



Effectiveness Of 7.5 Percent Povidone-Iodine In Comparison To 1 Percent Clotrimazole In The Treatment Of Otomycosis

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Abstract

Background: Otomycosis or fungal otitis externa is a condition seen in any otolaryngology setup and can be quite frustrating for the patient and the doctor due to its recurring nature. It is a superficial, sub-acute, or chronic infection of the outer ear canal, usually unilateral characterized by inflammation, pruritus, pain, and scaling. Prevalence is more in tropical and subtropical humid climates. Candida and Aspergillus are the most common fungi isolated. The most common Aspergillus isolate was the niger species followed by the species of flavus and fumigatus. Treatment mainly comprises of thorough lavage of the ear and clearing all fungal debris mainly seated in the anterior recesses of the ear canal. Predisposing factors must be addressed and topical antifungals initiated. Clotrimazole is the most commonly used antifungal. This drug acts on the fungal wall making them to be more permeable and leading to their instability and later cell death. Povidone iodine is a widely used antiseptic, easily available, cheap, and seen to be effective in the treatment of bacteria, fungi, viruses, protozoa, and spores. No resistance is known so far to this antiseptic.

Aim & objective: This was a prospective randomized case-control study and its objective was to establish the effectiveness of povidone-iodine in the treatment of otomycosis to a commonly used antifungal, clotrimazole. Our secondary objective was to identify the most common fungal isolate in our hospital. The two drugs were compared to the improvement in symptoms and signs of the affected individuals.

Methodology: We conducted a prospective randomized case-control study of individuals who were clinically diagnosed with otomycosis in our ENT OPD at Apollo Institute Of Medical Sciences & Research, Chittoor, Andhra Pradesh, India in the year 2020. 270 individuals who satisfied the inclusion criteria were randomized, and blinded to the drug they would receive. The symptoms and signs were noted and a pretreatment ear swab was taken for culture. On follow-up after 2 weeks, their symptoms and signs were noted and a post-treatment ear swab was taken. Each of the pretreatment and post-treatment variables was compared and the efficacy of the drug was assessed.

Results: 34 patients, clinically diagnosed with otomycosis who fulfilled the inclusion criteria were assessed, and 8 were lost to follow-up. In our study, the condition was more prevalent in females below the 30 age group. Unemployed individuals topped the list followed by housewives. The left ear was most commonly affected involving 74 % of the cases. Pruritus was seen in 76.5% of our patients followed by otorrhoea. There was a close relationship between self-cleaning and the absence of wax. Mixed infection was more common (35.4%) and Aspergillus niger formed 60.86% of fungal isolates. Pseudomonas aeruginosa and non-fermenting GNB was the most common bacterial isolate. Both drugs showed a good response in symptoms and signs after

treatment and though comparable, were not statistically significant (p value >0.05). The result of this study supports the use of Povidone-iodine in the treatment of otomycosis, thus avoiding the emergence of resistant organisms.

Keywords: Otomycosis, fungal otitis externa, fungi, antifungals, clotrimazole, povidone-iodine, aspergillus, candida

Introduction

Fungal external otitis (otomycosis) is a common disease throughout the world. Its frequency varies according to different geographic zones. It is a prevalent disease in the tropics (1) and is sometimes associated with complications, involving the middle ear (2). It has been an entity that has perplexed many an otologist because of its recurrent nature. Since its description about 100 years ago by Andral and Cavarret in 1843 and by Mayer in 1844, (3) many attempts have been made in the diagnosis and the treatment of this condition. The disease is seen worldwide and it is estimated to constitute approximately 5-25% of the total cases of otitis externa (4). In a routine otolaryngology clinic, its prevalence ranges from about 9 percent to about 30.4 percent in individuals presenting with otitis externa. It was believed that fungi were secondary invaders in external canal infections and that one-third of the external otitis was caused due to fungi and the remaining were attributed to gram-negative bacilli (5). Traditionally, the treatment of otomycosis revolved around good personal hygiene and avoidance of self-cleaning. But the management varied as time progressed which ranged from copious lavage to insertion of meta cresyl acetate wick, boric acid, sulphathiazole ointment, topical ketoconazole, cresylate otic drops, and aluminum acetic drops in the affected ear (5). In recalcitrant cases, treatment with 75 rads of X-rays (6) has also been attempted. The use of metacresylacetate however had produced dermatitis and hence its use was discontinued. The medical treatment has abundant literature describing the use of various classes of drugs mainly antifungals in the topical treatment of otomycosis (7). However, there has never been a study that evaluated the role of iodine as an antifungal in otomycosis. It is a well-known fact that iodine is a routinely used antiseptic solution in surgical wards, because of its antibacterial

property which has never been resisted or conquered by any organism. (8)

