https://doi.org/10.37939/jrmc.v27i3.2372

Comparison Of Isoconazole Nitrate Versus Nystatin For The Treatment Of Otomycosis

Amna Kausar[1], Sadia Chaudhry[2], Nighat Qamar[3], Ansa Umara Akram[4], Ashar Alamgir[5], Wajid Hussain[6]

Abstract

Objective: To compare the efficacy and local adverse effects of Isoconazole Nitrate versus Nystatin for the treatment of patients having Otomycosis.
Study Design: Group experimental study.
Study Setting & Duration: Department of Otolaryngology, Head & Neck Surgery at Rawalpindi Teaching Hospital, Rawalpindi. The duration of the study was 6 months after approval by the Ethical Committee from Feb 2023 to July 2023
Materials and Methods: A total of 64 patients were selected. The study participants were individuals who, according to operational definitions had Otomycosis and who had presented for evaluation at the Department of Otolaryngology Rawalpindi Teaching Hospital, Rawalpindi. They also met all inclusion and exclusion criteria requirements and these requirements were strictly adhered to to control confounders and bias. Isoconazole nitrate ointment was used to treat patients in Group A and Nystatin ointment was used to treat instances in Group B. Patients were chosen by randomization using a lottery method. SPSS 28 was used to determine the frequencies in the data.
Results: 64 individuals (32 cases in each group) were chosen for the study by the ENT outpatient clinic. Out of which 33 (51.6%) being female and 31 (48.1) being male. The age ranged from 12 to 80 years, with a mean age of 44.29 ±19.13. After two weeks, there was a substantial improvement in 25 (39.06%) of the group A patients (p=0.08), a moderate improvement in 7 (10.9%), and a minor improvement in 5 (7.81%) patients (p=0.37) while in group B exhibited a substantial improvement in just 19 (10.9%) (p=0.08), a moderate improvement in 9 (39.0%) (p=0.38), and a small improvement in 7 (42.19%) (p=0.37). After four weeks 21 (32.81%) in Group B showed insignificant improvement, while 26 (40.63%) in Group A exhibited better improvement than Group B. The treatment for group A, which included isoconazole nitrate, was substantially more successful than the Nystatin treatment for group B. Isoconazole was found insignificantly more effective than nystatin (p=0.08). The majority of patients in both groups didn't notice any adverse reactions.
Conclusion: Nystatin was shown to be significantly less efficacious than isoconazole nitrate ointment in treating otomycosis.
Keywords: Otomycosis, Isoconazole, Nystatin.

[1,4] Post-Graduate Trainee, ENT, Rawalpindi Teaching Hospital, Rawalpindi; [2] Associate Professor, ENT, Rawalpindi Teaching Hospital, Rawalpindi; [3] Associate Professor, ENT, Riphah International University, Rawalpindi; [5] Assistant Professor, ENT, Holy Family Hospital, Rawalpindi; [6] Assistant Professor, Fauji Foundation Hospital, Rawalpindi.
Correspondence: Dr. Sadia Chaudhry, Associate Professor, ENT, Rawalpindi Teaching Hospital, Rawalpindi. **Email:** sadiaaatif@yahoo.com
Cite this Article: Kausar, A., Chaudhry, S., Qammar, N., Akram, A. U., Alamgir, A., & Hussain, W. (2023). Comparison Of Isoconazole Nitrate Versus Nystatin For The Treatment Of Otomycosis. *Journal of Rawalpindi Medical College*, *27*(3). https://doi.org/10.37939/jrmc.v27i3.2372.
Received August 08, 2023; accepted August 31, 2023; published online September 26, 2023

