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Evaluation of Different Methods for Management of Difficult Cases of Otomycosis

Mostafa M. El said[1], Ahmed S. Abdelgelil[1], Ibrahim H. Bayomy[2] and Mahmoud M. Abd Elkhalek[1]

[1]Department of Otorhinolaryngology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[2]Department of Medical Microbiology and Immunology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
Email: emanal95@gmail.com

Abstract: Background: Otomycosis is one of the most common conditions encountered in general ENT practices. Otomycosis is mainly used to describe external fungal infections and also known as fungal otitis externa where fungal infection occurs at the external auditory canal, auricle, eardrum, and rarely middle ear [(1)]. **Objective:** This study aims to identify the most common pathogens encountered in difficult cases of otomycosis and evaluation of the most effective protocol for management of such cases**. Subjects and methods:** This prospective study was conducted at the otolaryngology outpatient clinic of Shubra General Hospital, Ministry of Health between April 2018 and June 2019 after approval of the study protocol by local ethical committee. An informed consent was obtained from all patients enrolled in this work. This study comprised a total of 50 patients clinically diagnosed with otomycosis and were divided into: **Group 1:** (20) patients without tympanic membrane perforation and **Group 2:** (30) patients with tympanic membrane perforation. **Group 1**patients have been divided into 2 groups: Group 1a and group 1b. (Group 1a): 10 patients were treated by topical antifungal cream (Clotrimazole 1%). (Group 1b): 10 patients were treated by topical antifungal ear drops (clotrimazole 1%). **Results:** -Group 1A (received topical antifungal cream); 9 cases cured within 5 days and only one cured within 10 days. -Group 1B (received topical antifungal drops); 7 cases cured within one month and 3 within 1.5 months. -Group 2: 30 patients group with tympanic membrane perforation (treated with topical antifungal cream); 27 cases cured within 5 days, 2 cured within 10 days and only one cured within 15 days. **Conclusion:** From this prospective randomized study it can be concluded that application of local antifungal agent in the form of cream is more effective than application of the same agent as drops in treatment of otomycosis.

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Key words: Otomycosis, fungal infections, antifungal cream, antifungal drops.

1. Introduction:

Otomycosis is one of the most common conditions encountered in general ENT practices. Otomycosis is mainly used to describe external fungal infections and also known as fungal otitis externa where fungal infection occurs at the external auditory canal, auricle, eardrum, and rarely middle ear [(1)].

Various predisposing factors including a humid climate, instrumentation of the ear, increased use of topical antibiotics / steroid preparations, immunocompromised host, undergoing open cavity mastoidectomy, wearing hearing aids with occlusive ear mold, poor hygiene and lower socioeconomic status, bacterial otitis externa, swimming, dermatomycoses, and insertion of foreign objects into the ear [(2)].

Otomycosis is occasionally difficult to distinguish from other forms of otitis externa especially diffuse bacterial otitis externa. Mixed infection sometimes occurs. Swabs from infected ears should be submitted for both bacterial and fungal culture. [(3)]

Difficult cases of otomycosis as cases with chronic suppurative otitis media accompanied by perforated tympanic membrane and or immunocompromised patients (e.g. diabetes, chemotherapy, malignancy and steroid administration [(4)].

Eradication of otomycosis is more difficult in ears with perforated tympanic membrane. Direct instillation of antifungal solution with a dropper is associated with burning sensation. Dermatologic antimycotic solutions are irritant to middle ear mucosa and may be ototoxic to the cochlea. Insertion of an ear wick saturated with antifungal solution or cream may be used to increase the contact time with metal skin and limit the seepage of the irritant solution to the middle ear. [(5)]

2. Patients and Method:

This prospective study was conducted at the otolaryngology outpatient clinic of Shubra General Hospital, Ministry of Health between April 2018 and June 2019 after approval of the study protocol by ethical committee.

An informed consent was obtained from all patients enrolled in this work.