Methodology: We conducted a prospective randomized case-control study of individuals who were clinically diagnosed with otomycosis in our ENT OPD at Apollo Institute Of Medical Sciences & Research, Chittoor, Andhra Pradesh, India in the year 2020. 270 The individuals who satisfied the inclusion criteria were randomized and blinded to the drug they would receive. The symptoms and signs were noted and a pretreatment ear swab was taken for culture. On follow-up after 2 weeks, their symptoms and signs were noted and a post-treatment ear swab was taken. Each of the pretreatment and post-treatment variables was compared and the efficacy of the drug was assessed. All patients with clinically diagnosed otomycosis, who satisfied the following inclusion and exclusion criteria. Inclusion Criteria: Age group- individuals from age 15-70 years. Exclusion Criteria: 1. Age group – less than 15 years and more than 70 years. 2. Chronic suppurative otitis media 3. Postoperative mastoidectomy cases. 4. Malignant otitis externa 5. Uncontrolled Diabetics 6. Patients with hearing aids. 7. Patients receiving chemotherapy and post-chemotherapy. The drugs were given in an open method. The drug was dispensed by a trained staff nurse. The principal investigator, staff nurse, and the patient were unaware of the drug being administered. The study was done in the ENT department at our tertiary hospital. All patients who presented in the outpatient department with symptoms of pruritus of the ear, ear ache, ear discharge, blocked sensation in the ear, tinnitus, or hard of hearing, were evaluated. The ear was inspected with an otoscope and a clinical diagnosis of otomycosis was made based on the history and presence of matted hyphae, spores, or curdy precipitate in the external auditory canal. The position of the otomycotic debris in the ear canal was

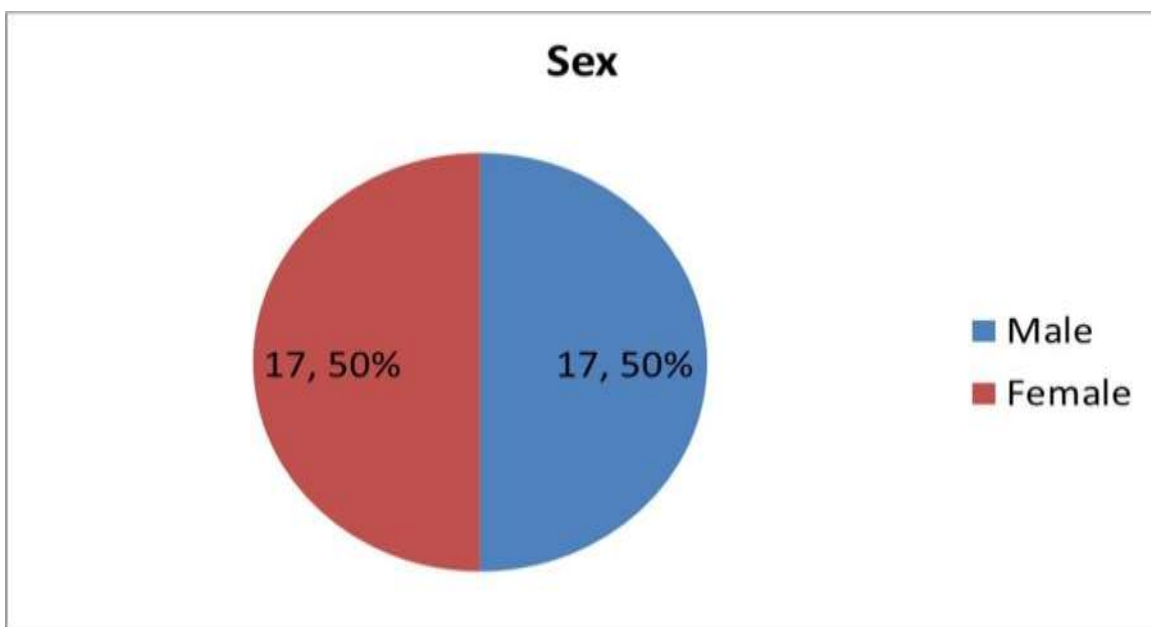
noted as lying in the isthmus, in the bony canal, or the cartilaginous canal. The presence of any erythema over the cartilaginous canal and bony canal was noted and the status of the tympanic membrane whether congested or perforated was noted. The presence of tragal tenderness or mastoid tenderness was looked for. Otomycotic debris was scooped out with a sterile swab and put in a sterile test tube containing 2 ml of normal saline. The sample was immediately sent for a fungal smear. The rest of the fungal debris was removed using a sterile suction tip. Fungal debris was teased onto a slide and stained with gram stain. The presence of fungi and bacteria was looked for. The ear swabs for this study was inoculated onto Blood agar (BA), Sabouraud's dextrose agar (SAB) with antibiotics & thioglycolate broth. BA was incubated at 37°C in a CO2 atmosphere and SAB & thioglycolate broth at 37°C for 18 hours. If there was a suspicion of fungal growth at the point of inoculation, the plates were incubated for a further 24 to 48 hours till sporulation occurred to facilitate identification. Fungal growth was identified by doing Lacto Phenol Cotton Blue (LPCB) preparation. After thorough toileting of the ear, the patient was sent to the ENT treatment room for administration of the study drug or the control drug by the sister in charge. At the beginning of the study itself, the drugs were sterilized according to the