1. Introduction

Otomycosis also known as fungal otitis externa occurs as a frequent disorder that is mostly used to characterize superficial fungal infections of the external auditory canal including the auricle. Otomycosis is regularly seen in outpatient otolaryngology clinics. Less frequently, it may affect the mastoid cavity after an open mastoidectomy including the middle ear if the drum is ruptured which is very challenging to treat. Itching, discomfort, auditory fullness, aural discharge, hearing loss, edema, redness and tinnitus are typical symptoms but can be asymptomatic in some cases.[1] Superimposed bacterial infections are frequently present alongside otomycosis. The patient's medical history, physical examination, microscopic otoscopic examination, and laboratory fungal detection are used to make the diagnosis of otomycosis [2]. Otomycosis was associated with numerous fungal species. While several species may be implicated in the illness, Aspergillus and Candida species are the most often found fungal pathogens in otomycosis patients.[1] But Aspergillus niger in particular appeared to be the most prevalent causal agent. The genera Penicillium, Fusarium, Mucoraceae, Scopulariopsis, Alternaria, Malassezia, and Candida, as well as several dermatophytes, are among the other fungal agents.[3]
Due to weakened local host defences brought on by bacterial infection, it is unclear whether the fungi are the actual infectious agents or merely colonization

species. A humid environment, the existence of cerumen, ear instrumentation, increasing topical antibiotic and steroid use, immunocompromised hosts, patients who have had open cavity mastoidectomy, and people who use hearing aids with occlusive ear moulds are just a few of the contributing variables. The infection is typically unilateral and is characterized by otalgia, scaling, and inflammatory pruritus. Local debridement, topical and systemic antifungal medications and stopping topical antibiotics have all been suggested as treatments. Avoidance of swimming and hygienic clothing habits are also recommended. Otomycosis can occasionally be difficult to treat and monitor over the long term, yet its probability of recurrence rate is still high.[4]Complications can also occur if proper treatment is not taken.

The external ear canal's cerumen, debris, and fungal components have to be cleaned out as part of the primary treatment for otomycosis, which is then followed by the application of topical antifungal drops. For the eradication of otomycosis, a variety of substances with different antifungal qualities are frequently employed, including azole group antifungals, amphotericin B, mercurochrome, aluminium acetate in the solution, boric acid, etc. [5]. Isoconazole nitrate (ISN) is an antifungal medication in the azole class. Dermatophytes, candida species, aspergillus species, as well as gram-positive bacteria like Staphylococcus species as well as Streptococcus species, are all susceptible to ISN's broad spectrum of antimicrobial activity. Numerous studies have evaluated the effectiveness of different azole group antifungals like clotrimazole, fluconazole and miconazole in the management of otomycosis [6].

Our study's goal was to compare two locally administered antifungal medications to determine the most effective and efficient plan for treating otomycosis and to compare their local adverse effects.

2. Materials & Methods

This group comparison study was conducted in the Department of Otorhinolaryngology Rawalpindi Teaching Hospital, Rawalpindi after approval from the Hospital Ethical Committee. A sample size calculation was made by using online sample size calculation software (Kane, 2017)Using the study conducted by Khan MA et al.,2021. The sample size was calculated as 32 in each group. Randomization of participants was done using the lottery method. The study was conducted on both male and female patients. 64 Patients (32 in each group) who suffered from otomycosis as per operational definitions were included. Itching, pain, deafness, clogged ears, tinnitus, and otoscopic observations of hyphae, spores, or curd-like white or grey discharge in the patient's external auditory meatus are some of the symptoms of the disease.

Patients with a diagnosis of otomycosis from both genders and all age groups were included in the study. For inclusion in the subject study, the clinical diagnosis was regarded as sufficient. Patients who were immunocompromised or taken immunosuppressants, had concurrent otitis media or a fungal infection on any other area of their body, such as tenia corporis were excluded.

Upon enrolment in the study, a comprehensive medical history and clinical assessment were performed on each participant. Symptoms, usage of ear wooden sticks, ear plugs, use of topical or systemic antibiotics or steroids, etc. were all thoroughly recorded in the patient's history.

