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Original Article

Comparison of Clinical Outcomes of Topical Clotrimazole 1% and Betadine 10% In The Treatment of Otomycosis at Tertiary Care Hospitals in Lahore

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ABSTRACT

Objectives: To determine the preferred treatment option in cases of otomycosis by comparing the clinical outcomes of treatment between topical Clotrimazole lotion 1% and Betadine drops 10%.

Study Design: Quasi-Experimental Study

Place and Duration of Study: CMH Lahore Medical College and Services Institute of Medical Sciences, Lahore, Pakistan, from Oct 24 to Jan 25.

Methodology: Sample size was calculated to be 200, with 100 patients at each center. Group-1 received treatment regimen R1, which consisted of each of the patients having received 01cc topical Clotrimazole 1 % while Group-2 received treatment regimen no 2 represented as R2, which consisted of each of the patients having received 03 drops of topical Betadine 10 % in his/her external ear canal. Six parameters of symptoms (pain, pruritus, and blockage) and signs (fungal debris, erythema of the external auditory canal, and erythema of the tympanic membrane) were compared for the two treatment regimens over a period of four weeks, and the data were analyzed using SPSS version 26.0.

Results: The results of our study found that 1% Clotrimazole lotion was significantly more effective than Betadine 10% drops in alleviating both symptoms (otalgia, pruritus, blockage) and signs (erythema and debris) associated with otomycosis.

Conclusion: The conclusion reached is that clotrimazole, as compared to Betadine, was more effective in alleviating the symptoms and signs of otomycosis

Keywords: Antifungal agents; Betadine; Clotrimazole; Drug therapy.

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INTRODUCTION

Otomycosis, or fungal otitis externa, is a superficial fungal infection of the external auditory canal with a global prevalence of 9-30%.[1] Otomycosis is a challenging fungal infection of the ear canal, affecting 3-5% of the population chronically.[2] It is more common in tropical and subtropical regions, affecting males slightly more than females, with the 30-40 age group most susceptible.[3] Risk factors include ear canal manipulation, antibiotic use, and immunocompromised conditions.4 The most frequent causative agents are Aspergillus species, particularly those in the Aspergillus section Nigri, and Candida species.[5] Emerging pathogens such as Aspergillus sydowii have also been reported.[6] Common symptoms include hearing loss, pruritus, otorrhea, and otalgia.[7] Diagnosis relies on clinical presentation and laboratory confirmation via microscopy and culture.[8] Treatment typically involves mechanical debridement and antifungal medications, with systemic antifungals reserved for severe cases. Treatment typically involves ear cleaning followed by topical antifungals, particularly azoles like clotrimazole, which are widely used because they are affordable and readily available.[9] However, some cases may be resistant to conventional treatments, necessitating alternative approaches.

Recent studies have explored the efficacy of various treatments for otomycosis. Clotrimazole, a commonly used azole antifungal, has shown effectiveness comparable to other treatments such as iodine tincture and acidifying agents. However, evidence comparing clotrimazole to other azoles remains limited and of very low certainty. A meta-analysis found that both antifungal drugs and traditional antiseptic medications effectively relieved otomycosis symptoms, with different associated complications. Further research, particularly randomized controlled trials with long-term follow-up, is needed to develop comprehensive guidelines for otomycosis treatment.[10]

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Pakistan's humid climate, limited awareness of ear hygiene, and unregulated medication use may contribute to recurrent otomycosis. Limited local evidence highlights the need to evaluate affordable and accessible treatment options. This study compares the clinical outcomes of topical Clotrimazole lotion 1% and Betadine drops 10% in patients with otomycosis. It aims to identify the preferable treatment in terms of efficacy, recurrence prevention, and quality-of-life improvement. The findings may help optimize cost-effective treatment and minimize prolonged use of topical ear medications in the local population.