randomization order generated by a computer, and the sister in charge was given sealed envelopes that contained the drug to be administered to the patient in a serial order. In the case of bilateral otomycosis, the more severely affected ear was taken as the test ear. The patient was advised to put 3 drops of the drug into the affected ear once a day. The patient was advised to clean his/her hands or the helper's hands before the installation. The instillation was done with the patient lying on his non-affected side or the side with fewer symptoms. The affected ear was placed upright and the pinna was pulled upwards, backward, and outwards to straighten the canal. The drops were instilled and the patient asked to remain in that position for about 10 minutes. He /She was asked to repeat this step every day for the next 13 consecutive days. At the end of the 2 weeks, the patient was reviewed in the OPD, and questioned regarding relief, persistence, or worsening of any symptoms or appearance of any new symptoms. The ear was re-examined under the microscope and the findings were noted and the repeat culture was taken from the ear. If there was no debris noted, a smear from the canal wall was taken.

Statistical analysis - All statistical analyses were performed using the statistical package for social science version 21.0 (SPSS Inc, Chicago, IL).

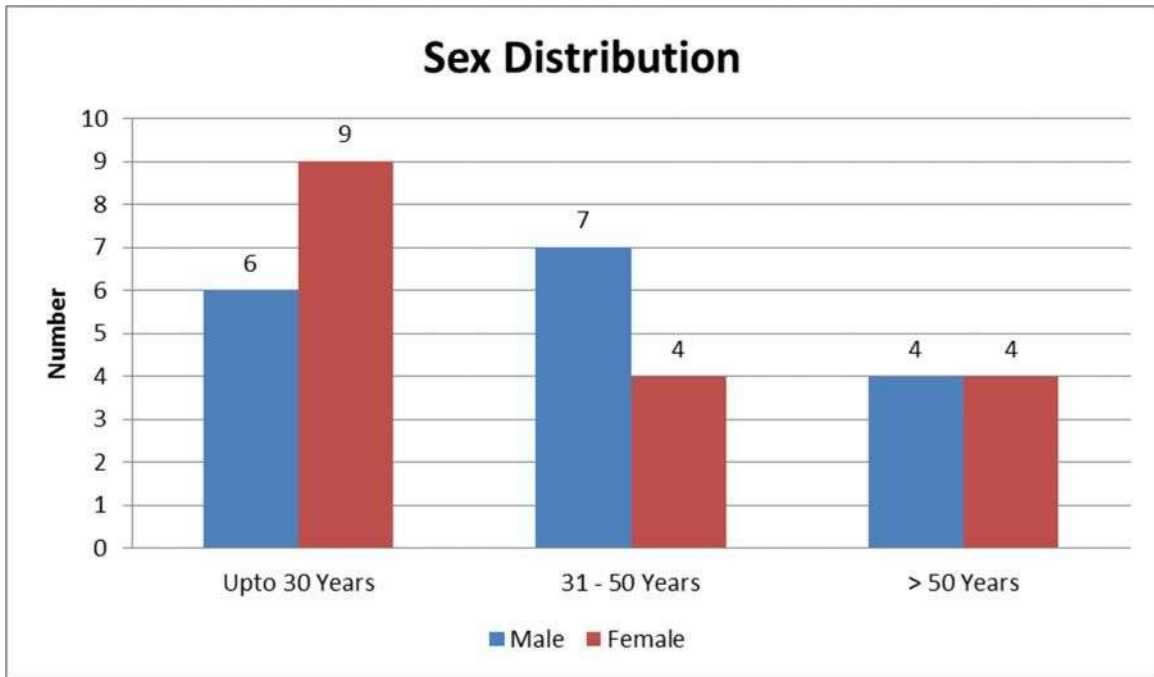
Results

Fig.1 Demographic details



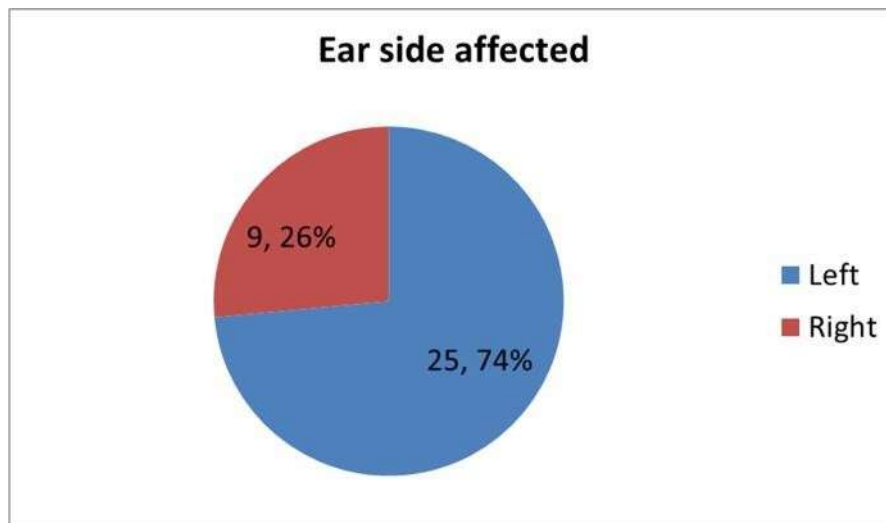
