

Clotrimazole Cream versus Ear Drops for Otomycosis: A Randomized Trial

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Rijul Sharma,¹ Syed Mohd Ahmad,¹ Singh Nitya,¹ Nehad Dahiya¹

ABSTRACT

Introduction

Otomycosis is a superficial fungal infection of the external auditory canal with a global prevalence ranging from 9% to 30%. The increased use of antibiotic ear drops has contributed to its rising incidence. This study aimed to compare the effectiveness of clotrimazole cream and clotrimazole ear drops in managing otomycosis.

Materials and Methods

A prospective, randomized controlled trial was conducted on 300 patients diagnosed with otomycosis. Patients were divided into two groups: Group A received clotrimazole cream administered by ENT specialists, and Group B used clotrimazole ear drops as self-medication. All participants were followed for four weeks, with clinical evaluations performed weekly.

Results

After one week, Group A (clotrimazole cream) achieved a 98% resolution rate, while Group B (clotrimazole drops) achieved an 86% resolution rate. The cream group showed fewer treatment failures and recurrences compared to the drop group ($p < 0.001$).

Conclusion

Clotrimazole cream is more effective than ear drops in treating uncomplicated otomycosis. Its occlusive application and higher compliance may contribute to superior clinical outcomes.

Keywords

Otomycosis; Clotrimazole; Topical Anti-Fungals; Cream versus Ear Drops

Otomycosis is a common superficial fungal disease that affects the External Auditory Canal (EAC).¹ The disease may show as acute, sub acute, or chronic, and is regularly one-sided, with the respective frame being more common in immunocompromised patients.² The disease is shown all-inclusive, with predominance extending from 9% to 30% in patients with the signs and indications of EAC disease.³

Otomycosis is ordinarily caused by inclining components, such as the passage of foreign bodies into the ear canal, traumatic insemination of wood particles, plant materials and soil into the ear canal, scratching and control of the ear canal with non-sterile hardware, living in dusty zones or damp climate, stickiness of the ear canal after swimming and showering, and fungal nail contamination and dermatophytic injuries around the ear.^{4,5} It is a global disease but is more common in adults than in kids and females than in males.⁶ Fungi are ordinarily found within the external ear as colonizers since

this surface contains the vital necessities for their development: proteins, carbohydrates, humidity, temperature and adequate Ph.⁷

Otomycosis is related to numerous complications including inclusion of the internal ear with mortality in uncommon cases. Formation of a fungus ball or fungal mass of mycelia, epithelial cells, and wax within the ear canal: exposure of this mass to the tympanic membrane are cause of hearing loss and sometimes perforation.⁸ The mycosis can have a destitute prognosis in immunocompromised people, particularly in cases of cellular immunodeficiency and neutropenia.⁹ The infection presents numerous challenges, both for patients and for

1 - Department of ENT, Hind Institute of Medical Sciences, Mau, Ataria, Sitapur

Corresponding author:

Dr. Rijul Sharma

email: dr.rijul05@gmail.com

ENT specialists, and may recur despite long-term treatment and follow-up.¹⁰ *Aspergillus* and *Candida* genera are the major etiologic agent for otomycosis. Beside this, third group which caused otomycosis included *Dermatophytes* (*Trichophyton mentagrophytes*). In rare cases, other saprophytic fungi have been isolated from otitis discharge including *Fusarium* spp., *Penicillium* spp. *Mucor* spp. and *Geotrichum* spp.^{11,12}

These days otomycosis treatment has made challenges both for patients and specialists in show disdain toward of the need for the long process of treatment and the credibility of relapse. Treatment recommendations incorporate reliable debridement of fungal agents from the ear canal, combined with the application of local and systemic anti-fungal.^{13,14} The primary line of treatment depends on the type of fungus isolated and incorporates commonly used, anti-fungal agents. More recently, azoles in the form of topical ketoconazole, miconazole and clotrimazole have become the pillar of treatment choices for otomycosis. Topical clotrimazole cream has been to a great extent utilized to treat otomycosis with variable success rates. Among topical anti fungals, topical clotrimazole cream and clotrimazole ear drops show up to be a great treatment option.^{15,16}

Accordingly, this research was done to compare improvement rate of otomycosis treated with topical medications; clotrimazole cream and clotrimazole ear drops. Relative frequency of response to treatment in both groups was assessed amid three periods. Finally, it was tested whether relative recurrence contains a noteworthy difference regarding reaction to treatment when comparing clotrimazole cream with clotrimazole ear drops based on clinical perceptions regarding the adequacy of each agent. The objective of this study was to compare the effectiveness of clotrimazole cream and clotrimazole ear drops in managing otomycosis.

