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Original Research Article

The efficacy of oral itraconazole in the treatment of otomycosis accompanied by a perforated tympanic membrane

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ABSTRACT

Background: Managing otomycosis in patients with an existing tympanic membrane perforation can pose challenges. However, this study underscores the efficacy of oral itraconazole as a viable treatment option for such instances.

Materials and Methods: The research encompassed 34 individuals experiencing both otomycosis and a perforated tympanic membrane. These participants received a combination of oral itraconazole and antibiotic ear drops as treatment. Over a period of six weeks, their progress was monitored to assess the treatment's effectiveness and to observe any potential instances of recurrence.

Results: Out of the total 34 subjects examined in the study, 25 individuals achieved complete recovery after just one week of oral itraconazole treatment. Among the remaining 9 patients, 6 experienced a successful resolution of the condition following two weeks of therapy. For 3 patients, an extended treatment duration was required, and in a singular case, a recurrence of the condition was observed at the six-week mark.

Conclusion: Oral itraconazole treatment presents as an efficacious substitute for conventional approaches in addressing otomycosis accompanied by tympanic membrane perforation.

1. Introduction

The incidence of otomycosis has surged in recent times. This escalation can be attributed to the excessive application of antibiotic ear drops and the utilization of Q tips.[1] Patients with compromised immune systems, such as those with diabetes mellitus and HIV, face an elevated susceptibility to stubborn otomycosis. Notably, chronic otitis media accompanied by a perforated tympanic membrane often correlates with otomycosis due to the sustained moisture within the ear canal.[2]

The primary challenge in managing individuals with otomycosis and a tympanic membrane perforation lies in the complications associated with using topical antifungal ear drops. When these antifungals penetrate the middle ear, certain patients endure intense pain and a pronounced burning sensation. In such cases, the utilization of topical antifungal ear drops is avoided. Instead, the ear canal is filled with antifungal cream or a cream-coated ear wick after a thorough initial cleaning process.[3] This cream or wick necessitates periodic replacement every few days until a complete recovery is achieved. Consequently, patients contend with the discomfort of a blocked ear throughout the treatment period and are required to make multiple visits to the ENT clinic. Recognizing the effectiveness of oral itraconazole as a potent treatment for a wide range of fungal infections, we endeavoured to investigate its efficacy when combined with meticulous initial suctioning and antibiotic ear drops. This combination serves as a substitute for the conventional use of topical antifungal ear drops or repetitive ear packing in the treatment of otomycosis accompanied by chronic otitis media.

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2. Materials and Methods

Conducted at a tertiary care center, this prospective study spanned a duration of one year, commencing in August 2022 and concluding in August 2023. The study encompassed all individuals who visited the ENT outpatient department with symptoms of otomycosis and a perforated tympanic membrane. Diagnosis of otomycosis was established through clinical assessment, wherein the presence of fungal hyphae within the ear canal was ascertained by microscopic examination.

A sample was collected from the ear through an ear swab, and this specimen was subsequently submitted for fungal culture analysis. The primary objectives of this step were to validate the diagnosis and pinpoint the specific fungal organism responsible. Individuals with chronic liver or renal conditions, those with a known hypersensitivity to itraconazole, and those exhibiting squamous-type chronic otitis media were intentionally excluded from the study.

The study included a cohort of 37 patients who had been diagnosed with both otomycosis and tympanic membrane perforation. Each patient underwent an evaluation that encompassed their initial symptoms, duration of discomfort, any previous occurrences of similar issues, and otoscopic observations, including an assessment of the perforation's size. Comprehensive medical assessments, such as blood sugar measurement and liver function testing, were conducted for all participants. As part of the initial treatment process, meticulous microscopic suctioning was performed to eliminate fungal debris from the ear canal.

Subsequently, the patients were initiated on an oral regimen of 100 mg itraconazole twice daily for a duration of 7 days. Alongside, they received antibiotic ear drops administered as 2 drops thrice daily for 7 days, aimed at managing bacterial co-infections within the middle ear. Following this initial treatment phase, all participants underwent a follow-up examination after one week. Additionally, they were continuously monitored for any potential adverse effects arising during the course of itraconazole therapy. The condition of the ear canal was observed through a microscope to assess the treatment's effectiveness. For individuals still displaying signs of fungal infection, a repeat suction clearance procedure was performed, and the oral itraconazole regimen was extended for an additional week. Patients were advised to return for follow-up evaluations at the 3-week and 6-week marks after discontinuing itraconazole treatment.