Our study showed an equal predilection in both genders (Fig 1).

Fig.2. sex distribution



The number of males and females in the three age groups was compared and it was found that there is a female predominance in the first age group, a male predominance in the second age group, and equal predominance of both genders in the third age group. The ‘p-value was 0.524. Since there is no significant difference between the sexes in each age group (p value>0.05), the groups are comparable (Fig.2).

Fig.3 ear side effected



74% of the individuals had involvement in the left ear, with the remaining 26% having involvement in the right ear (Fig 4).

Table :1 Symptoms- Pre-Treatment

Variables	Number of patients	Percentage
Pruritus		

Yes	26	76.5
No	8	23.5
Ear Discharge		
Yes	19	55.9
No	15	44.1
Otalgia		
Yes	18	52.9
No	16	47.1
Tinnitus		
Yes	10	29.4
No	24	70.6
Deafness		
Yes	7	20.6
No	27	79.4

Table :1 Pruritus was the most common symptom seen in 76.5% of the study followed by ear discharge, ear fullness, otalgia, tinnitus, and deafness in a descending order

Table:2 Signs- Pre-Treatment

Variables	Number	Percentage
Tragal Tenderness		
Yes	15	44.1
No	19	55.9
Cartilaginous canal wall erythema		
Yes	16	47.1
No	18	52.9
Cartilaginous canal wall edema		
Yes	12	36.4
No	21	63.6
Bony Canal wall erythema		
Yes	20	58.8
No	14	41.2
Bony Canal wall edema		

Yes	10	29.4
No	24	70.6
Ear discharge in the canal		
Yes	12	35.3
No	22	64.7
Tympanic membrane congestion		
Yes	23	67.6
No	11	32.4

