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COMPARISON OF EFFICACY OF 5%, 7.5%, AND 10% POVIDONE-IODINE IN TREATING OTOMYCOSIS IN NONDIABETICS: A RANDOMIZED CONTROLLED TRIAL

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Abstract

The primary objective of this research was to determine the rate of clinical improvement and mycological cure in non-diabetic patients with otomycosis treated with 5%, 7.5%, and 10% povidone-iodine solutions over a specified treatment period. A randomized controlled trial (RCT) was carried out on 90 patients admitted to the outpatient department of Otorhinolaryngology at Saveetha Medical College and Hospital Chennai, from July 2023 to April 2024 with clinical and microbiologically confirmed otomycosis .The epidemiological data regarding age, sex, and symptoms were recorded. Participants were randomly allocated into three groups: Group A, which received treatment with 5% povidone-iodine; Group B, which received treatment with 7.5% povidone-iodine; and Group C, which received treatment with 10% povidone-iodine. Treatment consisted of aural toileting followed by povidone-iodine wash on day 0,4,7,10,14 in different groups. Base line total scores were recorded on day 0 by clinical and oto-endoscopic findings. Scores were measured and compared between different groups on day 7 and day 14. Patients ranged from 18 to 65 years. 10% of povidone-iodine demonstrated rapid response by day 7 in terms of symptomatic and clinical improvement ($p < 0.001$) compared to 5% and 7.5% of povidone-iodine. By the 14th day, 7.5% iodine group and 10% iodine group had comparable outcomes($p = 0.226$) , while 5% iodine group continued to have consistently poorer outcomes compared to both 7.5% and 10% iodine groups at both time points. The data collected from this study show that higher concentrations, such as 10% offer superior antifungal activity or quicker resolution of symptoms. This study reinforces the role of povidone-iodine as an effective treatment for otomycosis . Further research could explore long-term outcomes and the potential for resistance with different concentrations to optimize otomycosis management strategies.

Keywords: Otomycosis; Povidone Iodine; Aural Toileting; Fungal KOH; Nondiabetics.

INTRODUCTION

Otomycosis is a prevalent superficial fungal infection that affects the external auditory canal (EAC). The most common causative agents of otomycosis are molds of the genus Aspergillus and yeasts of the genus Candida, particularly the Aspergillus niger and Candida albicans[2]

Otomycosis is typically associated with various symptoms, including itching, otorrhea, ear pain, and ear blockage. The diagnosis of otomycosis is primarily based on the patient's history, clinical presentation, and otoscopic examination of the ear canal and eardrum. However, additional tests, such as microbiological analysis, may be necessary to confirm the diagnosis[1]

The antifungal treatments currently used for otomycosis include clotrimazole, bifonazole, miconazole, and tolnaftate. Antifungals such as clotrimazole or nystatin can be effective against Candida, but they do not cover Aspergillus.[*6].* Due to the rising prevalence of drug resistance among Aspergillus species causing otomycosis, it is crucial to select an appropriate treatment regimen. Additionally, the excessive and

unnecessary use of antifungals can lead to overgrowth of the organism in the external ear canal. Iodine, commonly used as an antiseptic has been introduced as an alternative, with no documented resistance to date [7]. Povidone iodine has been known to demonstrate activity against mature bacterial and fungal biofilms both in vitro and ex vivo[9].

Aural toileting, which involves cleaning the ear canal to remove debris and discharge, enhances the penetration and efficacy of povidone-iodine. This combination not only ensures thorough eradication of the fungal infection but also addresses the persistent problem of biofilm formation, which is a common cause of treatment failure and recurrence with topical antifungals.

In our study, we compared the efficacy of 5%, 7.5%, and 10% povidone-iodine, combined with aural toileting, in treating otomycosis to determine the most effective concentration. Our research aims to identify the optimal concentration of povidone-iodine for clinical use, potentially improving treatment outcomes and reducing the reliance on traditional antifungals.

AIM AND OBJECTIVE

AIM: To evaluate and compare the efficacy of 5%, 7.5%, and 10% povidone-iodine solutions in the treatment of otomycosis in non-diabetic patients.