Isoconazole nitrate ointment was used to treat patients in Group A, and Nystatin ointment was used to treat patients in Group B. The patients were explained how to apply ointment. Patients underwent evaluation after two and four weeks of treatment and the success of the treatment was determined by how well the symptoms had improved (lessened discomfort, itching, and discharge). An ear examination was used to assess clinical progress. Clinical improvement was indicated by a decrease in ear canal edema, a decrease in discharge, a decrease in debris, and a decrease in discomfort and tenderness. Also, adverse effects like local irritation and allergic reactions were compared between the 2 groups.

Improvement was evaluated clinically by asking the patients if their symptoms had improved, and it was then classified as a mild, moderate, or remarkable improvement. Whenever there was only a slight reduction in the intensity of symptoms, such as discomfort, swelling and discharge, ear blockage, etc., improvement was considered to be minor. Similar to how improvement was described, symptom severity showed a moderate and noticeable reduction.

To assess all of the data, SPSS-28 was used. For quantitative factors, mean and SD were calculated. For

quantitative data, rates and proportions were determined. Chi-square was utilized to compare the improvement between the two groups' qualitative outcomes.

3. Results

The Otolaryngology outpatient department selected 64 patients for the study (32 cases in each group). 33 (51.6%) of the 64 patients were female, and the remaining 31 (48.1%) were male. The mean age calculated was 44.29 ± 19.13. After two weeks, 25 (39.06%) of the group A patients showed a significant improvement (p=0.08), 7 (10.9%) a moderate improvement (p=0.38), and 5 (7.81%) a minor improvement (p=0.37). In contrast, after two weeks, 19 (10.9%) (p=0.08) in group B showed a significant improvement, 9 (39.0%) (p=0.38) showed a moderate improvement, and 7 (42.19%) (p=0.37) showed a minor improvement. Similarly, after four weeks, 21 (32.81%) in Group B showed no improvement, while 26 (40.63%) in Group A exhibited better improvement than Group B. The majority of patients in both groups didn't notice any adverse reactions like local allergic reactions.

Table 1 Age in years

	Mean	SD	Range
Age in years	44.29	19.13	12_80

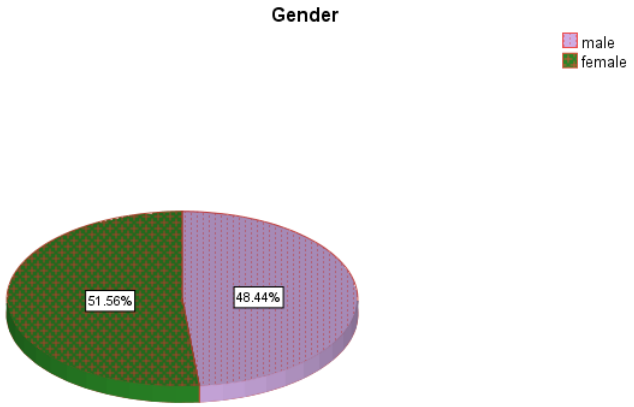

Figure-1 Frequency distribution of gender

5. Discussion

Otomycosis is a condition that is frequently seen in otorhinolaryngology outpatient clinics. In our study, women made up the majority, which is consistent with earlier studies. 51.56 % were females and 48.44% of the participants in our study were males. Otomycosis is said to be more common in nations on or near tropical coasts. This study was conducted in Rawalpindi. Summers in the Rawalpindi district are lengthy, humid and oppressive, with temperatures ranging from 39 to 105 F and infrequently falling below 34 F or rising over 112 F. [7]

Table 2 Marked improvement among study groups

Marked improvement	Group A: Isoconazole nitrate ointment N=32	Group B: Nystatin ointment N=32	P Value
Yes	25	19	.08
No	7	13	
Total	32	32	

From May to September, there is a hot summer. The humid season in Rawalpindi lasts from June through September. The increase in otomycosis instances in Rawalpindi during this season is caused by the hot weather. Fungi grow best in hot, humid environments.[7] The outer part of the external auditory meatus is covered in skin. Similar to the skin on the rest of the body, this skin is constricted and shaped like a meatal inlet. It may create favourable conditions for the growth of fungi.