Materials and Methods

This research is a clinical trial conducted on 300 patients who were diagnosed with otomycosis.

A controlled, randomized, open clinical trial was conducted within the otorhinolaryngology and head and

neck surgery department of Hind Institute of Medical Sciences, Sitapur, in western UP from September 2024 to February 2025. Patients diagnosed with clinical otomycosis (visualization consistent with fungal debris was done through microscopic examination) were allocated to one of two treatment groups according to a computer-generated randomization table. Statistic and clinical data were collected, and two samples of affected EAC were taken from each patient with the help of an ear pick and/or suction cleaner and then placed in a sterile transport medium for direct microscopic examination and culturing to distinguish the pathogenic organisms involved. For the direct examination, the material was mixed with saline solution on a slide, secured with a cover slip and visualized beneath the optical microscope at 10X and 40X magnifications. For the culture, the sample was embedded in a Saboraud dextrose agar medium incubated at 27-30! for a least 7 days. All patients underwent EAC cleaning and debridement. Clotrimazole cream was applied to the patients in Group A with a sterile, fresh 5 ml syringe and was left for 7 days; after that time, the cream residue was removed from the EAC, and the otic conditions were re-evaluated. Patients in Group B were instructed to apply Clotrimazole solution, 4 drops every 6 h for 7 days, after which time the otic conditions were re-evaluated.

The ideal clinical result comprised of an asymptomatic patient with a clean and dry EAC affirmed through microscopic examination. In both groups, in case the infection proceeded, the EAC was cleaned once more and a second treatment with the same drug was done. Dry ear care and avoidance of identified predisposing factors were advised.

The degree of improvement was assessed by comparing the symptoms and findings within the physical examination each week as well as one week after the resolution of the infectious disease to assess resolution or relapse.

The data collected were entered into an SPSS database, demographic variables and baseline characteristics were analyzed, including measures of central tendency and data dispersion, analysis of categorical variables using Chi square and comparison of continuous variables with

Student's t-test. A $p < 0.05$ was considered significant. An intention-to-treat analysis was conducted. Cases lost

to follow-up were considered as failures as long as follow-up visits were performed.