OBJECTIVE: To determine the rate of clinical improvement and mycological cure in non-diabetic patients with otomycosis treated with 5%, 7.5%, and 10% povidone-iodine solutions over a specified treatment period.

MATERIALS AND METHODS

This randomized controlled trial (RCT) was conducted in the Department of Otorhinolaryngology at Saveetha Medical College and Hospital Chennai, from July 2023 to April 2024. This study was done to evaluate and compare the efficacy of 5%, 7.5%, and 10% povidone-iodine solutions in the treatment of otomycosis in non-diabetic patients. This study was approved by the Institutional Review Board, and Ethical Committee of Saveetha University, and the study was conducted by ethical standards established by the Declaration of Helsinki (2000). All patients were explained about the study and written informed consent was obtained before participation. A total number of 90 patients were included in this study. Our objective was to determine the rate of clinical improvement and mycological cure in nondiabetic patients with otomycosis treated with 5%, 7.5%, and 10% povidone-iodine solutions over a specified treatment period

Inclusion Criteria:

- Aged between 18 and 65 years.
- Patients with clinically and microbiologically proven otomycosis, confirmed by potassium hydroxide (KOH) preparation.
    - Patients with Intact tympanic membrane integrity.
    - HbA1c ≤ 5.6%, indicating non-diabetic status.
    - Willingness to participate and provide informed consent.
    - Able to attend follow-up appointments.

Exclusion Criteria:

- Aged below 18 and above 65 years
- Active/ Inactive chronic otitis media (COM) with disrupted tympanic membrane integrity.
- History of previous ear surgeries with mastoid cavities.
- Pre-diabetic or diabetic status (HbA1c > 5.6%).
- Presence of other immunocompromised states (e.g., HIV/AIDS, cancer, use of immunosuppressive drugs).
- Known hypersensitivity or allergy to povidone-iodine.
- Pregnant or breastfeeding women.
- Inability to follow study procedures or attend follow-up visits.
- Patients who were not willing to participate in the study.

Research Design:

All patients aged 18-65 years who meet the inclusion and exclusion criteria are enrolled in the study. Each patient had first undergone a clinical examination and otoendoscopic evaluation. A fungal KOH swab had been taken to confirm the diagnosis of otomycosis microbiologically. Subsequently, patients were assigned a baseline score based on clinical symptoms and otoendoscopic findings, which included the following.

EAR ITCHING	0-No symptom	1-Mild	2-Moderate	3-Severe
EAR DISCHARGE	0-No symptom	1-Mild	2-Moderate	3-Severe
EAR PAIN	0-No symptom	1-Mild	2-Moderate	3-Severe

EAC ERYTHEMA	0-No erythema	1-Mild	2-Moderate
EAC OEDEMA	0-No edema	1-Mild	2-Moderate

