

## A COMPARATIVE STUDY OF EFFICACY OF CLOTRIMAZOLE AND FLUCONAZOLE EAR DROPS IN OTOMYCOSIS

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### ABSTRACT

#### BACKGROUND

Otomycosis is a clinical term to describe fungal infection of the external auditory canal. Most common fungi implicated in this infection are Aspergillus and Candida. Treatment of choice for fungal otitis externa includes thorough debridement followed by topical application of antifungal agents.

#### MATERIALS AND METHODS

120 patients with otomycosis were selected and divided into two cohorts. Patients in Group A were put on 1% Clotrimazole ear drops and those in Group B were put on 0.3% Fluconazole ear drops. All patients were reviewed weekly for 4 weeks for reduction in symptoms and signs.

#### RESULTS

Baseline characteristics of the study participants are comparable and there was no significant difference between the groups. Pain was the main presenting feature in both the groups followed by itching and ear block. Symptoms lasted for 1- 10 days. Aspergillus Niger was most common fungus isolated, followed by Aspergillus flavus, Aspergillus fumigatus and Candida. Comparing the two groups, the effectiveness of fluconazole was found to be better than clotrimazole at the end of 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week.

#### CONCLUSION

In our study, we have observed that topical Fluconazole is more effective than Clotrimazole to treat otomycosis.

#### KEYWORDS

Otomycosis, Fluconazole, Clotrimazole.

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#### BACKGROUND

Otomycosis is a clinical term to describe fungal infection of the external auditory canal. It is a common condition faced by an ENT practitioner and accounts for nearly 10% of ENT outpatient cases<sup>1</sup>. It is particularly common in hot, humid climates (Tropical and subtropical areas). Abuse of topical antibiotics in the ear is often a precipitating factor. Immunocompromised states predispose to the condition. Common clinical finding is a black, grey, green or white discharge with debris that is often said to resemble a wet newspaper. Sometimes fungal hyphae with spores can also be appreciated clinically.

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Aspergillus accounts for 80-90% of cases and Candida being responsible for the remaining 10-20%.<sup>1,2</sup> Treatment of choice for fungal otitis externa includes thorough debridement followed by topical application of antifungal agents. Acidifying agents, topical antifungals and antiseptics have been used for otomycosis with variable degree of cure rates.

#### MATERIALS AND METHODS

We conducted a Randomised Prospective Comparative clinical study for a period of 1 year in the ENT Department in association with the Microbiology Laboratory, Chettinad Health centre and Research Institute, Kelambakkam.

120 patients with otomycosis were included in the study based on the following criteria.

#### Sample Size Determination

- Sample size calculation was done on the basis of efficacy of two drugs in treating otomycosis. With the help of previous literature findings, anticipated incidence of both the drugs was calculated.
- Anticipated incidence (Persistence of infection) at the end of 4 weeks treatment with clotrimazole =20%

- Anticipated incidence (Persistence of infection) at the end of 4 weeks treatment with fluconazole = 4%
- Keeping 95% Confidence interval (5% alpha error) and 80% power of the study,
- Sample size for two independent group and categorical outcome was calculated with software clinicalc,
- Sample size arrived was 64 per group.

**In our Study, Sample Size of 60 were Recruited in each Group-**

**Study Participants Allocation**

Study participants who fulfilled inclusion criteria were randomly allocated in to two groups with the help of random table numbers. The ratio of allocation was 1:1. Odd number lot were allocated to group A to receive 1% Clotrimazole ear drops and even number lot were allocated to Group B to receive 0.3% Fluconazole ear drops.

**Statistical Analysis**

Data was analysed with Statistical Package for Social Sciences (SPSS IBM) version 21.0. The qualitative variables are described in the form of proportions and quantitative variables are described in the terms of mean and standard deviation. Baseline characteristics of the two group was checked for homogeneity. Data was checked for normality before applying appropriate tests of significance. Significance of difference in proportions (Qualitative variables) was calculated using chi square test. Significance of p value was taken as p<0.05

**Inclusion Criteria**

1. Age > 12 years.
2. Patients of either sex.
3. Culture positive fungal otitis externa.
4. Both immunocompetent and immunocompromised patients.

**Exclusion Criteria**

1. Culture negative cases.
2. Ootomycosis associated with otitis media.
3. Prior usage of topical antifungals.
4. Patients not consenting for participation.
5. Noncompliance with medication/follow-up.

This study was conducted after the approval of the institutional ethical committee and obtaining an informed consent from each patient. 120 patients with otomycosis were selected based on the criteria mentioned above. They were equally divided into two cohorts- A and B. All the patients underwent a microscopic suction clearance and the material forwarded for fungal smear and culture. Patients in Group A were put on 1% Clotrimazole ear drops and those in Group B were put on 0.3% Fluconazole ear drops in the dosage of 3 drops thrice daily. Patients in both the groups used the ear drops for a period of 3 weeks. All the patients were educated on the importance of re-establishing a dry ear and about water precautions. All patients were reviewed weekly for 4 weeks for reduction in symptoms and signs.

