Clinical audit of the microbiology of otorrhoea referred to a tertiary hospital in Singapore

Crystal Shuk Jin Cheong[1], MBBS, MRCS, *Licia Mei Ling Tan*[1], MB BCh, *Raymond Yeow Seng Ngo*[1], MRCS, FAMS

INTRODUCTION Otorrhoea is a common complaint in Ear, Nose and Throat clinics. This study aimed to establish the pathogens involved in cases of otorrhoea in Singapore, their sensitivity patterns and the effectiveness of empirical management.

METHODS A retrospective chart review was conducted on 91 patients with otorrhoea who had undergone swab cultures between July 2010 and February 2011.

RESULTS Of the 91 cases, 53% were diagnosed empirically as bacterial otitis externa and 25% as otomycosis. Aerobic bacteria accounted for 35.8% of the microorganisms cultured, while 34.7% were fungi and 29.5% were anaerobic bacteria. *Pseudomonas* (*P.*) *aeruginosa* and *Staphylococcus* (*S.*) *aureus* made up 31.6% and 21.0% of the microorganisms, respectively. 20% of *S. aureus* grown was methicillin-resistant. *Aspergillus* was the most common fungus and 19% of cultures were polymicrobial. 38% of patients had their treatment changed on the basis of culture results, as no improvement was observed on follow-up. *P. aeruginosa* was sensitive to ciprofloxacin and gentamicin in 81.8% and 76.0% of patients, respectively, while *S. aureus* was sensitive to cloxacillin in 93.8% and clindamycin in 87.5% of patients.

CONCLUSION The common microorganisms involved in otorrhoea in Singapore are *P. aeruginosa*, *Aspergillus* and *S. aureus*. Resistant strains of *Pseudomonas* spp. are now present. Methicillin-resistant *S. aureus* is increasingly prevalent and highly sensitive to vancomycin. Aminoglycoside and fluoroquinolone-containing eardrops are suitable first-line topical antimicrobials. Cloxacillin may be started should a concomitant oral antimicrobial be warranted empirically or for *S. aureus* infections. Otomycosis should be considered in patients who show no improvement with antibiotics.

Keywords: chronic suppurative otitis media, ear discharge, otitis externa, otomycosis, otorrhoea
Singapore Med J 2012; 53(4): 244–248

INTRODUCTION

Otorrhoea is a common complaint in Ear, Nose and Throat (ENT) clinics worldwide.[1] Otitis externa, an inflammatory condition involving the ear canal, is a usual cause of ear discharge. Otitis media, in both the acute and chronic form, with perforation of the tympanic membrane can also lead to otorrhoea. The microbiology of these conditions has traditionally been primarily due to aerobic bacteria, followed by anaerobic bacteria and then fungi. However, the treatment of otorrhoea is not straightforward due to the polymicrobial nature of the disease.[2] The rise of resistant strains in recent years has highlighted the need for culture-directed treatment, particularly in chronic or seemingly recurrent cases.[3] The climate of the geographical area studied also influences the spectrum of microorganisms implicated.[4] Aural toileting is important in the successful treatment of otorrhoea, in addition to assisting in the procurement of discharge for ear cultures. In this study, we documented the pathogens that caused otorrhoea in our patient sample and their resistance patterns in Singapore, as well as the effectiveness of antimicrobials started in the community and a tertiary hospital clinic.

METHODS

A retrospective chart review was conducted on patients who presented with otorrhoea and had undergone swab cultures during their first consultation at the ENT clinic in the National University Hospital (NUH), Singapore from July 2010 to February 2011. All patients with otorrhoea had been offered an ear swab by the department as part of an internal audit since 2010. Patients for this study were gathered by electronically retrieving the swab cultures undertaken during the above period and selecting those who met the inclusion criteria for our study. Approval for this study was granted by the National Healthcare Group (NHG) Domain-Specific Review Board. The swab was obtained under microscopic guidance prior to aural toileting for patients, and sent for culture and sensitivity testing on routine bacteriological media.

