Type of Antifungals: Does it Matter in Empirical Treatment of Otomycosis?

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Abstract To evaluate the efficacy of clotrimazole, miconazole and fluconazole in empirical treatment of otomycosis in our tertiary care hospital and to appraise possible better outcome in otomycosis. Two hundred and ninety five patients who presented with clinical otomycosis at our Melmaruvathur Adiparasakthi Institute of medical sciences were incorporated in this study. Two hundred and fourteen patients who satisfied our criteria were recognized and they were randomly alienated into three groups A, B, C. Group A patients were advised to instill clotrimazole ear drops by themselves. Miconazole cream instillation were done by our trained personal in group B patients. Group C patients were advised to use fluconazole ear drops. Patients were educated to keep ear dry and instructed to come for evaluation in first and second week after initial visit. A randomized double blinded prospective study. In the first week, clotrimazole had a good response than miconazole and fluconazole in our patients and in the second week, our patients showed a drastic response in patients instilling flucanazole ear drops compared to those using micanozole and clotrimazole. This better outcome doesn't show statistical significance since p value is 0.882. Clotrimazole drops, miconazole cream and Fluconazole drops showed almost same therapeutic efficacy in Otomycosis

Keywords Otomycosis · Topical antifungals · Miconazole · Topical azoles · Fungal otitis externa

Introduction

Otomycosis is the term coined to denote fungal infection of the external auditory canal. Nowadays it is one of the common clinical conditions seen in otorhinolaryngology department due to widespread usage of broad spectrum antibiotics, steroids and antibiotic ear drops [1]. Prevalence of otomycosis depends on geographical area (well seen in tropical and subtropical humid climates) and environmental factors like temperature, humidity and time of the year. Naturally cerumen has a protective role against the growth of fungi and bacteria due to its contents [2], but Raymanundo Munguia accused cerumen as a supporting element for fungal growth [3]. Aspergillus and candida are the common organisms found in otomycosis. Aspergillus Niger is found to be predominant organism [4, 5].

Controversy exists in between the authors regarding the selection of treatment in otomycosis. Some authors believe that treatment of otomycosis depends on the identification of species and its susceptibility [6, 7]. Another set of authors suggested that treatment depends on the drug's efficacy regardless of the causative agent [8, 9]. Pertaining to treatment of otomycosis, various topical antifungal agents are available in markets. Many authors conducted both in vivo and in vitro studies for otomycosis. Nystatin, azole group, ciclopiroxolame, tolnaftate, mercurochrome, aluminium acetate drops [10], cresylate drops [10], boric acid [11] were used in vivo studies. Aqueous garlic extract [12], concentrated garlic oil [12], amphotericin, itraconazole, voriconazole [13], terbinafine [14] were tried in vitro studies. We were very interested to conduct a study in otomycosis and compare the clinical

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outcome of three easily available topical azoles i.e. clotrimazole drops, miconazole cream and fluconazole drops.

Materials and methods

This study was conducted in our hospital from September 2012 to April 2013. 295 patients of age (10–74) years who presented with clinical otomycosis were enrolled in this study. The criterion of clinical otomycosis was distinctive findings on otoscopic examination. The classical appearance was either grayish white mass similar to wet blotting paper or blackish spores in the external auditory canal. Patients with chronic suppurative otitis media, those who underwent surgery for chronic discharging ear and patients with bilateral disease were excluded from our study.

Detailed history were taken from two hundred and fourteen patients who fulfilled our criteria. Then samples were collected and sent to microbiological department for fungal identification and culture inoculation. Aural toileting were done in all the patients with suction in the OP department itself. To ensure double blindness and proper administration of medication, a trained nursing assistant, who was not involved in evaluating the patients was utilized. She grouped the patients randomly, applied the first dose of ear medication and instructed the patients to avoid water entering into their ears. Group A (72) patients were advised to instil clotrimazole 1 % ear drops, 3–5 drops three times a day. Group B (71) patients were treated with two application of miconazole cream, once during initial visit and second application during first week review for persistent disease. Miconazole was applied in the external auditory canal by loading in a 2 cc syringe attached with a regular 18 gauge suction tip. The viscosity of miconazole cream and the shape of the external auditory canal were considered to play a vital role in holding miconazole. Group C (71) patients were instructed to use fluconazole drops, 3–5 drops three times a day in affected ear. All of them were followed up in the end of first and second week. The patients and investigators remained blinded throughout the study.

Response to the treatment in three groups are tabulated as follows

Good response: External auditory canal is dry.

Moderate response: External auditory canal is filled with minimal secretion.

No response: External auditory canal is filled with full secretion.

Results

Out of 214 patients in our study, 128 (59 %) patients were female and 86 (41 %) patients were male. Right ear (67 %) involvement is more than left ear. The presenting complaints of otomycosis in the descending order are as follows: ear pain (49 %), ear block (28 %), ear itching (15 %) and ear discharge (8 %). All the 214 patients were randomly divided into three groups i.e. A, B, C (Fig. 1) and they were instructed to come for follow up in first week (Table 1).

Reports of all those in three groups i.e. microbiological confirmation of fungal growth either in smear identification or culture growth were collected (Table 2). Out of 214 patients, 116 (54.2 %) patients had *aspergillus niger*, *Candida albicans* in 53 (24.7 %), *Aspergillus flavus* in 9 (4.2 %), *Aspergillus fumigatus* in 6 (2.8 %), but 30 patients (14 %) had no fungal elements.