**RESULTS**

A total of 120 study participants were recruited of which group 1 constituted 60 participants and group 2 constituted 60 study participants. Group 1 were given clotrimazole and group 2 were prescribed fluconazole. 47% and 45% were males in group 1 and group 2 respectively. Baseline characteristics of the study participants are comparable and there was no significant difference between the groups. (Table 1)

Sl. No.	Baseline Characteristics of Study Participants	Group 1 N=60 N (%)	Group 2 N=60 N (%)	P value
1.	<b>Sex</b> Male Female	28 (46.7) 32 (53.3)	27 (45) 33 (55)	0.855
2.	<b>Age group</b> 0-18 years 19-60 years >60 years	10 (16.7) 49 (81.7) 1 (1.7)	10 (16.7) 47 (78.3) 3 (5)	0.594
3.	<b>Side of the ear affected</b> Both Right Left	10 (16.7) 21 (35) 29 (48.3)	5 (8.3) 29 (48.3) 26 (43.3)	0.211
4.	<b>Pain</b> Present Absent	49 (81.7) 11 (18.3)	51 (85) 9 (15)	0.624
5.	<b>Itching</b> Present Absent	16 (26.7) 44 (73.3)	19 (31.7) 41 (68.3)	0.547
6.	<b>Ear block</b> Yes No	18 (30) 42 (70)	13 (21.7) 47 (78.3)	0.202
<b>Table 1. Baseline characteristics of study participants. (N=120)</b>				

Among the study participants, pain was a presenting feature in 81.7% of group 1 and 85% of group 2. Itching of ear was seen in 26.7% and 31.7% of group 1 and group 2 respectively. Ear block was observed in 30% and 21.7% of group 1 and group 2 respectively. Ear discharge was seen in 11(18.3%) of group 1 and 7 (11.7%) of group 2 participants. Duration of the symptoms were ranging from 1- 10 days in group 1 and 1-7 days in group 2. Predisposing factors were - history of use of ear buds for cleaning (72% and 68%), history of water entry into ear canal (18% and 14%), Diabetes mellitus (6% and 14%). Other factors were oil instillation (2% and 4%), syringing into ear canal (2% and 0%).

Sl. No.	Otomycosis Features	Group 1 N=60 N (%)	Group 2 N=60 N (%)
1.	<b>Spores</b> Present Absent	19 (31.7) 41(68.3)	24 (40) 36 (60)
2.	<b>Granulations</b> Present Absent	6 (10) 54 (90)	4 (6.7) 56 (93.3)

3.	<b>Otitis externa features</b>		
	Present	19 (31.7)	17 (28.3)
	Absent	41 (68.3)	43 (71.7)
4.	<b>Fungal organism</b>		
	Asp. niger	22 (36.7)	38 (63.3)
	Asp. flavus	18 (30)	9 (15)
	Asp. fumigatus	7 (11.7)	2 (3.3)
	Candida albicans	4 (6.7)	1 (1.7)
	Non albicans candida	3 (5)	3 (5)
	No growth	6 (10)	6 (10)
<b>Table 2. Presenting features and organisms in otomycosis. (N=120)</b>			

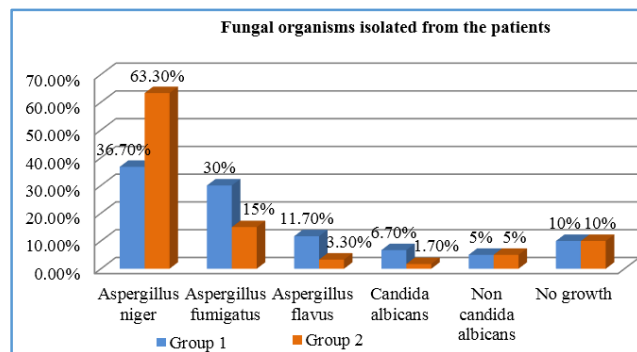


Figure 1. Bar diagram showing distribution of study participants according to fungal organism

The species of fungal infection among the study participants are varied. Out of 120 patients, Aspergillus Niger was most common (36.7% and 63.3%), followed by aspergillus flavus (30% and 15%), aspergillus fumigatus (11.7% and 3.3%) and other organisms. (Figure 1) Fungal spores were found in 31.7% of group 1 and 40% of group 2 patients. (Table 2)

At the end of four weeks of treatment, debris was observed in 13(21.7%) of clotrimazole treated group and in 12(20%) of fluconazole treated group. Comparing the two groups, it was observed that the effectiveness of the drug in terms of fungal colonization, fluconazole was found to be better than clotrimazole at the end of 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week. (p value = 0.000, 0.000, 0.000)

Sl. No.	Disease course	Week 1 N (%)	P value	Week 2 N (%)	P value	Week 3 N (%)	P value	Week 4 N (%)	P value				
1.	<b>Clotrimazole (N=60)</b>		0.175		0.00		0.00		0.00				
	NAD	0		1 (1.7)		6 (10)		23 (38.3)					
	Minimal	1 (1.7)		4 (6.7)		14 (23.3)		24 (40)					
Debris	59 (98.3)	55 (91.7)		40 (66.7)		13 (21.7)							
2.	<b>Fluconazole (N=60)</b>												
	NAD	0		5 (8.3)		27 (45)		46 (76.7)					
	Minimal	6 (10)		23 (38.3)		22 (36.7)		12 (20)					
Debris	54 (90)	32 (53.3)		11 (18.3)		2 (3.3)							
<b>Table 3. Comparison of study participants of two groups according to course of disease. (N=120)</b>													

NAD- No abnormality detected, Chi square test applied p value <0.05 is significant.