This study comprised a total of 50 patients clinically diagnosed with otomycosis**.**

Inclusion criteria:

Difficult cases of otomycosis include:

1-Patients clinically diagnosed with otomycosis with chronic otitis media with perforated tympanic membrane.

2-Immunocompromised patients as those with malignancy, receiving chemotherapy or corticosteroids and diabetic patients with or without tympanic membrane perforation.

The exclusion criteria:

1-Tympanic membrane perforation caused by trauma.

2-Active middle ear infection.

3-Recent history of treatment with antifungal topical medication.

All patients were subjected to a complete history taking, clinical examination and laboratory investigation.

1-History taking including age, sex, occupation, diabetic status, trauma, history of ear surgery or any fungal infection in other parts of the body and laterality of symptoms. History of habits like use of oils /ear drops, wooden sticks or metal wax picks for removal of wax were also recorded.

2-Otological examination: Using otoscope for assessment of external auditory canal and tympanic membrane for presence of fungal mass.

Specimen preparation & processing:

After the clinical diagnosis was established, two Sterile cotton swabs were used for collecting debris, fungal elements from the external ear canal of patients showing symptoms of otomycosis. All samples were transported to the laboratory of Shubra General Hospital within half an hour. A portion of the collected material was suspended in 1-2 drops of 10% potassium hydroxide with methylene blue (2:1) on a clean slide and a cover glass was placed over it avoiding air bubbles. It was examined under microscope for the presence of fungal hyphae or yeast cells. Another portion of the collected material was used for Gram staining, and examined for presence of inflammatory cells, bacteria, yeast cells or other fungal elements (***Fischer et al., 1998).***

The second swab was inoculated on two Sabouraud's dextrose agar (SDA) plates with chloramphenicol. One plate was incubated at (22^{o} C) and another at (37^{o} C) for 1 -2 weeks. Both plates were observed for fungal growth daily. Fungal growth was identified by standard procedures at The Regional Center for Mycology and Biotechnology, Al-Azhar University.

The second swab was inoculated on blood agar and MacConkey's agar plates, incubated at (37^{o}C) for 24 – 48 hours and examined for bacterial growth. Identification of bacterial isolate was done by standard procedures at The medical microbiology and immunology department research lab, faculty of medicine, Al-Azhar University.

Management:

Treatment with aural toileting (suction aspiration and dry mopping) of the debris in the EAC and the patients were put on topical antifungal regimens as the following:

*Group 1:*20 Patients without tympanic membrane perforation have been divided into 2 groups: Group 1a and group 1b.

(Group 1a): 10 patients were treated by topical antifungal cream (Clotrimazole 1%).

(Group 1b): 10 patients were treated by topical antifungal ear drops (clotrimazole 1%).

Group 2: The other 30 patients with tympanic membrane perforation were treated by topical antifungal cream installed into the external auditory canal by using ear suction tips *(Figure 17)* and syringe containing about 2 ml of pure antifungal cream (clotrimazol).

Follow up of management:

a. Follow up of management:

1-For patients whose culture revealed mixed (fungal and bacterial) infection, medication was changed to mixed (antifungal and antibacterial) agents.

2-Then all patients were followed every 5 days by clinical examination for presence of fungal infection till complete recovery "approved by –ve culture".

-With any follow up setting with negative clinical examination for fungal infection, a swab was obtained for culture to make certain of complete care of fungal infection.

-Patients with sustained fungal infection (either: positive clinical examination or positive swab) have a repeated courses of the same treatment.

b. Follow up for recurrence:

10 cases were examined again after 1 and 2 months from the beginning of management with topical antifungal cream to assess the rate of recurrence.

Statistical analysis:

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, analysis of variance (ANOVA) test and chi-square test, linear correlation coefficient by SPSS V.25. P-value <0.005 was considered significant.

3. Results:

Our study included 50 patients of age group ranging from (25-68) years (*Table 1*). Maximum number of cases were between 41 – 50 years of age (38%).

Our study showed increased incidence of otomycosis among females (62%) more than males (38%). (Table 2)

In our study, the incidence of otomycosis was 60% bilateral and 40% unilateral (*Table 3*). Among the unilateral cases, {the right side (22%) showed predominance over the left side (18%)}.