One hundred and seventy seven patients who attended our OP department in the first week, 19 patients came with negative report in microbiological analysis of fungus (Table 3) and remaining 158 patients were advised for second week review (Table 4).

The treatment response in the first and second week visits were properly collected (Table 5). In the first week follow up, Group A (Clotrimazole) has a good response than Group B (miconazole) which is followed by Group C (fluconazole). Surprisingly in the second week, Group C (fluconazole) had a good response than Group A (Clotrimazole) which is followed by Group B (miconazole).

Discussion

We conducted this study because otomycosis is a very common condition in our OP department. This disease is well prevalent in people coming from rural area surrounding our institution. There is a female predominance (59 %) in our study, which well correlates with the studies by Jia X [15] and Yehia MM [16]. The most common presenting complaint in our study is ear pain, which is same in Tang Ho study [10], but Kurshid Anwar coded hearing loss as the most common presentation in otomycosis [17]. Right ear involvement is appreciated more in

Fig. 1 Distribution of patients in three groups

Table 1 Attendance of patients in first week review

Follow up	Frequency	Percent
Absent	37	17.3
Reviewed	177	82.7
Total	214	100.0

Table 2 Microbiological results in total subjects

Microbiological confirmation of fungus	Frequency	Percentage
Positive	184	85.99
Negative	30	14.01
Total	214	100.0

Table 3 Microbiological results in combination with first week attendance

Follow up	Positive frequency	Percent	Negative	Percentage	Total
Absent	26	70.27	11	29.73	37
Reviewed	158	89.27	19	10.73	177
Total	184	85.98	30	14.02	214

Table 4 Attendance in second week review

Follow up	Frequency	Percent
Absent	13	8.23
Reviewed	145	91.77
Total	158	100.00

our study which may be because of ear manipulation with unsterile objects to alleviate ear itching in right handed individuals. Sathish also described right ear predominance

in the involvement of otomycosis [18]. We got histories of oil instillation, scratching with sharp instruments like keys, hairpins in the ear canal, turban usage while working in agricultural fields in our patients. This triggered us to evaluate predisposing factors in detail and local practices to clean the ear. The major predisposing factors in 184 microbiological positive cases were ear trauma (63.6 %), eardrops and oil instillation (51.6 %), turban usage (34.7 %) and swimming (16.8 %). Ashish kumar expressed concomitant dermatomycosis as the commonest predisposing factor and swimming as the least predisposing factor [19]. In our study, we have not seen even one single case of associated dermatomycosis.

All the patients with clinical otomycosis were routinely treated with antifungal topical medication even without sending to microbiological examination. We were surprised to view the negative microbiological results in 14 % of clinical diagnosed otomycosis, which is also documented by Ahmad Yaganeh moghadam [20] in his study.

Solubility, viscosity, tonicity, surfactant and preservatives were usually considered in the preparation of topical ear medications. Viscosity is very important in keeping the medication to work in the ear canal. Thin medication will easily drain out of the ear canal whereas thick medication won't reach inner recess of the ear. There is always many merits and demerits in using various types of topical medications. Cream is roughly a mixture of half water and hair oil. Cream formulation will spread easily, it will be well absorbed and less sticky compared to ointments. So it is very useful in treating oozing and "wet" skin conditions like otomycosis. Ointments has 80 % oil and 20 % water content which helps in treating "dry" conditions in skin. We selected miconazole in cream base for our study because of well absorption. While using Clotrimazole

Table 5 Treatment response in three groups

		First week						Total			By using Friedman test <i>P</i> value
		No response		Moderate response		Good response					
		Count	%	Count	%	Count	%	Count	Total	% of the study population	
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		First week									0.371
A	Clotrimazole	13	25.49	15	29.41	23	45.10	51	32.28		
B	Miconazole	16	29.09	17	30.91	22	35.42	55	34.81		
C	Fluconazole	17	32.69	21	40.38	14	28.89	52	32.91		
Total		46	29.11	53	33.54	59	37.34	158	100		
		Second week									0.882
A	Clotrimazole	4	8.70	5	6.82	37	83.00	46	31.72		
B	Miconazole	3	6.00	4	12.77	43	81.60	50	34.48		
C	Fluconazole	2	4.08	4	6.98	43	84.30	49	33.79		
Total		9	6.21	13	8.97	123	84.83	145	100		

drops (oil base), Fluconazole (water base), we advised our patients to maintain head position for 5 min after instillation of ear drops.

In the first week of follow up, we elicited best results with clotrimazole among the three groups. Sufian Alnawaiseh found a good response with miconazole cream than clotrimazole drops in the whole of the 2 week study [21]. we were surprised to see good response with fluconazole than others in the second week, which very well correlates with Sathish study [18]. Though Fluconazole exhibited good response in our study comparing with miconazole cream and clotrimazole, this difference doesn't show statistical significance since p value is 0.882. This insignificant statistical response may be because of small scale study and patient's noncompliance in review. Our comparison of three azole antifungal groups in three different forms (water base, oil base, cream base) shows almost the same therapeutic effects in otomycosis. Though we are discussing more about the topical antifungals, there may be need of aggressive systemic antifungal therapy in immunocompromised patients because of possibility of invasive otomycosis

Conclusion

Clotrimazole drops, miconazole cream and Fluconazole drops had same therapeutic efficacy in our study. So we have a liberty to choose any one of topical azoles in otomycosis and also they are considered to be safe since they had no ototoxic property which was already proved by many authors.

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