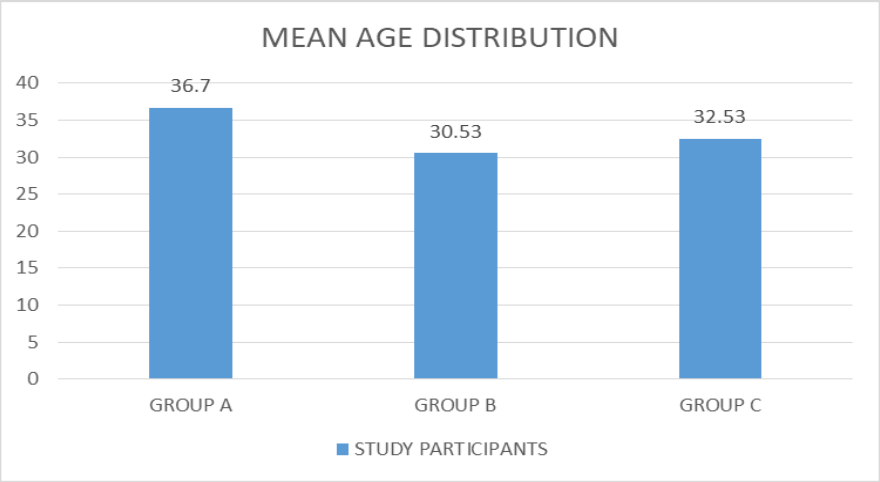
EAC DEBRIS	0-No Debris	1-Debris

Participants were randomly allocated into three groups: Group A, which received treatment with 5% povidone-iodine; Group B, which received treatment with 7.5% povidone-iodine; and Group C, which received treatment with 10% povidone-iodine. This was a double-blind study (both participants and investigator), with 90 lots prepared, 30 each labelled as Group A, Group B, and Group C. Each patient picked a lot and gave it to the nurse, who then prepared and administered 10 ml of either 5%, 7.5%, or 10% povidone-iodine solution in a 10 ml syringe to the investigator. Aural toileting was performed by suctioning under otoendoscopic visualisation, and the wash was administered with povidone-iodine at the assigned concentration. Participants were reviewed on days 4, 7, 10, and 14, during which aural toileting and povidone-iodine wash were administered at subsequent visits. Scores were calculated based on symptomatic and otoendoscopic findings on days 7 and 14 and compared with the baseline scores of day 0. On day 14, a KOH swab was taken from the external auditory canal to determine the presence or absence of fungal elements before aural toileting. Any participants with a positive KOH swab on day 14 were given topical antifungal ear

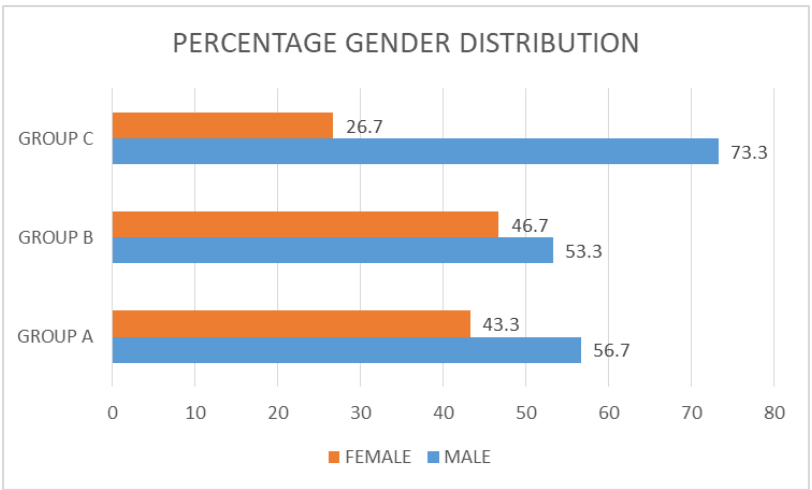
drops and followed up until cured. Statistical analysis was carried out using SPSS software version 19. The characteristics of the sample were summarized using mean (standard deviation) / median (interquartile range) and frequency(percentages) for quantitative and qualitative variables respectively. ANOVA/Kruskal Wallis test was used to compare the quantitative measurements between the three groups for the normally/not normally distributed data, followed by post hoc multiple comparisons, adjusted by Bonferroni correction. The chi-square test was used for categorical variables and the statistical significance was considered at 5% (p value<0.05)

RESULTS

The mean age of participants in Group A was 36.7 years (SD = 17.723), in Group B was 30.53 years (SD = 11.970), and in Group C was 32.53 years (SD = 14.260). There was no statistically significant difference in the mean ages among the three groups (p = 0.263).



Gender distribution also did not show a statistically significant difference among the groups (p = 0.235) In Group A, 17 participants were male (56.7%) and 13 were female (43.3%). Group B had 16 males (53.3%) and 14 females (46.7%). Group C comprised 22 males (73.3%) and 8 females (26.7%).