Table 1): Age group (Total cases).

Age group	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
20:30 Years	4	40.00	0	0.00	6	20.00	10	20.00	14.614	0.067
31:40 Years	1	10.00	0	0.00	5	16.67	6	12.00		
41:50 Years	2	20.00	3	30.00	14	46.67	19	38.00		
51:60 Years	2	20.00	4	40.00	3	10.00	9	18.00		
61:70 Years	1	10.00	3	30.00	2	6.67	6	12.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

Table (2): Sex distribution

Sex	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Male	4	40.00	4	40.00	11	36.67	19	38.00	0.057	0.972
Female	6	60.00	6	60.00	19	63.33	31	62.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

Table (3): Laterality

Bilatera	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Bilateral	7	70.00	4	4000	19	63.33	30	60.00	4.525	0.340
Right ear	3	30.00	3	30.00	5	16.67	11	22.00		
Left ear	0	0.00	3	30.00	6	20.00	9	18.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

In our study (*Table 4*) the predominant complaints were pain, itching, block sensation and ear discharge. 18 % of patients had itching, 14 % of patients had pain and itching, 16 % of patients had pain and block sensation and 24 % of patients had pain and hearing loss. Clinical examination revealed canal skin erythema and fungus debris in all cases.

Table (4): Symptoms

Symptoms	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Pain	2	20.00	1	10.00	2	6.67	5	10.00	8.622	0.568
Itching	0	0.00	0	0.00	9	30.00	9	18.00		
Pain + Itching	1	10.00	2	20.00	4	13.33	7	14.00		
Pain + Discharge	2	20.00	2	20.00	5	16.67	9	18.00		
Pain + Block sensation	2	20.00	2	20.00	4	13.33	8	16.00		
Pain+ Hearing loss	3	30.00	3	30.00	6	20.00	12	24.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

In our study 68% of the patients gave history of manipulation / trauma to the EAC with either stick *(Table 5)* feather, metal picker, pin etc, 24% of patients gave history of using either antibiotic ear drops, antibiotic -steroid ear drops, or use of nonsterile oil into ear. Also, 12% of our patients gave history of previous swimming in water pool or introduction of water into the external auditory canal.

Table (5): Predisposing factors

Predisposing factors	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Antibiotic ear drops	2	20.00	3	30.00	1	3.33	6	12.00	10.033	0.123
Steroid drops	1	10.00	2	20.00	3	10.00	6	12.00		
Truama	5	50.00	5	50.00	24	80.00	34	68.00		
Swimming	2	20.00	0	0.00	2	6.67	4	8.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

The associated medical conditions in our study *(Table 6)* of the patients were as the following: 7 patients had diabetes (14%), 5 patients (10 %) had cancer (3 had lung cancer and 2 had prostatic cancer and were on radiotherapy), three patients (6%) were on systemic corticosteroids as they had multiple sclerosis, 9 (18 %) patients had history of chronic otitis media with tympanic membrane perforation, and 26 patients (52 %) had history of diabetes associated with tympanic membrane perforation.

Table (6): Associated medical conditions.

Associated medical condition	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
DM	8	80.00	6	60.00	4	13.33	18	36.00	4.313	0.828
Cancer	2	20.00	3	30.00	2	4.67	7	14.00		
Systemic Steroids	0	0.00	1	10.00	3	10.00	4	8.00		
Chronic otitis media with tympanic membrane perforation	0	00.00	0	00.00	9	30.00	9	18.00		
DM + chronic otitis media with tympanic member perforation	0	00.00	0	00.00	12	40.00	12	24.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

In our study *(Table 7)* the swab cultures showed that 42 patients (84 %) had pure fungal infection and 8 patients (16 %) had mixed fungal and bacterial infection. Patients who had mixed fungal and bacterial infection (3 had uncontrolled diabetes and 5 had tympanic membrane perforation). Cultures that showed bacterial infection (5 were klebsiella and 3 were staphylococcus aureus).