3. Results

A total of 37 patients were initially included in the study but 3 patients did not come for the follow-up, thus making the total number in the study group to be 34. In this study the peak incidence of otomycosis with perforation of tympanic membrane was noted in the age group of 31 - 40 years (38%). The ratio of males to females was 1.13 to 1, comprising 18 males and 16 females. (Figure 1).

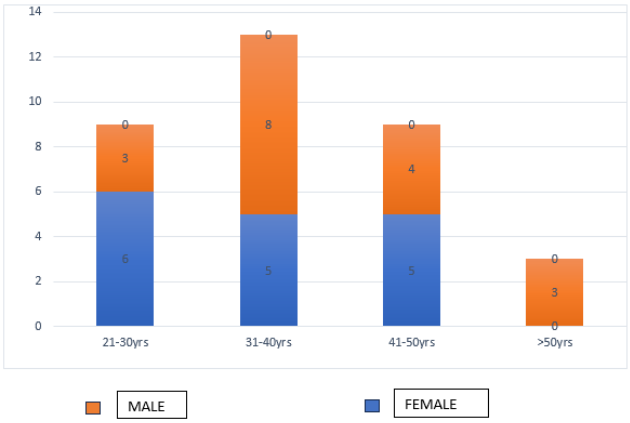

Figure 1: Age and sex distribution

Prominent symptoms among the patients included earache, otorrhea (ear discharge), ear blockage, and pruritus (itchiness). Among the participants, nine were identified as individuals with pre-existing diabetes who were already undergoing medication for the condition. Clinical examinations revealed fungal debris with hyphae present in the ear canals of all patients, with varying degrees of severity. This ranged from minimal presence on the floor of the canal to complete filling of the canal. In this study, the predominant fungal isolates were from the Aspergillus species, specifically A. niger and A. fumigatus, followed by Candida species. The study's patient distribution included 16 individuals with large-sized central perforations of the tympanic membrane, 14 with moderate-sized central perforations, and 4 with small central perforations.

Nearly all patients experienced significant symptom relief within one week of treatment. Upon examination at the conclusion of this initial week, 25 patients (74%) exhibited a complete absence of fungal material, leading to the discontinuation of oral itraconazole for these individuals. For the remaining 9 patients, an additional week of treatment involving repeat suctioning and continued itraconazole therapy was administered. By the end of the second week, a total of 31 patients (91%) were observed to be entirely symptom-free (refer to Figure 2).

The three patients who exhibited no positive response to the initial treatment had uncontrolled diabetes, and consequently, they required an extended course of itraconazole therapy. Among this subgroup, one patient achieved a complete cure following three weeks of treatment, while the remaining two attained recovery after four weeks of treatment. During the follow-up period, a diabetic patient who had initially been successfully treated with a one-week itraconazole regimen experienced a recurrence three weeks after discontinuing the medication.

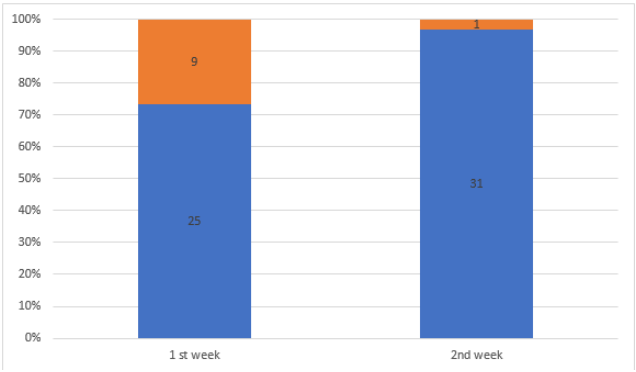

Figure 2: Treatment outcome

This patient was subsequently treated with the same regimen but with a two-week course of itraconazole, resulting in complete recovery. Throughout the entire study, all other patients underwent a six-week follow-up without any instances of otomycosis recurrence. Furthermore, no adverse effects stemming from itraconazole were reported by any of the patients involved in the study.

4. Discussion

Otomycosis refers to a fungal infection that targets the superficial layers of the external ear canal. This infection can manifest in either an acute or chronic form and is marked by symptoms like inflammation, itching, scaling, and significant discomfort within the ear. Statistics suggest that approximately 7-15% of cases of otitis externa[2] can be attributed to otomycosis. This condition tends to thrive in warm, humid climates and is particularly prevalent among individuals aged between their second and third decades, often those with subpar hygiene practices. Common predisposing factors for otomycosis include frequent swimming, eczema, excessive use of cotton swabs, a narrow ear canal, allergies, chronic drainage, exposure to radiation, obstructive earwax, post-mastoidectomy radical cavity, use of earplugs, and prolonged use of topical antibacterial treatments. The condition tends to be more severe in diabetic and immunocompromised patients. In cases of tympanic membrane perforation, otomycosis can extend to involve the middle ear, and in some instances, it might also affect the auricle (outer ear).[4]