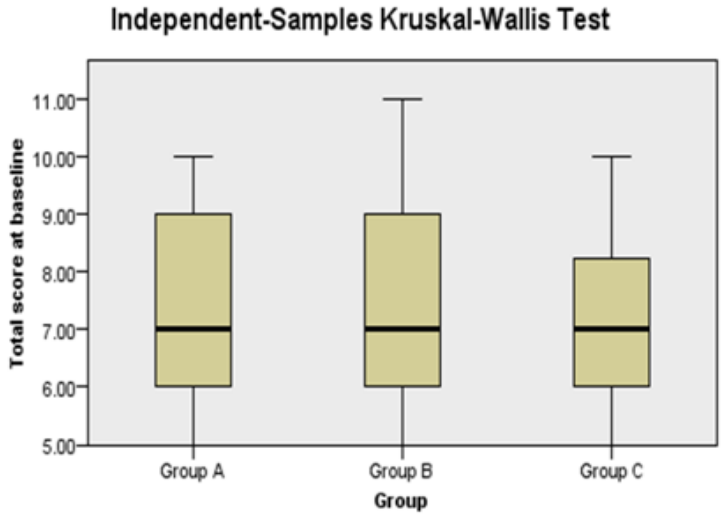


In group A 14 participants (46.7%), Group B 15 participants (60%), and in group C 14 participants (46.7%) were seen to have otomycosis in the right ear. Left-side otomycosis was observed as Group A had 15 participants (50%), Group B had 13

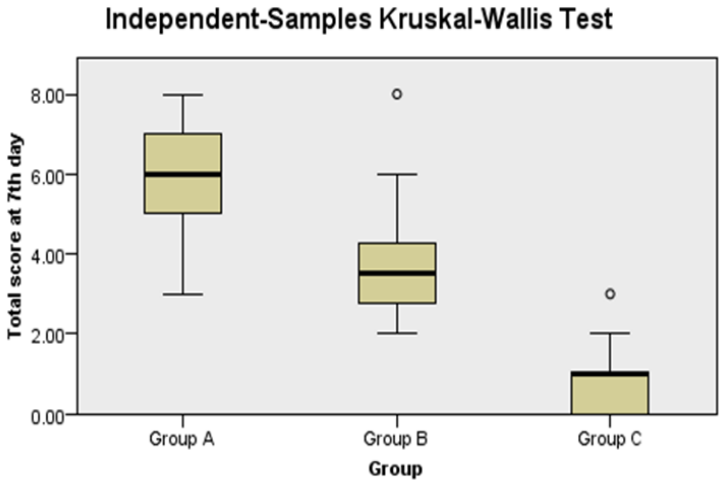
participants (43.3%), and Group C had 15 participants (50%). Both ear otomycosis was observed as Group A had 1 participant (3.3%), Group B had 2 participants (6.7%), and Group C had 1 participant (3.3%). There was no statistically significant difference in the distribution of the affected side among the three groups (p = 0.947).

At baseline (Day 0), the study compared three groups of 30 participants each across various clinical variables. For itching, ear discharge, and ear pain the severity ranged from grade 0 to grade 3. There was no statistically significant difference among the groups in terms of itching (p = 0.114). Pain levels varied across the groups without significant differences (p = 0.535). Ear discharge severity also showed no significant variation (p = 0.487).

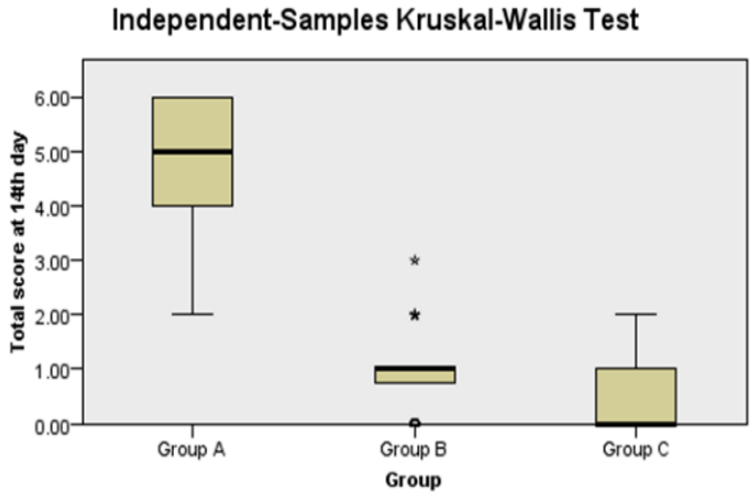
External auditory canal erythema and edema were similarly distributed among the groups, with p-values of 0.727 and 0.294, respectively. All participants in each group exhibited the presence of debris in the external auditory canal. The total scores on day 0, representing an aggregate measure, did not differ significantly among the groups (p = 0.389). The median baseline scores had no statistically significant differences across the groups for the assessed clinical variables, demonstrating comparability among the groups at the start of the study.