Table (7): Type of infection

Infection	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Pure fungal	8	80.00	9	90.00	25	83.33	42	84.00	0.397	0.820
Mixed fungal bacterial	2	20.00	1	10.00	5	16.67	8	16.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

In our study *(Table 8)* infection with candida albicans was found in 28 (56%) of cases, infection with aspergillusniger was found in 14 (28%) of cases, aspergillusflavus was found in 3 (6%) cases and aspergillus fumigatus was found in 5 (10%) of cases.

Table (8): Pathogens

Pathogens	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Candida	5	50.00	4	40.00	19	63.33	28	56.00	12.079	0.060
Aspergillusniger	4	40.00	1	10.00	9	30.00	14	28.00		
Aspergillusflavus	0	0.00	2	20.00	1	3.33	3	6.00		
Aspergillus fumigatus	1	10.00	3	30.00	1	3.33	5	10.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

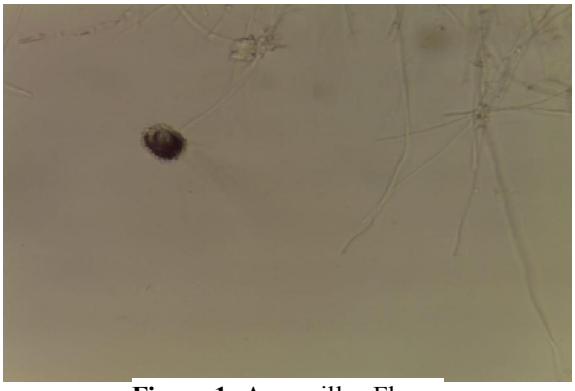

Figure 1: Aspergillus Flavus

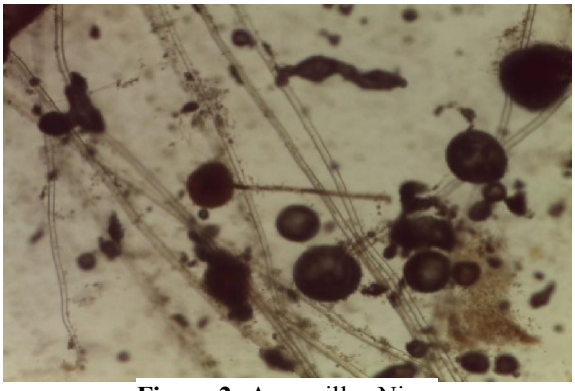

Figure 2: Aspergillus Niger

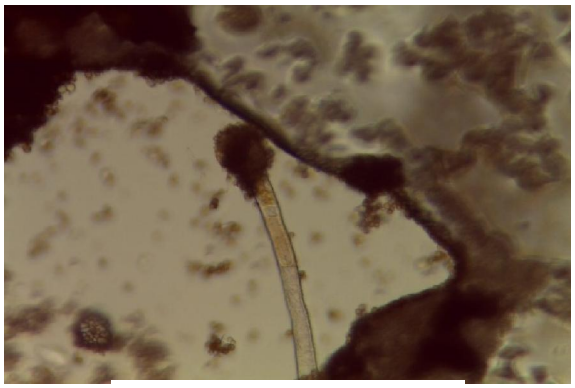

Figure 3: Aspergillus Fumigatus

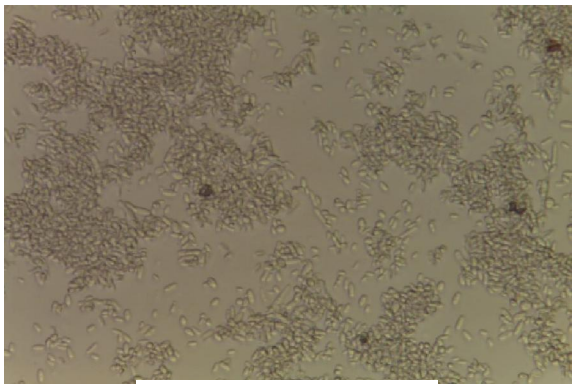

Figure 4: Candida Albicans

In our study *(Table 9)* 40 patients (80%) had the symptoms of otomycosis for the third time, 9 patients (18%) had the symptoms for the second time and only one patient for first time.