METHODOLOGY

A quasi-experimental trial was conducted at two centers, which include the Departments of Otorhinolaryngology, CMH Lahore Medical College and Services Institute of Medical Sciences, Lahore, Pakistan, from Oct 24 to Jan 25. The study was approved by the Institutional Review Board (IRB) of CMH Lahore Medical College (vide letter no. Case# 97/ERC/CMH/LMC dated 21 /10/2024). A non-probability convenience sampling technique was used. Sample size (n) was calculated as 199 using the WHO calculator, with the proportion of good response (p1) against Povidone Iodine and Clotrimazole(p2) P1=40% and P2=54% respectively 11, with 80% power and a 95% confidence interval, which was rounded off to 200. The total sample was divided into 100 each for data collection at two research centers. Informed written consent for the study was obtained from all patients for this research study.

Inclusion Criteria: All patients between the ages of 18 and 60 years, of either sex, diagnosed with otomycosis after confirming the presence of the following symptoms (Pain in the ear, itching in the ear, and ear blockage sensation) along with the following signs (Fungal debris in the external auditory canal, erythema of the external auditory canal, and erythema of the tympanic membrane), with an intact tympanic membrane.

Exclusion Criteria: Patients having acute diseases (either infectious or non-infectious) requiring hospitalization, sensitive to the above-mentioned drugs, having ear wax, otitis media, malignant otitis externa, eczema, psoriasis, seborrheic dermatitis, and diabetic, immunocompromised, and debilitated patients.

The total sample was divided into 100 each for data collection at two research centers. Informed written consent for the study was obtained from all patients for this research study. These 100 patients at each center were randomly divided by lottery method into two groups. Group-1 consisted of 50 patients and received treatment regimen 1, represented as R1, consisting of each patient having 01cc topical clotrimazole 1% in his/her external ear canal three times daily for 4 weeks. Group-2 consisted of 50 randomly distributed patients and received treatment no. 2, represented as R2, consisting of each of the patients having received 03 drops of topical Betadine 10 % in his/her external ear canal twice a week for 4 weeks. Six parameters of symptoms (pain, pruritus, and blockage) and signs (fungal debris, erythema of the external auditory canal, and erythema of the tympanic membrane) were compared for the two treatment regimens over a period of four weeks. The responses of patients to symptoms after receiving the treatment regimens were measured for pain on the visual analog scale from 0 to 10, while pruritus and ear blockage were measured on a perception score from 1 to 10. The observed signs in patients after receiving the treatment regimens were measured on assessment scores from 1 to 10. The responses of patients' perception scores and assessment scores after receiving both treatment regimens were categorized into three categories according to scores. Good response was categorized with scores from 6 to 10, partial response was categorized with scores from 4 to 6, and poor response was categorized from 1 to 3. All the patients were followed up weekly for 04 weeks, and results were obtained at the end of follow-up with the help of a standardized proforma attached. The standardized performa consisted of two sections, first part about the demographic information (Name, Age, Sex, Address) and second part about measured symptoms and signs of disease and treatment regimen administered related information (OPD registration No; Group:1/2; Treatment Regimen: R1/R2; Pain score (VAS 0 to 10); Pruritus (Perception score 1 to 10); Blockage sensation (Perception score 1 to 10); Fungal debris on examination (Assessment score 1 to 10); Erythema in external auditory meatus (Assessment score 1 to 10); Erythema on TM (Assessment score 1 to 10);). All the data collected were entered and analyzed using SPSS version 26.0. For descriptive analysis, median and interquartile ranges were calculated for age, and frequencies with percentages were calculated for gender variables, and post-treatment symptoms and signs responses were also displayed as frequencies. Normality for symptoms and signs response scores was assessed through the Shapiro–

Wilk Test. A nonparametric *Mann–Whitney U Test* was applied for between-group (treatment regimen; R1 and R2) comparison. The privacy of participants was respected, and there was no identification of anyone participating in this study. All information obtained from participants was kept confidential.