Additionally, narrowed external auditory meatus increases the risk. An important risk factor that damages the skin barrier is the manipulation of the auditory meatus using objects such as pins, keys, sticks, and various other metallic things. It is also typical to use earbuds to reduce itching.

Table 3 Moderate improvement among study groups

Moderate improvement	Group A: Isoconazole nitrate ointment N=32	Group B: Nystatin ointment N=32	P Value
Yes	7	9	.38
no	25	23	
Total	32	32	

Table 4 Minor improvement among study groups

Minor improvement	Group A: Isoconazole nitrate ointment N=32	Group B: Nystatin ointment N=32	P Value
yes	5	7	.37
no	27	25	
Total	32	32	

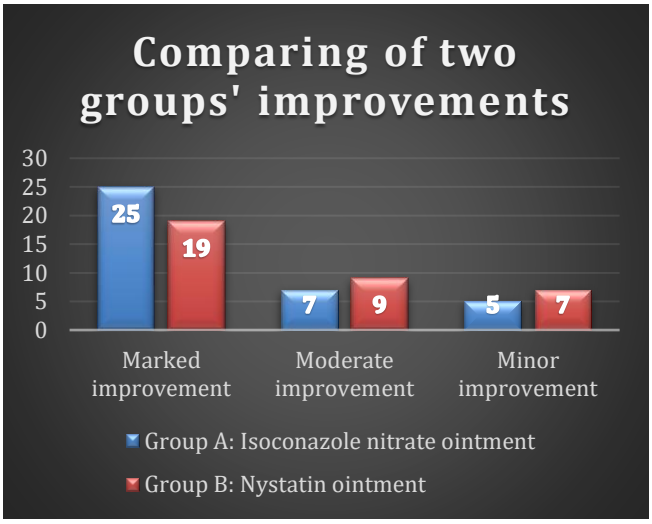

Figure 2 Comparing two groups

All of the aforementioned actions can harm the ears and increase the risk of otomycosis. When the aforementioned risk factors are present and the surrounding environment is hot, humid, as well as acidic, which encourages the growth of fungi and results in otomycosis.

Table 5 Improvement at 4th weeks among study groups

Improvement in 4th week	Group A: Isoconazole nitrate ointment N=32	Group B: Nystatin ointment N=32	P Value
Yes	26	21	.12
No	6	11	
Total	32	32	

Otomycosis must be treated in these situations in addition to any primary or secondary fungus infections on the body to prevent chronic or recurrent infections.

There is a difference of opinion regarding the prescription of the various types of antifungals among otorhinolaryngologists. In this study, we compared nystatin with isoconazole comparing their local side effects as well. In another study from 2021, Ambrose Lee compared different azole antifungals for the treatment of otomycosis. [5]

The socioeconomic factors and the associated delay prevent routine mycological sample cultural and sensitivity testing. There are very rarely other species of fungi implicated besides common Candida or Aspergillus unless the person is immunocompromised (severe diabetes, on high dosage corticosteroids, taking immunosuppressant, suffering from HIV or Tuberculosis, etc.). Both nystatin and isoconazole have sufficient anti-Aspergillus and anti-Candida effects. Nystatin is an Ionophores member that is related to Amphotericin B. It attaches to ergosterol, a crucial part of the fungus membrane, to perform its antifungal function. It creates pores in the fungus membrane, and forms ion channels which causes potassium to leak out and kill the fungus. [8]

Table 6 Adverse (unwanted) effects among study groups

Adverse (unwanted) effects	Group A: Isoconazole nitrate ointment N=32	Group B: Nystatin ointment N=32	P Value
severe allergic reactions	3	3	.31
burning or itching	2	6	
No side effect	27	23	
Total	32	32	

Isoconazole nitrate is an azole derivative on the other side. Reduced ATP concentration and cell wall destruction are two ways that isoconazole nitrate harms fungal cells. it alters the stability and permeability of the membrane. A broad-range antimycotic medication called isoconazole nitrate has efficacy against some gram-positive bacteria in addition to being an efficient antimycotic. It absorbs quickly and has little overall negative effects. [9]