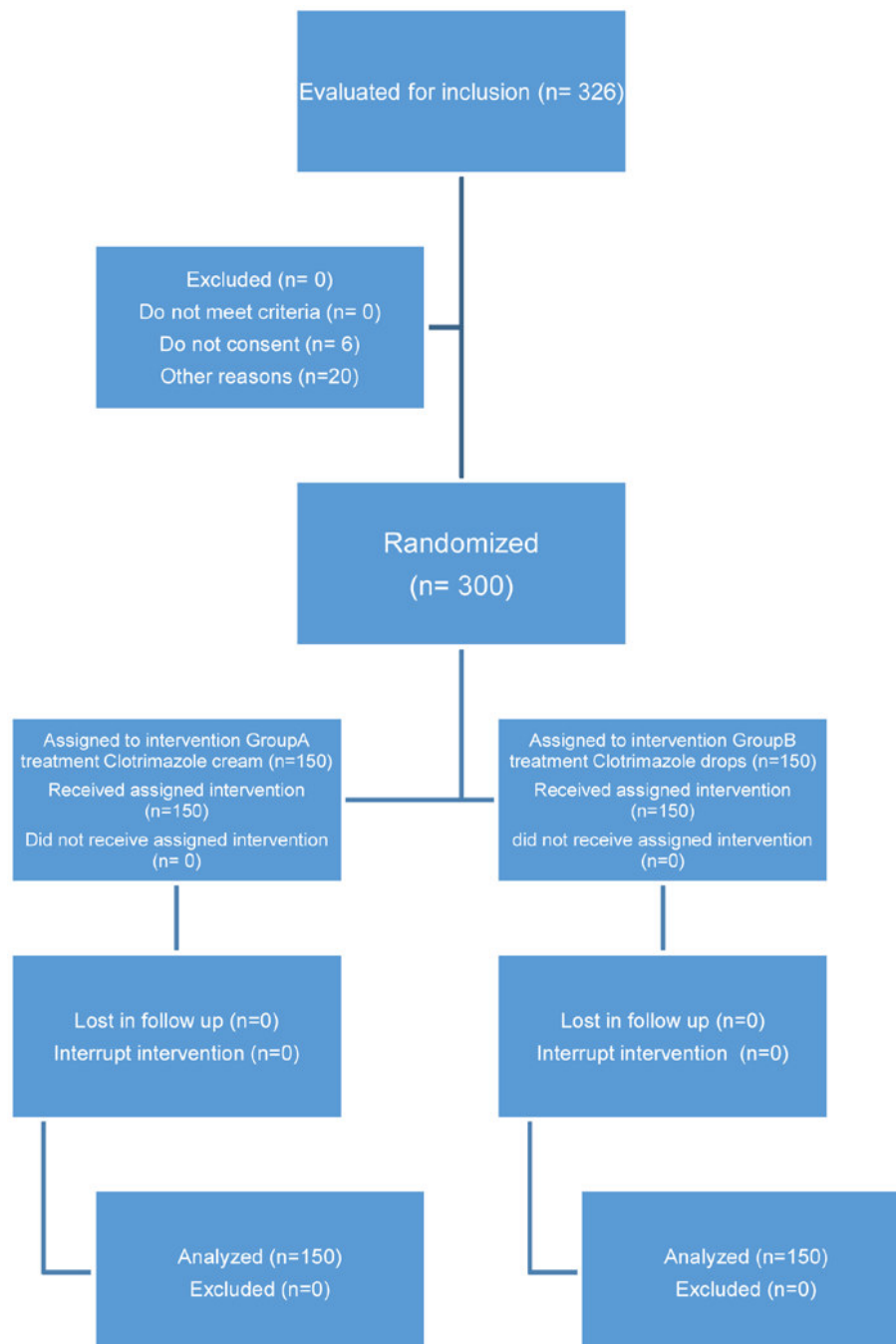


Fig.1. Flow Chart of Method

Results

There were 300 otomycosis patients in the current research.

Age : In the current study, 176 patients (58.66%) were

under 50 years old, 60 cases (20%) were between the ages of 31 and 40, 36 cases (12%) were between the ages of 21 and 30, and 28 cases (9.33%) were between the ages of <20. The research participants' average age was 36.4 years.