Patients who had previous ENT consultations in our hospital for otorrhoea in the last three months, or previous operations on the involved ear were excluded. Prior treatment received in the community was recorded. The relationship between the antimicrobials started empirically at initial presentation, the culture results and effectiveness of empirical treatment was recorded in percentages. Facultative anaerobic bacteria were classified as anaerobes for the purpose of this study. 'Prior treatment' was defined as the use of topical and/or oral antimicrobials within the seven days before presentation at our clinic. 'Symptom resolution' was defined as an absence of otorrhoea and other commonly

[1]Department of Otolaryngology, Head and Neck Surgery, National University Health System, Singapore
Correspondence: Dr Raymond Ngo, Consultant and Assistant Professor, Department of Otolaryngology, Head and Neck Surgery, National University Health System, 1E Kent Ridge Road, NUHS Tower Block, Level 7, Singapore 119228. raymond_ngo@nuhs.edu.sg

Table I. Diagnoses of patient at initial presentation (n = 91).

Diagnosis	No. of cases (%)
Bacterial otitis externa	48 (52.7)
Otomycosis	23 (25.3)
Chronic suppurative otitis media	16 (17.6)
Acute otitis media with tympanic membrane perforation	3 (3.3)
Myringitis	1 (1.1)

Table II. Spectrum of microorganisms cultured.

Microorganism species	No. of cultures (%)
Pseudomonas aeruginosa	30 (31.6)
Aspergillus	19 (20.0)
Methicillin-sensitive *S. aureus*	16 (16.8)
Candida	14 (14.7)
MRSA	4 (4.2)
Acinetobacter baumannii	3 (3.2)
Enterobacter cloacae	2 (2.1)
Streptococcus anginosus	1 (1.1)
S. lugdunensis	1 (1.1)
Acinetobacter haemolyticus	1 (1.1)
Bacteroides fragilis	1 (1.1)
Peptostreptococcus spp.	1 (1.1)
Escherichia coli	1 (1.1)
Prevotella	1 (1.1)

S.: *Staphylococcus*; MRSA: Methicillin-resistant *Staphylococcus aureus*

associated complaints such as ear itch, otalgia, as well as a swollen or erythematous external auditory canal.

RESULTS

A total of 91 patients (48 male and 43 female) underwent swab culture for otorrhoea between July 2010 and February 2011. The patients were aged 5–96 (mean 39, median 35) years. The empirical diagnoses made on initial presentation are shown in Table I. 53% of the patients were diagnosed as having bacterial otitis externa, while 25% were diagnosed as having otomycosis and 18% were diagnosed with chronic suppurative otitis media (CSOM).

The full spectrum of microorganisms cultured is shown in Table II. Aerobic bacteria formed the majority of the microorganisms cultured (35.8%), followed by fungi (34.7%) and anaerobic bacteria (29.5%). *Pseudomonas* (*P.*) *aeruginosa* was the most prevalent strain, accounting for 88.2% of all cultured aerobic bacteria. *Staphylococcus* (*S.*) *aureus* constituted 71.4% of the anaerobes grown, one-fifth of which were methicillin-resistant *S. aureus* (MRSA). Table III demonstrates the polymicrobial background of otorrhoea – 62.6% of cultures yielded a single microorganism, while 19.8% grew at least two microorganisms. The composition of microorganisms is further subdivided in Table IV. Aerobic and anaerobic bacteria were grown in 9.9% of cultures, while 5.5% grew both fungi and bacteria. Treatment

Table III. Polymicrobial nature of cultures.

No. of microorganisms per culture	No. of cultures (%)
1	57 (62.6)
2	13 (14.3)
≥ 3	5 (5.5)
Normal flora	8 (8.8)
No growth	8 (8.8)

Table IV. Composition of microorganisms cultured.

Composition	No. of cases (%)
Solely aerobic bacteria	23 (25.3)
Solely anaerobic bacteria	13 (14.3)
Aerobic and anaerobic bacteria	9 (9.9)
Solely fungi	25 (27.5)
Fungi and bacteria	5 (5.5)
Normal flora	8 (8.8)
No growth	8 (8.8)

had been given by general practitioners in the community or emergency departments in 55 out of 91 (60.4%) cases. Of these, topical antibiotics had been prescribed to 42 patients and oral antibiotics to 34 patients, of which 27 were amoxicillin +/– clavulanic acid. 21 patients had been prescribed antibiotics via both the topical and oral routes. None had been started on antifungal medications. The primary cause for failure of therapy started in the community was found to be inappropriate antimicrobial selection in 37 patients. The most common cause was a failure to treat for fungal infection in 21 of the 37 patients.