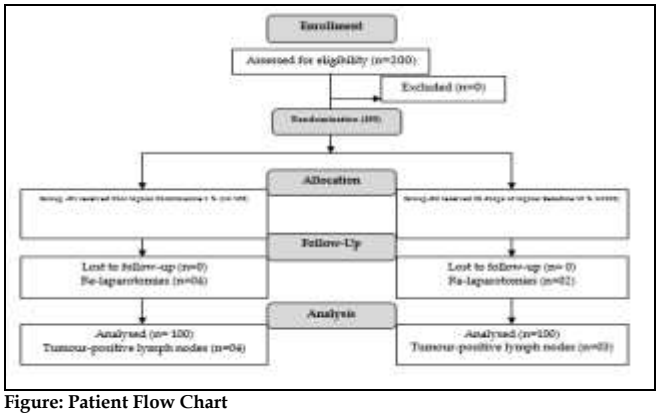


Figure: Patient Flow Chart

RESULTS

Out of the total sample size of 200 patients, 100 patients were allocated to each group at the two centers, with equal proportions of R1 and R2 treatment regimens administered. The average age of both groups was approximately equal. The gender distribution was also equal in proportion for males and females in both groups. Comparison of age and gender across both groups was non-significant. Demographic characteristics were displayed in Table-I.

Table I: Demographic characteristics of patients (n=200)

Variables	Categories	R1, n=100	R2, n=100	*p*-value
Age of participants (in years)	Median (IQR)	29.50(38.0-24.0)	28.0(35.0-24.0)	0.157a
Gender, n (%)	Female	42(42)	44(44)	0.082b
	Male	58(58)	56(56)	

**a Mann-Whitney U test, b Chi-square test*

Frequency distribution of post-treatment symptoms and signs responses was presented in both groups as in Table-II. Responses were graded between 1 and 10 and categorized into three types of responses: poor response (Visual analog 1-3 score), partial response (Visual analog 4 -6 score), and good response (Visual analog 7-10 score). Likewise, the signs were also graded between 1 and 10 and categorized into three types of responses: poor response (Assessment score 1-3), partial response (Assessment score 4 -6), and good response (Assessment score 7-10). The highest frequencies of patients were shown in the good response category for symptoms and signs after using both treatment regimens.

Table-II: Frequency Distribution of Post-Treatment Symptoms And Signs Responses (n=200)

Symptoms	Responses	R1, n=100	R2, n=100
Pain (Visual Analog Score 0-10)	Good Response (7-10)	70	60
	Partial Response (4-6)	25	29
	Poor Response (1-3)	5	11
Pruritus (Perception Score 1-10)	Good Response (7-10)	60	50
	Partial Response (4-6)	30	38
	Poor Response (1-3)	10	12
Blockage Air (Perception Score 1-10)	Good Response (7-10)	70	55
	Partial Response (4-6)	25	30
	Poor Response (1-3)	5	15
Signs	**Responses**	**R1, n=100**	**R2, n=100**
Fungal Debris (Assessment Score 1-10)	Good Response (7-10)	80	75
	Partial Response (4-6)	15	20
	Poor Response (1-3)	5	5
Erythema External Auditory (Assessment Score 1-10)	Good Response (7-10)	60	50
	Partial Response (4-6)	30	35
	Poor Response (1-3)	10	15
Erythema Tympanic Membrane (Assessment Score 1-10)	Good Response (7-10)	80	70
	Partial Response (4-6)	17	25
	Poor Response (1-3)	3	5

Table III: Comparison of post-treatment symptoms and signs responses between the two treatment regimens (n=200)