On Day 7, significant differences were observed among the three groups across several clinical variables. Group C showed the highest improvement in itching, with 73.3% of participants reporting no itching, compared to 23.3% in Group B and 13.3% in Group A (p < 0.001). For pain, 86.7% of Group C participants reported no pain, compared to 53.3% in Group B and 13.3% in Group A (p < 0.001). Ear discharge was absent in 96.7% of Group C, 20% of Group B, and 6.7% of Group A participants (p < 0.001). External auditory canal erythema was absent in 83.3% of Group C, 53.3% of Group B, and 3.3% of Group A participants (p < 0.001). External auditory canal edema was absent in 76.7% of Group C, 30% of Group B, and 3.3% of Group A participants (p < 0.001). External auditory canal debris was absent in 86.7% of Group C, 70% of Group B, and 16.7% of Group A participants (p < 0.001). The median total scores were 1 for Group C, 3.5 for Group B, and 6 for Group A, further reflecting significant differences among the groups (p < 0.001). These results indicated that Group C exhibited the most substantial improvements in all measured clinical variables.

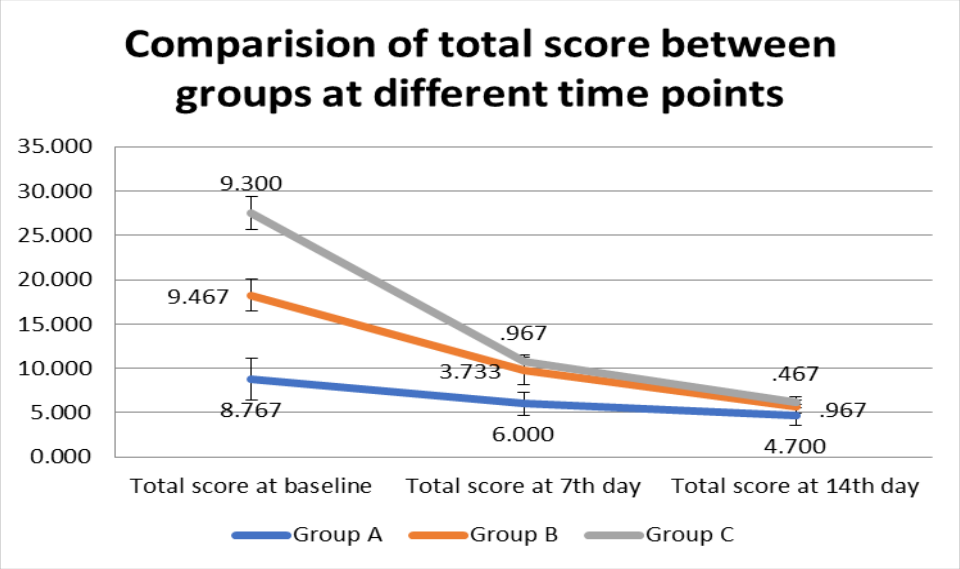


At the end of the study, On day 14 significant differences were observed among the three groups across various clinical variables. For itching, 93.3% of Group C participants reported no itching compared to 76.7% in Group B and 36.7% in Group A ($p < 0.001$). In terms of pain, 100% of Group C had no pain, compared to 80% in Group B and 23.3% in Group A ($p < 0.001$). Ear discharge was absent in 93.3% of Group C, 90% of Group B, and 6.7% of Group A participants ($p < 0.001$). External auditory canal erythema was absent in 86.7% of Group C, 93.3% of Group B, and 33.3% of Group A participants ($p < 0.001$). External auditory canal edema was absent in 80% of Group C, 73.3% of Group B, and 10% of Group A participants ($p < 0.001$). Additionally, debris was absent in 96.7% of Group C, 86.7% of Group B, and 23.3% of Group A participants ($p < 0.001$). The KOH test was negative for 90% of Group C, 83.3% of Group B, and 26.7% of Group A participants ($p < 0.001$). The median total scores were 0 for Group C, 1 for Group B, and 5 for Group A ($p < 0.001$).