About 38% of patients underwent a change in antimicrobial treatment, guided by culture results due to persistent ear discharge seen on follow-up visits (Fig. 1). Following the change in therapy, 57.1% of cases were documented to have resolved, while the remaining cases were lost to follow-up and thus presumably resolved. Of the 25 cultures that grew solely fungi, only 14 had been diagnosed as otomycosis, and the patients were started on antifungal agents on their initial visit to our clinic. *P. aeruginosa* was found to be sensitive in 18 out of 22 (81.8%) patients tested with ciprofloxacin and in 19 out of 25 (76.0%) patients tested with gentamicin. Methicillin-sensitive *S. aureus* demonstrated sensitivity to cloxacillin in 15 out of 16 (93.8%) cases and to clindamycin in 14 out of 16 (87.5%) cases. All of the four MRSA cases in our study were sensitive to vancomycin, while 75.0% of cases were sensitive to fusidic acid and 25.0% to co-trimoxazole.

DISCUSSION

It has been shown in the literature that the most common bacteria involved in otitis externa and chronic suppurative otitis media worldwide are *P. aeruginosa* and *S. aureus*.[2,3,5] A study conducted at the same hospital (NUH) in 1998 by Loh et al found that coagulase negative *Staphylococcus* was the most common bacterium isolated in acute diffuse otitis externa in Singapore and *Aspergillus* the most common fungus.[6] Our study has shown

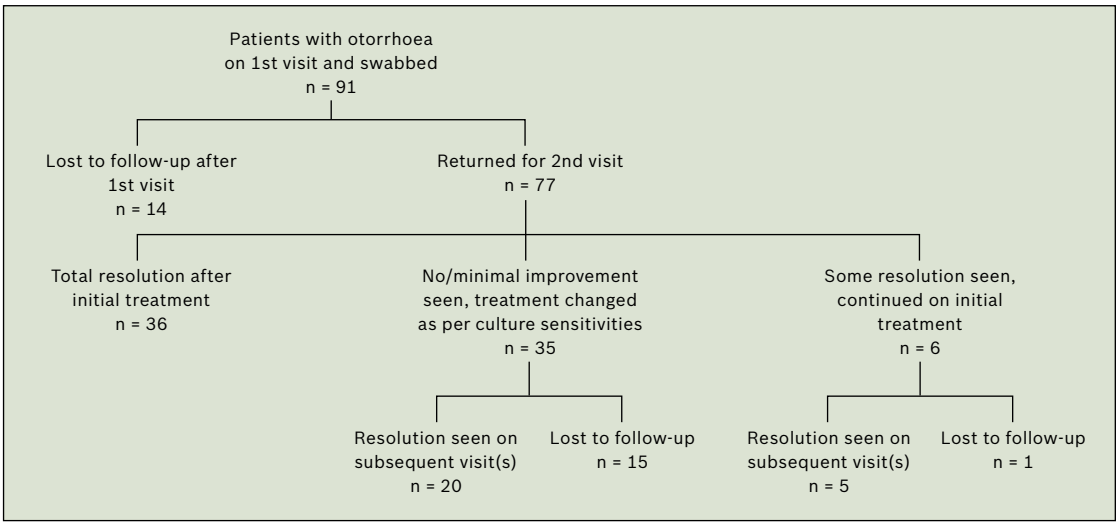

Fig. 1. Diagram shows the course of action taken following ear swab on initial presentation by patients.