Table (9): Past recurrence rate.

Past recurrence rate	Groups								Chi-Square	
	Group IA		Group IB		Group II		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
3rd time	0	0.00	10	100.00	30	100.00	40	80.00	50.000	<0.001*
2nd time	9	90.00	0	0.00	0	0.00	9	18.00		
1st time	1	10.00	0	0.00	0	0.00	1	2.00		
Total	10	100.00	10	100.00	30	100.00	50	100.00		

In our study:

-Group 1A (received topical antifungal cream); 9 cases cured within 5 days and only one cured within 10 days.

-Group 1B (received topical antifungal drops); 7 cases cured within one month and 3 within 1.5 months.

-Group 2: 30 patients group with tympanic membrane perforation (treated with topical antifungal cream); 27 cases cured within 5 days, 2 cured within 10 days and only one cured within 15 days.

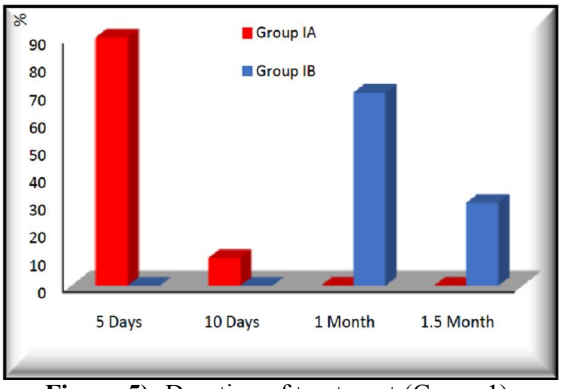

Figure 5): Duration of treatment (Group 1).

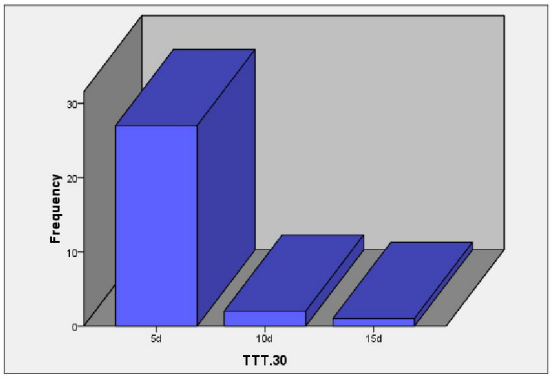

Figure (6): Duration of treatment (Group 2)

Table (10): Duration of treatment (Group 1)

Recovery	Groups				P-value
	Group IA		Group IB		
	N	%	N	%	
5 Days	9	90.00	0	0.00	0.028
10 Days	1	10.00	0	0.00	
1 Month	0	0.00	7	70.00	
1.5 Month	0	0.00	3	30.00	
Total	10	100.00	10	100.00	

Table (11): Duration of treatment (Group 2)

Recovery	Number of patients	Percent
5days	27	90%
10days	2	6.6%
15days	1	3.3%
Total	30	100%

4. Discussion:

Otomycosis is a common condition encountered in ENT Outpatient department which consists of fungal infection of the external auditory canal wall. [6]

The patient mainly presents with otalgia, pruritis, block sensation, and otoscopy finding shows presence of matted hyphae, spores, or curdy precipitate in the external auditory canal. [6]

In our study, pain in the form of otalgia was the main complaint of patients with otomycosis either alone or associated with others representing symptoms. 82% of cases which is in accordance with findings of other studies. Accordingly, absence of pruritis does not exclude the possibility of otomycosis.