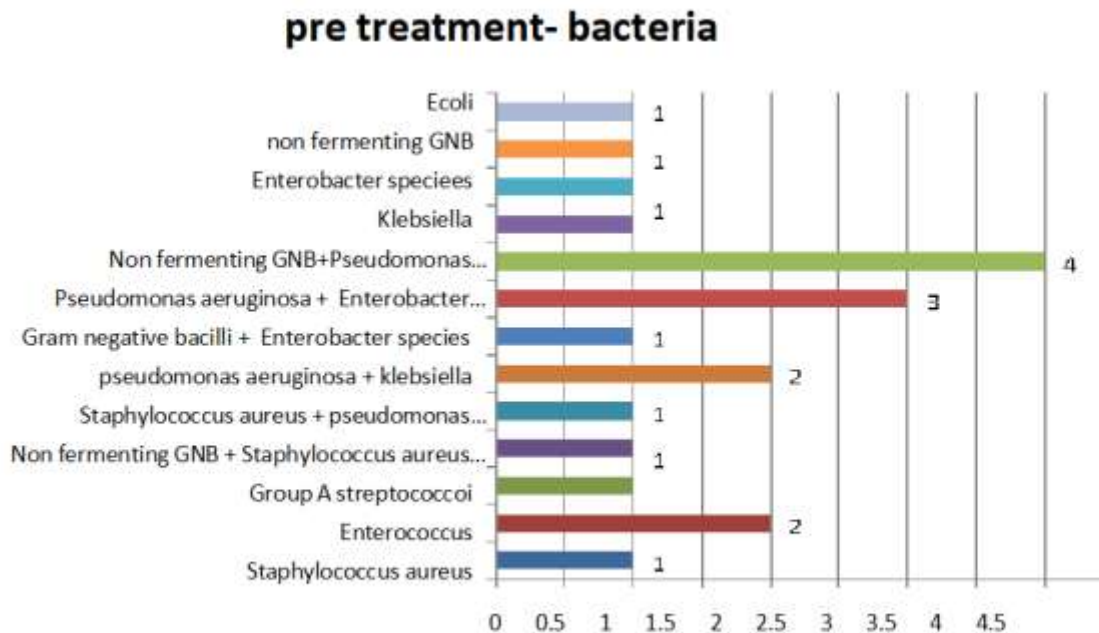
Tab.2. Tympanic membrane congestion was found in 67.6% of the individuals, followed by bony canal wall erythema, cartilaginous canal wall erythema, tragal tenderness, cartilaginous canal wall edema, ear discharge in the canal, bony canal wall edema in the descending order.

Table :3 Self -Cleaning And The Presence Of Wax

Variables	Number	Percentage
Self-Cleaning		
Yes	24	70.6
No	10	29.4
Wax		
Yes	10	29.4
No	24	70.6

Out of 34 individuals, 24 had a history of self-cleaning and 24 had no wax in the ears.

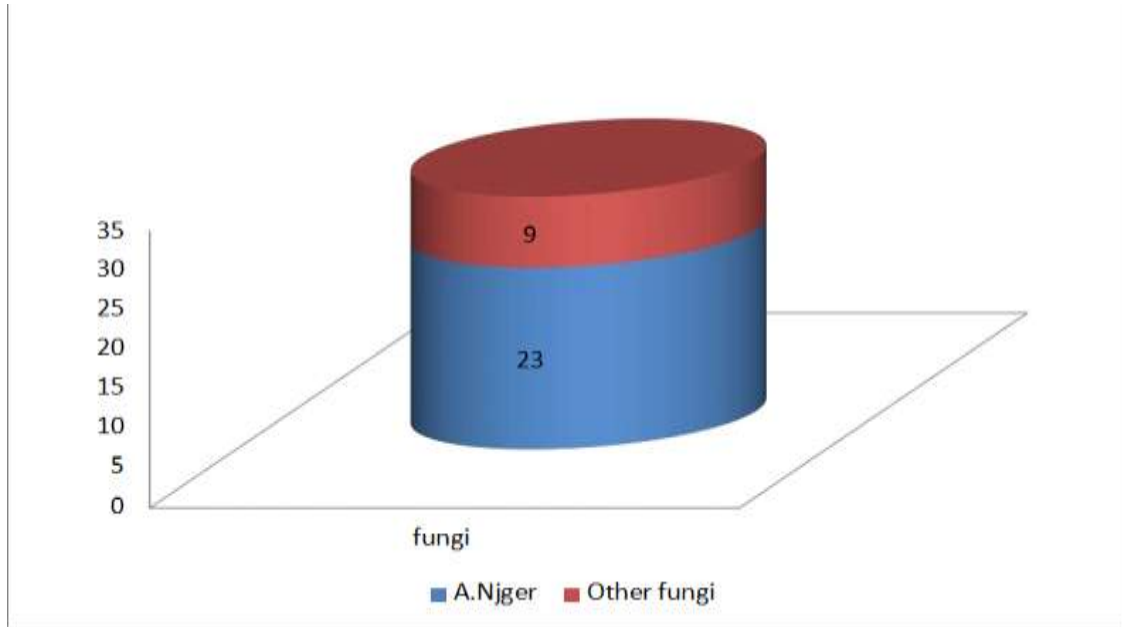
Graph:4 PRE-TREATMENT SWAB BACTERIAL FLORA



Graph :4

In pre-treatment ear swabs, (non fermenting GNB + pseudomonas aeruginosa) accounted for 11.8% of the cases, and (pseudomonas aeruginosa + enterobacter) species and staphylococcus aureus formed 8.8% of the cases. Among the fungi, aspergillus niger and aspergillus flavus was most commonly isolated (23.5%) and (aspergillus niger with yeast) formed 11.7% of the cases. Aspergillus niger was the most common fungi isolated, forming 60.86% of the isolates either in association with other fungi or in isolation and hence was the most commonly isolated species in our institution.