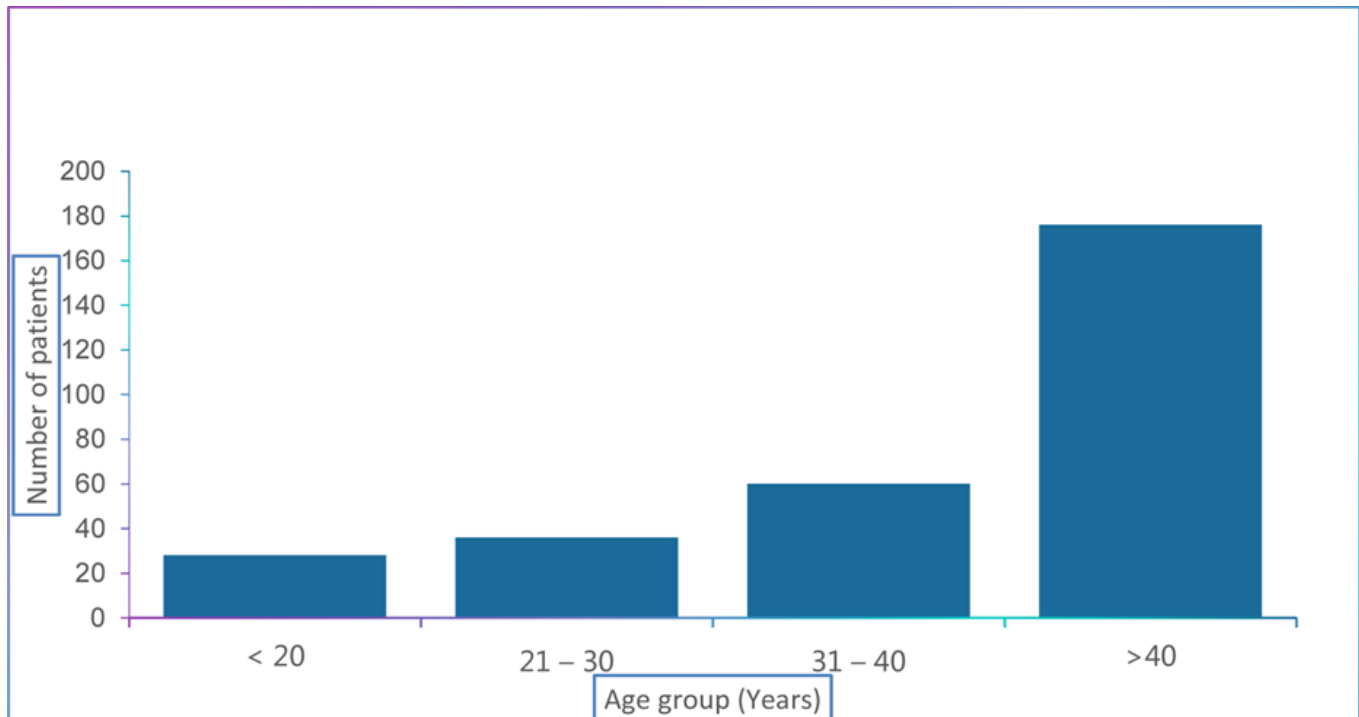


Fig. 2. Age Distribution

Gender : Of the participants in this study, 186 (62%) were men and 114 (38%) were women.

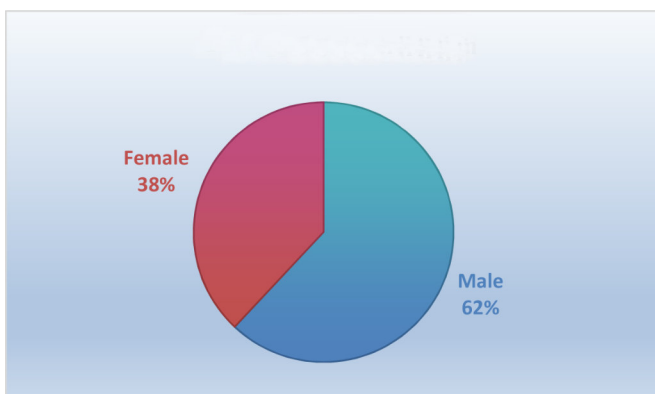


Fig. 3. Gender Distribution

Occupation: 98 (32.66%) of the study's participants were housewives, 134 (44.66%) were laborers, 24 (8%) were students, 10 (3.33%) were business owners, and 34 (11.33%) were farmers.

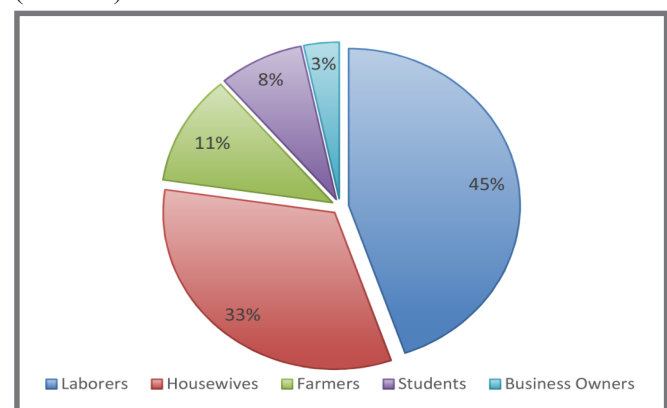


Fig. 4. Occupational Distribution

Presenting Complaints: Right ear pain accounted for 256 (85.3%) of the study's participants' most commonly presenting complaints.