Study by Pradhan et al., suggested pruritis as the main symptom of otomycosis whereas study by Ho Tang et al reported it to be 23%. [7]

In the study by Ali et al, the most common symptoms of otomycosis were pruritis (92.16%) and otalgia (50.98%). [8]

Regarding the most common organisms causing otomycosis, the predominant fungal pathogens in otomycosis were different in various literature reports, including: A. flavus, Aspergillus fumigates and Candida. [9]

In our study, 28 patients (56 %) of cases were caused by Candida albicans, 14 patients (28%) by Aspergillusniger, 3 patients (6%) by Aspergillusflavus and 5 patients (10%) by Aspergillus fumigatus. This is in accordance with other studies. [10]

In the study by Ali et al, A. niger (50.98%) was the most common isolated organism, followed by Aspergillusflavus (33.33%), and then by Candida species (14.7%). [8]

We refer this difference to the variability in geographic distribution and environmental factors.

There is no proper agreement regarding the effect of various antifungal agents used for otomycosis and various agents have been used for the same. Though, use of appropriate antifungal agent along with mechanical debridement remains the mainstay of treatment. Amongst antifungals topical clotrimazole remains widely used agent. 1% Clotrimazole cream has been used for treatment of this condition with good efficacy. [(11)]

Ali et al said that "voriconazole and nystatin should have the upper hand in treatment of otomycosis. Moreover, it was informative enough to explain one of the main reasons for lack of response to commonly prescribed antifungals and high recurrence rate, which was recently observed in our practice with prescription of fluconazole as a first-line treatment for our cases". [(8)]

Regarding this we used Clotrimazole cream and drops 1%**.**

We aimed in this study to assess best way for application of local antifungal agents in treatment of otomycosis 'drops or cream'.

Patients using drops have to instill drops in affected ear three to four times a day. This can become very cumbersome for office going person. Besides, direct instillation of antifungal solution is also associated with burning sensation especially in cases of perforated drum. [(12)]

By using cream, we increased the contact time of the agent with the meatal skin so increasing effect of used antifungal agent with expecting better effect which was obvious in our study as follow:

-Group 1A (received topical antifungal cream); 9 cases cured within 5 days and only one cured within 10 days.

-Group 1B (received topical antifungal drops); 7 cases cured within one month and 3 within 1.5 months.

-Group 2: 30 patients group with tympanic membrane perforation (treated with topical antifungal cream); 27 cases cured within 5 days, 2 cured within 10 days and only one cured within 15 days.

Mishra et al., said that "From this prospective randomized study it can be concluded that use of 1% topical clotrimazole drops and 1% clotrimazole cream are equally effective in management of otomycosis. However when given a choice considering the fact of only single time application, patients prefer use of topical cream over drops for treatment of otomycosis [(7)]

The main drawback of topical cream was blocked sensation which was more in patients in whom topical cream was used which is a known fact as reported by Hurst et al. but this is less evident with application of cream by wick as reported by Abou Halawa et al. [(7)]

Also study by Abou Halawa et al used clotrimazole ointment for otomycosis and compared use of wick with regular application and found that self-application and wick application both have same efficacy for relief from otomycosis. [(7)]

The recurrence rate in our study was 2 % only.

Studies have reported that otomycosis recur in almost 8.89% of treated subjects. It takes around 2-3 weeks of to achieve cure from disease. Thus to reduce chance of recurrence and to improve patient wellbeing as well as considering the ease of installation study compared cream versus drops. [(13)]

The question asked to all patients at the end of treatment as to their preference of treatment modality went in favor of 1% clotrimazole cream. This may be due to the fact that patients prefers one time instilling of cream instead of self-medication of putting drops 3-4 times a day.

Limitation:

Unfortunately, our study had some limitations. The major limitations were being a single-centre study and the relatively small study population. So for further studies regarding this issue, we recommend a multicenter study with a large number of population followed through the study.

Conclusion:

From this prospective randomized study it can be concluded that application of local antifungal agent in the form of cream is more effective than application of the same agent as drops in treatment of otomycosis.

Cream leads to more block sensation during the first day when compared to drops. However when given a choice considering the fact of only single time application, patients prefer use of topical cream over drops for treatment of otomycosis.

The available number of cases in our study was small. So further prospective multicenter studies with large number of patients are needed to confirm the results of this study.

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