The post hoc multiple comparison results revealed significant differences between the groups on both the 7th and 14th days. On the 7th day, Group A showed significant differences compared to Group B ($p < 0.001$) and Group C ($p < 0.001$), and Group B differed significantly from Group C ($p = 0.002$). By the 14th day, significant differences

persisted between Group A and both Group B ($p < 0.001$) and Group C ($p < 0.001$), but the difference between Group B and Group C was no longer significant ($p = 0.226$). These results suggest that by the 14th day, Groups B(7.5% iodine group) and C(10% iodine group) had comparable outcomes, while Group A(5% iodine group) continued to have consistently poorer outcomes compared to both Groups B and C at both time points.



DISCUSSION

The surface of healthy EAC skin hosts a variety of microbial species, including Staphylococcus spp., Corynebacterium spp., Bacillus spp., Streptococcus spp., Gram-negative bacilli such as Pseudomonas aeruginosa and Escherichia coli, along with fungi, predominantly Aspergillus and Candida species.[3].These microorganisms are typically saprophytic but can become pathogenic if the balance between bacterial and fungal growth is disrupted, especially when the body's defense mechanisms are compromised[4]. The external ear canal offers an optimal environment for mold growth and reproduction, resulting in an increase in otomycosis cases among both immunocompromised and immunocompetent individuals. [1]. The optimal duration of treatment to prevent recurrence is still under research and debate, though prolonged treatment durations have shown better outcomes. Povidone-iodine wash with aural toileting is preferred over topical antifungals for otomycosis treatment due to its rapid and effective fungal load reduction. Its broad-spectrum activity against a wide range of pathogens, including bacteria and fungi. It is particularly beneficial in mixed infections, potentially reducing the need for prolonged antifungal therapy and minimizing the risk of resistant fungal strains.

Povidone-iodine is a stable, inexpensive substance with no reported bacterial or fungal resistance, making it a suitable choice for otomycosis treatment in developing countries due to its low cost, effectiveness, and lack of ototoxicity. Prior research has demonstrated the effectiveness of povidone-iodine in treating otomycosis.

Swain SK et al. reported that proper aural micro-suctioning followed by the placement of povidone-iodine-soaked gel foam in the ear canal resulted in complete cessation of

recalcitrant otomycosis highlighting the potent antifungal properties of povidone-iodine, aiding in the management of persistent fungal infections in the ear [11].

A comparison of the efficacy of betadine (povidone-iodine) with clotrimazole in treating otomycosis by Mofatteh MR et al., concluded that both treatments were equally effective [10]. This supports the use of betadine as a viable antifungal option, potentially helping to mitigate the risk of developing resistant organisms.The study indicated that improvements were comparable in both treatment arms, thereby underscoring the role of povidone-iodine in otomycosis management.

In a comparative study by Ajay Philip et al., 7.5% povidone-iodine otic drops were tested against 1% clotrimazole with lignocaine drops. The results showed that both treatment regimens led to significant improvements, demonstrating the antifungal efficacy of povidone-iodine at this concentration [12].

In the context of the current study, evaluating 5%, 7.5%, and 10% povidone-iodine concentrations provides additional insights into optimizing otomycosis treatment. The findings from previous studies suggest that povidone-iodine is effective at lower concentrations, such as 7.5%, and comparable to established antifungal treatments like clotrimazole. Therefore, assessing higher concentrations, such as 10% could determine whether increased concentrations offer superior antifungal activity or quicker resolution of symptoms.

The comparison revealed that 10% of povidone-iodine demonstrated rapid response by day 7 in terms of symptomatic and clinical improvement compared to 5% and 7.5% of povidone-iodine. By day 14, the response with 7.5% and 10% povidone-iodine were almost identical, with no significant difference. However, 5% povidone-iodine showed poorer results on both day 7 and day 14 compared to 7.5% and 10% povidone-iodine. No side effects were observed in any of the participant groups.

CONCLUSION

This study reinforces the role of povidone-iodine as an effective treatment for otomycosis, consistent with previous research. The varying concentrations offer a range of therapeutic options, enabling tailored treatments that can be adjusted for efficacy and patient-specific needs. Further research could explore long-term outcomes and the potential for resistance with different concentrations to optimize otomycosis management strategies.

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