Table I: Distribution in study group as per presenting complaints

PRESENTING COMPLAINTS	NUMBER	PERCENTAGE (%)
Pain in right ear	256	85.3
Pain in left ear	40	13.33
Pain in both ears	04	1.4
Itching in left ear	32	10.67
Itching in right ear	127	42.33
Itching in both ear	07	2.33
Aural fullness in right ear	198	66
Aural fullness in left ear	26	8.67
Aural fullness in both ear	02	0.7
Decreased hearing in right ear	19	6.33

Wax: Only 24 (8%) of the patients in this research had wax present in addition to their fungal infection, and 276 (92%) had only fungal debris visible during an otoscopic examination of their EAC.

Division of Laterality: In the current study, 270 patients (90%) had unilateral otomycosis, of which 192 (71.11%) cases involved the right ear and 78 (28.88%) involved the left ear. The remaining 30 patients (10%) had bilateral involvement.

Distribution of Fungi: *Aspergillus Niger* was the most frequently isolated organism in the current investigation, occurring in 164 (54.66%) of the patients; *Candida albicans* was observed in 78 (26%), *Aspergillus fumigatus* in 38 (12.6%), and *Aspergillus flavus* in 20 (6.66%) of the patients.

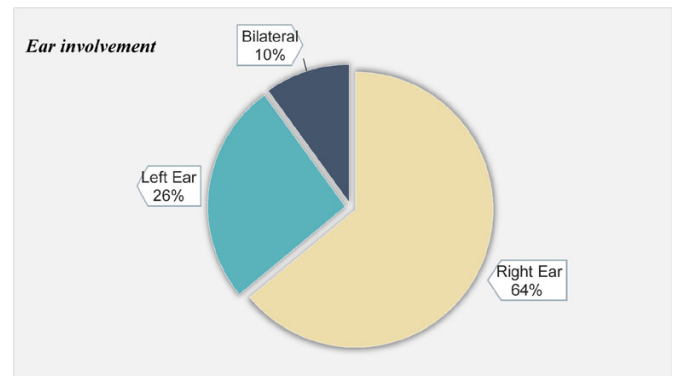


Fig. 4. Division of Laterality

Table II. Distribution in study group according to isolated organisms

ISOLATED ORGANISMS	NUMBER	PERCENTAGE
<i>Aspergillus niger</i>	164	54.66
<i>Candida albicans</i>	78	26
<i>Aspergillus fumigatus</i>	38	12.6
<i>Aspergillus flavus</i>	20	6.66
Total	300	100

Signs at the end of one week: After one week in the current study, 147 (98%) of the patients with persistent symptoms while on clotrimazole cream had no fungal debris and were asymptomatic, while 129 (86%), of the patients receiving clotrimazole drops had no fungal debris and were asymptomatic.

After updating the contingency table with the number of recurrences for each group, the chi-square statistic for all outcomes is approximately 34.394, with a p-value less than 0.001. This indicates a significant association between the type of treatment (Clotrimazole cream vs. Clotrimazole drops) and all observed outcomes, including resolution after the first, second, and fourth weeks of treatment, as well as the number of recurrences.

Table III. Comparison of treatment results in patients with Clotrimazole cream and Clotrimazole ear drops treatments

	GROUP 1 CLOTRIMAZOLE CREAM (n = 150)	GROUP 2 CLOTRIMAZOLE DROPS (n = 150)	p-VALUE
Resolution after 1st week of treatment	147	129	0.037
Additional patients with resolution after 2nd week of treatment	3	21	<0.001
Change in treatment	0	0	<0.001
Number of recurrences	3	21	<0.001
Complications	0	0	<0.001

Discussion

Otomycosis, a word for fungal infection of the external auditory canal, is commonly reported by ENT doctors and is diagnosed based on clinical presentation. The two most common fungi that have been linked to otomycosis pathogenic saprophytes are *Aspergillus* and *Candida*.^{17,18}

Aspergillus species accounted for 54.66% and *Candida albicans* for 26% of the etiological agents identified in this investigation. *Aspergillus* 41.1% (*A. Niger* 36.9%) and *Candida albicans* 8.2% were identified from 72 individuals in the investigation by Kour et al.¹⁹