Variables	Treatment Regimen		*p*-valuea
	R1, n=100	R2, n=100	
	Median (IQR=Q3-Q1)		
Symptoms (Min=1, Max=10)			
Otalgia/pain (Min=0, Max=10)	7.0(8.0-7.0)	7.0(8.0-5.0)	0.04*
Pruritus	7.0(8.0-5.3)	6.0(8.0-5.0)	0.04*
Ear Blockage	7.0(8.0-7.0)	6.0(8.0-5.0)	0.05*
Signs (Min=1, Max=10)			
Fungal Debris	7.0(8.8-7.0)	7.0(8.0-5.0)	0.09
Erythema EAC	7.0(8.0-6.0)	5.0(7.0-4.3)	<0.001*
Erythema TM	7.0(8.0-7.0)	7.0(8.0-5.0)	0.05*

**a Mann-Whitney U test with a p-value less than or equal to 0.05;*
Erythema EAC – Erythema annulare centrifugum; Erythema TM – Erythema of the tympanic membrane

Comparison of post-treatment symptoms and signs responses between the two treatment regimens was carried out and displayed in Table-III. Median (Q3-Q1) for symptom and sign scores were compared with nonparametric tests. Symptoms (Otalgia/pain; p=0.04, Pruritus; p=0.04, and Ear Blockage; p=0.05) and signs (Erythema EAC; p<0.001and Erythema TM; p=0.05) were found statistically significant with $p \leq 0.05$. This means that R1 is better than R2 based on the recorded score responses.

DISCUSSION

The results of our study found that 1% Clotrimazole lotion was significantly more effective than Betadine 10% drops in alleviating both symptoms

(otalgia, pruritus, blockage) and signs (erythema and debris) associated with otomycosis. The differences in treatment outcomes were statistically significant across five out of the six parameters evaluated, affirming Clotrimazole's superior efficacy in a clinical setting.

In support of our study, Shabbir *et al.*,[12] also showed a better response with clotrimazole as compared to iodine-soaked gel form but had a smaller sample size. Mofatteh *et al.*,[13] found no significant difference in efficacy between clotrimazole and iodine tincture, while Aziz *et al.*,[11] compared 7.5% Povidone-iodine with 1% Clotrimazole ear drops and lignocaine and found it to be a more effective antifungal agent in the treatment of Otomycosis. However, Yassin *et al.*,[9] conducted a comprehensive review comparing acidifying agents and clotrimazole, concluding that while both appear effective, there is insufficient evidence to definitively choose between them. They noted that eight studies favored clotrimazole for treating otomycosis symptoms such as pain, itching, swelling, and hearing loss. Wu S *et al.*,[14] conducted a meta-analysis and literature review showing that antifungal drugs and traditional antiseptic medication were effective in relieving symptoms in patients with otomycosis, and the two treatments were associated with different complications.

The critical analysis of Clotrimazole antifungal efficacy was supported by Anslay *et al* and Chavan *et al.*,[15,16], supported our research and compared the efficacy of Clotrimazole and Betadine suggest that while Clotrimazole is more targeted and symptom-effective, Betadine remains a viable, low-cost alternative as reported by Alhaleem *et al*.[17] In terms of clinical efficacy, this study complements our research showing that Clotrimazole's favorable safety profile, minimal ototoxicity, broad antifungal coverage, and proven efficacy make it an appealing first-line treatment for otomycosis in ENT OPD.[18] Future research in this area should include RCTs with long-term follow-up to guide the development of otomycosis guidelines to overcome some of the weaknesses found in the literature.

LIMITATION OF STUDY

The limitations of our study were two. Firstly, a small sample size; a larger sample size and longer duration could provide more robust conclusions regarding long-term efficacy and recurrence rates. Secondly, as the study is not double-blinded, observer bias could have influenced assessment outcomes. The recommendations of our study include the following: Firstly, future studies should incorporate a larger patient population from diverse geographical locations for generalizability of results; Secondly, blinding of both patients and assessors should be undertaken in future studies to improve the reliability of results.

CONCLUSION

The conclusion of this quasi-experimental study demonstrated that clotrimazole, as compared to betadine, was more effective in alleviating the symptoms and signs of otomycosis.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AAK & FR: Data acquisition, data analysis, critical review, approval of the final version to be published.

SHS & AR: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SN & MAK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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