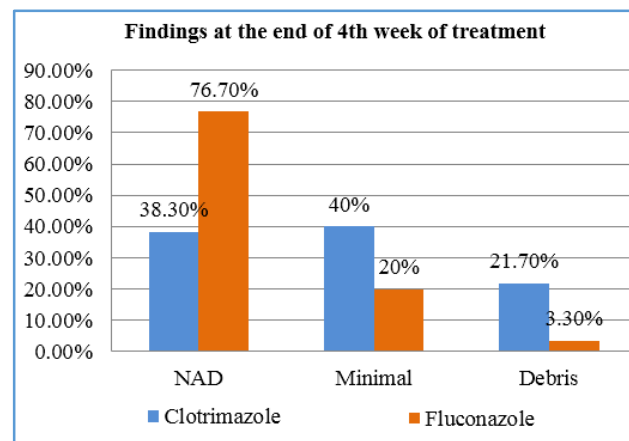
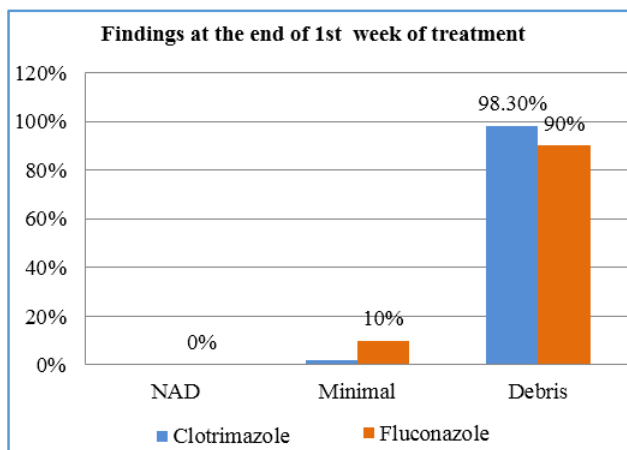


Figure 2. Bar diagram showing distribution of study participants according to findings of disease at the end of 1<sup>st</sup> and 4<sup>th</sup> week. (N=120)

**DISCUSSION**

Otomycosis is fungal infection of the external auditory canal and its associated complications sometimes involving the middle ear.<sup>2</sup> It occurs because the protective lipid/acid balance of the ear is lost.<sup>3</sup> Most common fungi implicated in this infection are *Aspergillus* and *Candida*. In the studies conducted by Chander et al, Paulóse et al, Mohanty et al, and Yassin et al, *Aspergillus* spp were the most common fungi isolated, and *C albicans* was the next most common.<sup>4-7</sup> Similarly in our study, *Aspergillus Niger* was most common, followed by *aspergillus flavus*, *aspergillus fumigatus* and *C albicans* and Non-*Candida albicans*.

Treatment of Otomycosis consists of debridement along with topical agents- acidifying agents, antifungal drugs and antiseptics. Topical preparations of Azole group of antifungals are widely used, the most common being 1% Clotrimazole ear drops. Bassiouny et al studied the effects of anti-fungal agents and found that clotrimazole and econazole were effective antifungal agents in the treatment of otomycosis<sup>8</sup>. According to Stern et al and Jackman et al, clotrimazole is an effective antifungal agent against most yeasts and fungi, and nystatin has the widest spectrum of activity among the antifungals<sup>9, 10</sup>. In a study by Yadav et al, fluconazole was found to be an effective antifungal agent in the treatment of otomycosis<sup>11</sup>. In a study conducted by Nagendran et al, in the first week, clotrimazole had a good response than miconazole and fluconazole and in the second week, there was a drastic response in patients instilling fluconazole ear drops compared to those using miconazole and clotrimazole. This better outcome did not show a statistical significance<sup>12</sup> since p value was 0.882.

In our study, it was observed that the clinical effectiveness of fluconazole was found to be better than clotrimazole at the end of 2<sup>nd</sup> week, 3<sup>rd</sup> week and 4<sup>th</sup> week, which was statistically significant.

**CONCLUSION**

Otomycosis is relatively a common clinical disorder in tropical climatic condition like ours. It usually affects one ear and bilateral involvement is more common in immunocompromised individuals. Use of ear buds, topical antibiotic drops and ear probing predispose to this infection. Most common pathogen involved is *Aspergillus*, followed by *Candida* sp. In a few immunocompromised patients, we have

observed tympanic membrane perforations. In our study, we have observed that topical Fluconazole is more effective than Clotrimazole to treat otomycosis.

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