Otomycosis can be treated in a number of ways, with some studies finding that azoles are particularly helpful in this regard. To examine the effectiveness of both drugs in a controlled clinical trial, it was chosen to compare the treatment of otomycosis with Clotrimazole Ointment vs Clotrimazole Ear Drops in the current study.^{20,21}

Clotrimazole, an imidazole antifungal agent, exerts its effect by inhibiting the cytochrome P450 enzyme lanosterol 14- α -demethylase, which is involved in ergosterol biosynthesis, an essential component of the fungal cell membrane. This inhibition disrupts membrane integrity, increases permeability, and ultimately causes fungal cell death²². According to the Malik²³ research, in terms of antifungals, the imidazole group demonstrated

an 80% resolution rate in the first application with a negligible chance of recurrence.

Studies by Vega-Nava CT et al. (2015)²⁴ Jadhav VJ et al. (2003)²⁵ Khan F et al. (2013), and Mun guía R (2008) demonstrated 50–100% efficacy rates of clotrimazole.

Clotrimazole is also listed by Jackman A as the most often used and efficient treatment.²⁶ In this study, 147 patients (98.0%) receiving therapy with a single dosage of clotrimazole cream and 129 (86%) receiving treatment with clotrimazole drops were symptom-free at the end of the first week following treatment. At the end of the first and four weeks of follow-up, the current study demonstrated a considerable improvement in symptoms with a single dosage of clotrimazole cream in cases of otomycosis. This is consistent with a research by Paulose KO, et al. (1989),²⁷ who discovered that clotrimazole treatment resulted in an improvement of 89%. Treatment failure rates ranged from 9 to 17%, according to studies by Jia X et al. (2012),²⁸ Anwar K (2014),²⁹ Nemati S et al. (2014),³⁰ and Naqi S et al. (2014).³¹

A comparative histological study done by Hamishehkar H, et al. (2015) discovered that Occlusive products can enormously influence skin hydration by forming a barrier on the skin following the topical administration of oil-based

formulations. These products repair the skin barrier by restoring the skin lipids as well.³²

Another study conducted by Hongbo Zhai and Howard I. Maibach in 2002 concluded that Occluded skin sites had a significant increase in *Trans-epidermal Water Loss* (TEWL) values (every-day and alternate-day schedule) when compared to unoccluded sites. Results indicated that post-exposure occlusive treatment markedly enhanced irritant response³³.

These results are consistent with our study, which found that 98% of cases treated with Clotrimazole cream resolved completely after one week of treatment; only 2% of Clotrimazole patients experienced recurrence, and the infection was treated with one more week of treatment without requiring a change in treatment; Clotrimazole application was also less expensive and easier for patients because it was done in the doctor's office and patients had weekly check-ups.

Additionally, following the first week of therapy, there was a significant difference in the resolution of otomycosis between the two treatment groups. Because the clotrimazole drops were administered at home once every 6 hours for 7 days, more patient adherence was necessary.

Since the cream covers the entire extent of the EAC skin and is in contact with this surface for a longer period than the drops, it is likely more effective than the latter. Additionally ear packing with cream forms an occlusive layer which may markedly enhance absorption of the drug and proving to be more beneficial than the drops.

The primary limitation of these investigations was the lack of treatment blinding, wherein patients as well as doctors were cognizant of the allocated treatment. Since topical drops were used at home for one group of patients and cream was administered at the doctor's office for the other, blinding became challenging when there were differences in treatment presentations. Additionally, the patient had to comply with the latter therapy more, which was evaluated at follow-up visits.

Further randomized controlled studies are required to validate our findings because our sample size is modest.

Conclusion

The therapy of otomycosis was shown to be slightly more effective with clotrimazole cream and drop regimens. Since *Aspergillus* species and *Candida albicans* are the most prevalent causes of otomycosis, our findings support the use of clotrimazole cream as a therapy for otomycosis due to its cost-effectiveness and adequate pharmacological effect. Resistance-developing organisms may be minimized with the administration of such therapy.

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