According to Filiz Gülüstan. isoconazole had a quicker onset of action, quicker relief from itching and better overall effectiveness as a treatment. [10]
Azoles are more successful than Nystatin in treating typical skin and ear fungal infections, according to in vivo and in vitro research.
In our study, we found that isoconazole ointment had exceeding recovery rates and clinical condition improvements than did nystatin ointment without any adverse effects. As a result, we advise using isoconazole rather than nystatin as the first-line therapy for otomycosis.

5. Conclusion

Treatment of otomycosis with isoconazole nitrate ointment was notably more effectual than with nystatin. The majority of patients in both groups didn't notice any adverse reactions.

CONFLICTS OF INTEREST- None

Financial support: None to report.
Potential competing interests: None to report

Contributions:

A.K - Conception of study
A.K, A.U.A, A.A, W.H - Experimentation/Study Conduction
S.C, N.Q - Analysis/Interpretation/Discussion
A.K, A.U.A, A.A, W.H - Manuscript Writing
S,C, N.Q - Critical Review
S.C, A.U.A, A.A, W.H - Facilitation and Material analysis

References

[1] Lotfali E , Ghasemi R, Masoumi N, Molavizadeh D, Sadeghi S, et al. Isolation, Characterization, and Antifungal Sensitivity Pattern of Fungal Species with Potential Resistance to Antifungal Drugs in Patients with Otomycosis. Arch Clin Infect Dis. 2022;17(4):e129169. https://doi.org/10.5812/archcid-129169.
[2] Xu S, Li J, Ding L, Gao K, Xie F, Han J, Zhou X. Efficacy and safety of terbinafine hydrochloride spray and 3% boric acid alcohol ear drops in otomycosis. Acta Otolaryngol. 2020 Apr;140(4):302-306. Doi: 10.1080/00016489.2020.1712474
[3] Haq M, Deshmukh P. Review of Recurrent Otomycosis and Clotrimazole in Its Treatment. Cureus. 2022 Oct 9;14(10):e30098. Doi: 10.7759/cureus.30098.
[4] Kiakojuri K, Rajabnia R, Mahdavi Omran S, Pournajaf A, Karami M, Taghizadeh Armaki M. Role of Clotrimazole in Prevention of Recurrent Otomycosis. Biomed Res Int. 2019 Dec 26;2019:5269535. doi: 10.1155/2019/5269535
[5] Dundar R, İynen İ. Single Dose Topical Application of Clotrimazole for the Treatment of Otomycosis: Is This Enough? J Audiol Otol. 2019 Jan;23(1):15-19. doi: 10.7874/jao.2018.00276.
[6] Lee A, Tysome JR, Saeed SR. Topical azole treatments for otomycosis. Cochrane Database Syst Rev. 2021 May 25;5(5):CD009289. doi: 10.1002/14651858.CD009289
[7] Khan MA, Akram S, Anwar K, Ahmad A, Khan M, Hakim A. Prevalence, clinical profile and seasonal variation of otomycosis in Pakistan. International Journal of Pathology. 2020 Oct 5:26-30.
[8] Hossain CM, Ryan LK, Gera M, Choudhuri S, Lyle N, Ali KA, et al. Antifungals and Drug Resistance. Encyclopedia [Internet] 2022;2(4):1722–37. Available from: http://dx.doi.org/10.3390/encyclopedia2040118
[9] Ghannoum MA, Rice LB. Antifungal agents: mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. Clin Microbiol Rev. 1999 Oct;12(4):501-17. doi: 10.1128/CMR.12.4.501.
[10] Gülüstan F, Abakay MA, Demir E. Efficacy of topical isoconazole nitrate in the treatment of otomycosis. Am J Otolaryngol. 2021 Jul-Aug;42(4):102961. doi: 10.1016/j.amjoto.2021.102961