Figure:5 Distribution Of Fungi



The number of individuals with pure fungal infection was 32.3%. Number of individuals with pure bacterial infection was 32.3%, and Mixed infections were seen in 35.4 percent of the individuals.

Figure:6 clinically diagnosed otomycosis

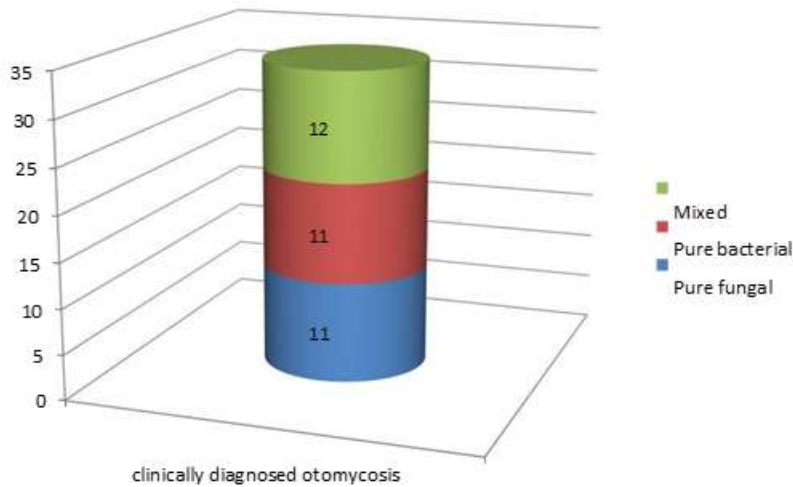


Figure .7. Post-treatment bacterial swab

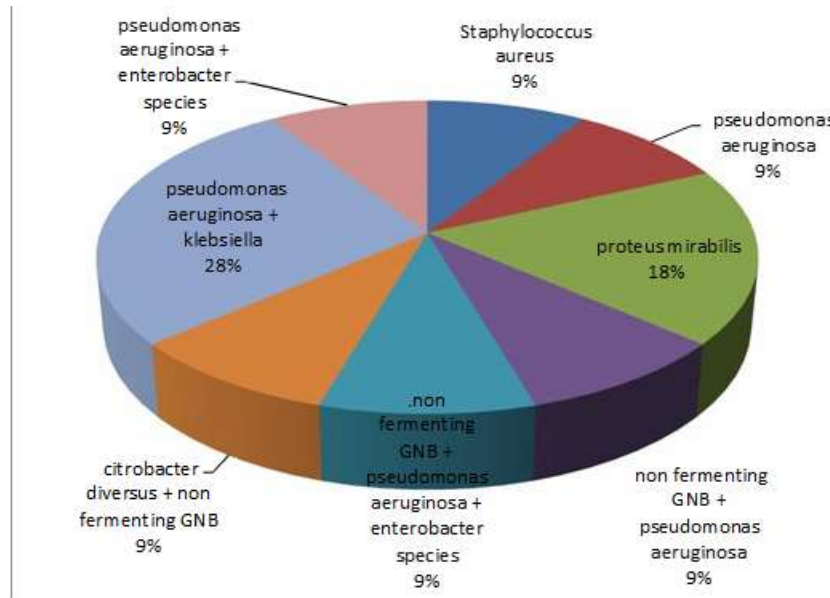
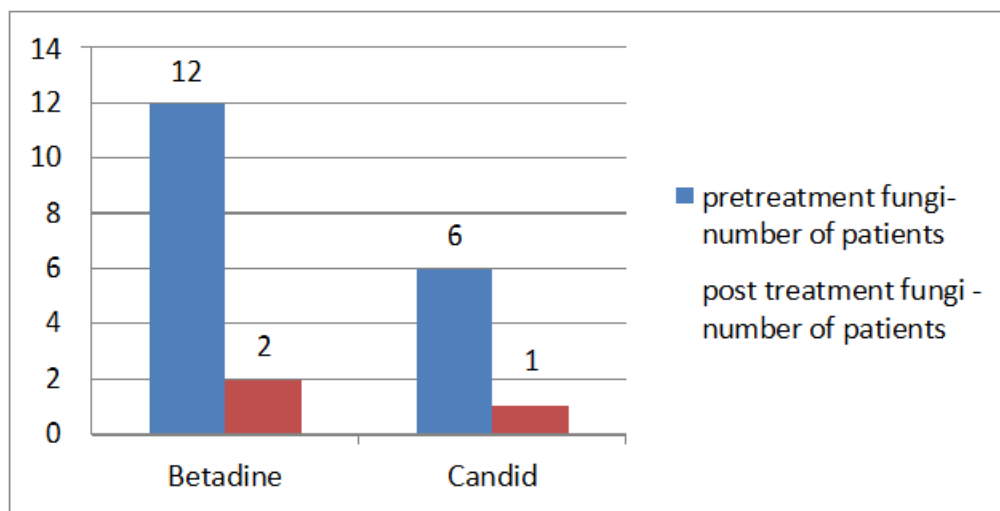