The typical culprits identified in otomycosis are Aspergillus niger and Candida albicans. According to a study conducted by Ashish Kumar involving 82 patients, the primary fungal isolates consisted of Aspergillus niger (52.43%), Aspergillus fumigatus (34.14%), Candida albicans (11%), and Mucor. Another investigation by Kurnatowski and Filipiak, which analysed 249 individuals with external otitis, revealed that 15% of cases had a combined bacterial and fungal origin, while 13% were solely attributed to fungal[5] causes.

Otomycosis is notorious for its tendency to recur if appropriate treatment measures are not implemented. Notably, there exists considerable disparity in the treatment approaches employed by different ear, nose, and throat specialists. These methods encompass the use of topical antifungal ear drops, application of antifungal ointments, utilization of ear wicks for canal packing, as well as the administration of oral antifungal medications. The complexity escalates when patients with a perforated tympanic membrane present with otomycosis. Moreover, cases of chronic otitis media[3,6] often involve concurrent bacterial infections alongside otomycosis.

When dealing with the conjunction of otomycosis and a tympanic membrane perforation, challenges emerge, notably the pronounced stinging pain and potential ototoxicity associated with the use of topical antifungal drops. These drops can directly reach the middle ear through the perforation. Consequently, an alternative strategy involves the application of medicated antifungal cream to entirely fill the ear canal or the use of a medicated ear wick. Both methods entail the discomfort of a blocked ear over several days, accompanied by the need for multiple follow-up visits to have the treatment removed and reapplied.

In such scenarios, a promising solution lies in the administration of oral antifungal medications like itraconazole, which yields a favourable rate of recovery. In our specific study, we adopted a treatment approach that involved the use of itraconazole along with antibiotic ear drops to manage bacterial infections in the middle ear. Prior to this, a meticulous microscopic suctioning procedure was carried out.

A brief regimen of oral broad-spectrum antifungal medication proves highly effective in managing challenging cases of otomycosis.[7] Itraconazole, being an antifungal agent with a broader spectrum of activity compared to Fluconazole, demonstrates particular efficacy against Aspergillus and Candida. In our current study, the findings indicate that a significant proportion of patients exhibited a positive response to treatment within the initial week, with a majority achieving full recovery by the conclusion of the second week. This underscores the efficacy of a two-week course of itraconazole therapy, combined with antibiotic ear drops, as a reliable approach for treating otomycosis in cases featuring a tympanic membrane perforation.

In our conducted research, instances that were further complicated by diabetes necessitated an extended treatment period spanning three to four weeks. In a study conducted by R. Venkataraman et al., a five-day regimen of Itraconazole at a daily dosage of 200mg demonstrated effectiveness in treating otomycosis among diabetic patients.[7] Notably, their study also highlighted that initiating Itraconazole therapy at an early stage aids in averting the development of more intricate manifestations of the condition in diabetic individuals. Additionally, oral Itraconazole was observed to

be valuable in alleviating pruritus (itchiness). In our own investigation, patients who underwent a minimum of two weeks of Itraconazole treatment exhibited no recurrence of symptoms during the six-week follow-up period.

Itraconazole was determined to be highly effective and well-tolerated in our investigation, with no reports of significant adverse effects among patients. Notably, oral Itraconazole therapy does not necessitate liver function monitoring if the baseline liver function tests are within normal ranges. A study by Ryo Amesara et al., involving 22 patients, also attested to the remarkable efficacy of oral Itraconazole. The study noted that the concentrations of Itraconazole present in cerumen (earwax) surpassed most of the Minimum Inhibitory Concentration (MIC) values, indicating a robust antifungal effect. However, it's important to acknowledge that our study's limitations include a relatively small patient cohort, which falls short of the ideal sample size for a comprehensive epidemiological study. Additionally, our study lacks a comparative analysis with alternative treatment methods.

5. Conclusion

While numerous treatment choices exist for otomycosis, certain approaches encounter constraints when dealing with cases involving a tympanic membrane perforation. Our study findings provide a clear conclusion: a two-week course of oral itraconazole therapy emerges as a highly effective option for managing otomycosis, particularly in scenarios where a tympanic membrane perforation is present. Moreover, this treatment avenue holds potential for being explored in instances of refractory or recurrent otomycosis even in the absence of tympanic membrane perforation.

6. Source of Funding

None.

7. Conflict of Interest

None.

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