливість, саліцилова кислота.

COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF PATHOGENETIC AND ETIOLOGICAL TREATMENT OF OTOMYCOSIS

Poladova L. R.

Abstract. Aim is to compare the effectiveness of treatment with salicylic acid and two drugs with direct antifungal action. To identify the spectrum of the most common pathogens of otomycosis in Azerbaijan and their sensitivity to the most used antifungal drugs.

Object and methods of research. A controlled randomized trial that included patients diagnosed with external fungal otitis, randomized into 3 treatment groups: 1) 2% alcohol solution of salicylic acid, 2) betadine solution, 3) 1% alcohol solution of clotrimazole. The diagnosis was made on the basis of otoendoscopy and laboratory data. The criterion for inclusion of patients in the study was the detection of elements of active fungal flora by microscopy of a smear of pathological material taken from a diseased ear, as well as the detection of fungal cultures when seeded on plates with dextrose Saburo agar. There were 30 people in each treatment group. The course of treatment lasted 14 days. The criteria for the effectiveness of treatment were the reduction and disappearance of complaints in patients, improvement of the otoscopic picture and the absence of elements of active fungal flora in the smear.

Evaluation of treatment results was carried out after 3 days, 7 days, 14 days, 6 months. Complications and relapses have been reported. The results were compared between the groups.

Results. The study included 90 patients aged 2 months to 86 years. Of these, 49 are women and 41 are men. In 51.7% of patients, the external auditory canal with the eardrum was affected. Isolated tympanic membrane lesion (myringitis) was observed in 3.4% of patients. *Aspergillus niger* was detected in 50.0%±5.2. *Candida albicans* in 25.5%±4.5 cases, *Penicillium natatum* – 18.1%±4.0. *Mucorales* were detected in 4.3%±2.1% of cases. The most common symptom was ear pain (75.6±4.5) and colored discharge (63.3±5.1). The most frequent predisposing factor in patients was traumatization of the external auditory canal with ear sticks (57.8±5.2). The most frequently detected flora was sensitive to ketoconazole (47.9±5.2), the majority showed resistance to fluconazole (91.7±2.8). The treatment regimen in group 1 showed the best results. Already on the 3rd day of treatment, patients noted a significant reduction in pain and itching. In groups 1 and 3, patients often complained of a burning sensation during instillation of the drug (53.3±9.1) and (40.0±8.9), respectively. In group 2, these complaints were rare (6.7±4.6).

Conclusions. Bypassing the lengthy process of diagnosis and determination of sensitivity to antifungal agents, in uncomplicated cases, a 2% alcohol solution of salicylic acid is more effective in the treatment of otomycosis compared with a povidone-iodine solution and a 1% alcohol solution of clotrimazole.

Key words: antifungal, otomycoses, susceptibility, salicylic acid.

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INFLUENCE OF VITAMIN D ON THE STATE OF CARBOHYDRATE METABOLISM IN COVID-19 RECONVALENTS WITH FIRST DIAGNOSED TYPE 2 DIABETES

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Vitamin D deficiency was detected in patients after COVID-19 with newly diagnosed type 2 diabetes mellitus (T2DM). Patients were divided into two groups. Group 1 consisted of patients receiving standard oral glucose-lowering therapy. The second group consisted of patients who, in addition to standard therapy, received a drug with a high content of vitamin D. It was found that the use of a drug with vitamin D in the treatment of these patients leads to compensation for carbohydrate metabolism disorders, improves the course of T2DM, restores the level of vitamin D, which helps to reduce the risk of cardiovascular disorders.

Key words: COVID-19, post-COVID syndrome, type 2 diabetes mellitus, vitamin D.

Connection of the publication with planned research works.

The work is a fragment of the research work "Development of differentiated personalised rehabilitation complexes for patients after coronavirus infection at the sanatorium stage", state registration number 0122U001261.

Introduction.

According to the WHO definition, the post-COVID syndrome is a post-COVID condition that occurs in people with suspected or confirmed SARS-CoV-2 infection, which usually manifests itself three months after the onset of COVID-19 with symptoms that cannot be explained by other causes and lasts at least two months [1]. Post-COVID (post-COVID syndrome) is a wide range of new, temporary or long-term health problems that can occur four or more weeks after the first infection with the covid virus [2].

NICE (the National Institute for Clinical Excellence) guidance published on 30 October 2020 defines post-COVID syndrome as a set of signs and symptoms that develop during or after a COVID-19 infection lasting more than 12 weeks and are not explained by an alternative diagnosis [3]. This definition describes post-COVID syndrome as a condition with symptoms that often overlap and can change over time and affect any system in the body [4].

Common symptoms after COVID-19 can include fatigue, shortness of breath, and decreased mental ability

such as memory or ability to concentrate (cognitive dysfunction). Symptoms may appear after an acute episode of COVID-19 or persist after the disease and may change or recur over time. The list of possible manifestations of post-COVID syndrome is not exhaustive as research is continued [5].

There are also quite serious long-term complications, especially in patients with severe COVID-19 who have been hospitalised (mostly older people with comorbidities):

- cardio-vascular (inflammation of the heart muscle);
- respiratory (lung function disorders);
- dermatological (rash);
- neurological (impaired sense of taste and smell, sleep disorders);
- psychological (depression, anxiety, mood swings) [6].

To date, it has been established that several endocrine pathologies can occur in COVID-19 convalescents. These include deterioration of control of existing diabetes, subacute thyroiditis and osteoporosis, etc., the emergence of endocrine regulation disorders along the hypothalamus-pituitary-adrenal axis, and impaired thyroid hormone secretion [7, 8].

Increased morbidity and detection of diabetes mellitus in people with COVID-19 is observed in almost all regions of our country and many countries of the world [9, 10]. The pathogenesis of the impact of SARS-CoV-2 coronavirus on the endocrine system is multifaceted [11]. It