Fig.8 Number of patients with residual disease – fungus



After treatment with povidone-iodine nine of the smears grew bacteria, pseudomonas aeruginosa was the most common isolate followed by Enterobacter.

After treatment with clotrimazole and lignocaine, 3 had grown bacteria, with pseudomonas aeruginosa forming the most common isolate followed by non-fermenting gram-negative bacilli. Post treatment 23 of the patients had no fungal growth, 8 were lost to follow up and 3 had residual fungal infection out of which 2 belonged to the povidone-iodine group and 1 to the clotrimazole group. In the symptom profile, the clotrimazole group showed a resolution of symptoms in pruritus, ear discharge, fullness, tinnitus, and

deafness of 83.3%, 91.7%, 83.3%, 91.7%, and 91.7% respectively. However, there was a 100% resolution of otalgia. In the povidone-iodine group, there was complete resolution of deafness and tinnitus, whereas pruritus, ear discharge, and ear fullness had 93.3% resolution. However, the otalgia was resolved only in 86.7% of the cases. Considering tragal tenderness, 100% had relief of the symptom using both ear drops. There was no statistical significance between the 2 groups (p value>0.05), hence the groups are only comparable. Povidone-iodine had shown 100% resolution of both the cartilaginous wall erythema and the edema whereas the clotrimazole group showed a favorable response of 83.3% and 91.7%

respectively. There was no statistical difference between the groups (p value >0.05), hence the groups are comparable. Bony canal erythema had resolved in 91.7% and 93.3 % of the cases respectively which was not statistically significant (p value >0.05) and hence the two groups were comparable. Clotrimazole showed a 100 % resolution in the bony wall edema, ear discharge, and tympanic membrane congestion whereas povidone-iodine showed a resolution of 93%, 100%, and 86.7 % respectively. Both drugs had a 100 percent cure regarding bony wall edema. It was not statistically significant ($p > 0.05$) and hence the two groups were comparable. In view of the above findings, it can be stated that both drugs were equally efficacious in resolving the above symptoms and signs. But this could not be established as the statistical value was insignificant. Hence we recommend a study with a larger sample size to gather further information.

Discussion

Chronic suppurative otitis media, post-operative mastoidectomy cavities, and immunocompromised individuals are well-documented predisposing factors for this condition. Hence in our study, we excluded the above conditions and tried to analyze if there are any other factors for otomycosis. For complete disease clearance, management should address the underlying factors. (9) The basic principles of management of fungal otitis externa include effective aural toilet, identifying the causative organism, and eliminating it using the appropriate antifungal agent. Though systemic antifungals have been attempted in otomycosis, topical preparations are commonly used as these fungi cause superficial infections only. (10) Frequent relapses of otomycosis have been encountered due to the persistence of spores. Studies have shown that sub-epithelial spores persist despite using topical antifungal eardrops and hence stressed the importance of a longer duration of treatment and follow up. However in our study, on examination after 2 weeks of treatment, no spores were encountered. (11) Hence we emphasize meticulous aural toileting, especially in the region of the isthmus and the anterior recess. Several topical antifungal treatments have been tried in the past, these include the application of antiseptics such as gentian violet, boric acid, cresyl ate and aluminum acetate (Burrows Solution) but these drugs fell out of favor given their ototoxicity, when the condition was associated with a

perforation. Clotrimazole is a common antifungal of the azole group used in the treatment of otomycosis. It is used most commonly in combination with either topical antibiotics or steroid preparations. The drug was found to be effective in most other studies, achieving a cure rate of 95 % (7). (12) We planned to look at the efficacy of 7.5 % of the povidone-iodine solution in the management of otomycosis. 1% clotrimazole with 2% lignocaine in propyl glycerol base was used as the control drug. Our primary aim was to find an alternative to clotrimazole in the treatment of otomycosis. (13) We selected povidone-iodine as it is easily available and has been proven to be effective in chronic suppurative otitis media which is one of the predisposing factors of otomycosis. It is chemically stable, and inexpensive, and resistance in bacteria and fungi is yet to be reported. (14) Excessive and indiscrete use of any topical antibiotic and antimicrobials may lead to the emergence of resistant organisms. Povidone iodine overcomes this problem as there are no studies to date showing the development of resistance, which is an increasing cause of concern in this antibiotic-resistance era. (15) In developing countries like India and third-world countries, where a cheaper and more effective form of medication without ototoxicity is a requisite, povidone iodine forms a better choice. We removed confounding factors such as immunocompromised individuals, patients with hearing aids, and tympanic membrane perforations as they would need a longer duration of therapy as 2 weeks of treatment may not have sufficed. Very few studies have described the sex and age distribution, and the affected individuals mainly belonged to the 30-40 years age group (16) In our study, a larger number of individuals belonged to the age group 15-30 with a female preponderance. This was however not statistically significant. Unemployed individuals were seen as more affected by the disease followed by housewives. (17) The various factors taken in comparison of the drugs such as the patient's symptoms and signs were compared with the pre-treatment and post-treatment and tabulated. This is the first study in literature where we have graded signs and noted the resolution of signs after the treatment and hence can propose grading of otomycosis based on the signs. The signs and symptoms in this study of each drug were later Chi-squared and found to be insignificant (p value >0.05) and so the groups were comparable. The

majority of our patients presented with pruritus followed by otorrhoea, ear fullness, otalgia, tinnitus, and deafness when compared with other studies such as that in which otalgia was the major symptom followed by otorrhoea and hearing loss. (17) Pruritus would have instigated the individual to self-clean his ear, traumatizing the epithelium leading to maceration, and causing the introduction of fungal and bacterial organisms thus leading to infection. In our study, repeated self-cleaning seemed to have a close relation to the absence of wax. The majority of the patients had their left ear affected. (18) This probably would have been related to the handedness of the general population. The general population comprises mostly right-handed individuals. Use of the non-dominant hand would have caused more epithelial damage and hence infection. Further studies can be done including the handedness of the individual and ear side affected. Looking at microbial flora growth, studies have shown that mixed infections are quite rare as the fungi generally tend to inhibit bacterial flora. (19) In our study of clinically diagnosed cases of otomycosis, infection due to the mixed flora topped the list and we propose it may be due to the formation of bio-films which are known to be quite resistant to the topical agents commonly used. This may also explain the recurrent nature of otomycosis. Further research will be necessary to confirm this. (20) The commensals residing in the ear of a normal individual are the *Staphylococcus epidermidis*, *Corynebacterium* spp, *Bacillus* spp, Gram-positive cocci (*Staphylococcus aureus*, *Streptococcus* spp, non-pathogenic micrococci), Gram-negative bacilli (*Pseudomonas aeruginosa*, *Escherichia coli*, *Haemophilus influenza* and *Moraxella cararrhalis*) and mycelial fungi of the *Aspergillus* genus or yeast-like fungi, particularly *Candida* spp. Our pretreatment smears had a predominance of Non fermenting GNB and *Pseudomonas aeruginosa*, and 75% of this group had an association with fungus. Our studies tallied with most of the others in isolating *Aspergillus niger* as the most common species. (21) Hydrogen peroxide is irritative to the skin and its application to an already erythematous ear canal may cause the patient more discomfort (66). It causes effervescence and must be only used under supervision. Alcohol rapidly destroyed biofilms of *staphylococcus epidermidis*. *Candida* has been known to form biofilms, especially

in dwelling catheters and studies are now suggesting biofilm formation of *aspergillus* species with bacteria. (22) There has been no literature showing biofilms as a cause for recurrent external auditory canal infection, hence we strongly suggest that the recurrence and persistence of the disease is not just a result of spores, but probably due to biofilm formation. Oral antibiotics are indicated when co-existing bacterial infection results in incomplete resolution of the canal infection or when cellulitis of the external auditory canal sets in. Unlike other studies which compared only the symptoms and the culture, we categorized the signs as confined to various parts of the ear canal, and the tympanic membrane and concluded that most of the patients had tympanic membrane congestion followed by bony and cartilaginous wall erythema. (24) Fungal debris was most commonly noted in the bony cartilaginous isthmus, suggesting a defective epithelial migration and failure of normal lateral excursion in the removal of the offending organism, thus forming a nidus for fungi to thrive on. (25)

Conclusions

The result of this study supports the use of Povidone-iodine in the treatment of otomycosis, thus avoiding the emergence of resistant organisms. Future studies in larger groups of patients are necessary to see which is more effective. This study has opened a window in the application of povidone-iodine in clinically diagnosed cases of otomycosis in humans in addition to the management of chronic suppurative otitis media.

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