that within our sample, otorrhoea was most frequently caused by *P. aeruginosa*, followed by *Aspergillus* and methicillin-sensitive *S. aureus*. By examining this study and Loh et al's study,[6] we can gain a better understanding of the changing spectrum of micro-organisms involved in ear infections in Singapore. Our study included all patients presenting with otorrhoea, regardless of the underlying diagnosis, as it can be difficult for medical practitioners in the community to make a diagnosis of otitis externa or suppurative otitis media. We also wanted to analyse the effectiveness of empirical treatment started without a preceding culture result. *P. aeruginosa* accounted for 48.4% of bacterial cultures in our study, while 32.3% yielded *S. aureus*, one-fifth of which were methicillin-resistant. In the study by Loh et al, which was limited to cases of bacterial otitis externa and otomycosis, 30% of the bacterial cultures grew *P. aeruginosa*, while 15.6% yielded *S. aureus*, none of which were methicillin-resistant.[6]

Agius et al showed that the most severe cases of otitis externa are usually secondary to *P. aeruginosa*.[7] 18% of *Pseudomonas* infections in our study were found to be resistant to ciprofloxacin, a percentage that was similar to that reported in other studies.[8] In contrast to the previously reported 100% susceptibility rate of *P. aeruginosa* to gentamicin by Loh et al,[6] our study found resistance in 24.0% of cases. The rise of aminoglycoside resistance in *P. aeruginosa* in recent years has also been noted in the study by Cantrell et al.[9] Our study found that 93.8% of methicillin-sensitive *S. aureus* cases were sensitive to cloxacillin and 87.5% were sensitive to clindamycin, suggesting that these would be good oral antibiotics to commence if topical antibiotics have not been effective in treating the otorrhoea. Studies have shown that there is no statistically significant difference in efficacy between fluoroquinolones and aminoglycosides in curing otitis externa and chronic suppurative otitis media.[10-13] We agree that aminoglycoside and fluoroquinolone-containing eardrops are suitable first-line topical therapies. However, in the event where the integrity of the tympanic membrane is uncertain, fluoroquinolones are recommended instead of aminoglycosides so as to avoid ototoxicity.[14,15]

MRSA has become an increasingly common pathogen since its first discovery in 1961.[16] The rise in the incidence of MRSA is clearly seen, as none of the cultures in the earlier study by Loh et al grew MRSA,[6] in contrast to 4.2% of cases in our study. Our incidence of MRSA is lower than the 7%–17% incidence rate reported worldwide.[8,17,18] MRSA has more often been implicated in chronic myringitis and CSOM,[3,17] and in our study, the four cases involving MRSA were equally divided between CSOM and otitis externa. MRSA accounted for 12.5% of our CSOM cases. This is significantly lower than that found in other studies, which reported 24.8% of CSOM cases or 45.9% of all *Staphylococcus*-related CSOM.[19]

Vancomycin has been demonstrated to be the gold-standard therapy for MRSA in multiple studies,[19-21] and our study has found that there was 100% sensitivity to vancomycin *in vitro*, while sensitivity to fusidic acid was 75.0% compared to 96.3% in the literature.[18] Only 25.0% was sensitive to co-trimoxazole, contrary to studies that reported sensitivity in 85%–88% of MRSA-related otorrhoea.[18,19,22] Vancomycin, and fusidic acid to a slightly lesser extent, is therefore an excellent treatment option in our local setting. Gentamicin and fluoroquinolones have been shown in various studies to be effective in treating MRSA, depending on whether the MRSA was hospital- or community-acquired,[23,24] but these antibiotics are not part of the routine battery of sensitivity tests conducted in our hospital laboratory. It would be beneficial to explore the susceptibility pattern of local MRSA strains against these antibiotics. This would assist in slowing the development of vancomycin resistance, a worrying scenario that is appearing and requiring the use of more powerful antibiotics.[25] Topical vancomycin is an effective treatment for MRSA otorrhoea, and aids to avoid the inconvenience and cost of intravenous therapy.[21]

Among our patients, 28% had fungal-positive cultures. The reported incidence of otomycosis is 1.7%–30.0%.[5,26] Otomycosis occurs more frequently in the tropics as compared to temperate countries due to the hot and humid environment, which predisposes to fungal growth.[27] The most common fungi

involved in otomycosis are *Aspergillus* spp. and *Candida* spp.[26,28] Geographical location appears to affect the prevalence of each species. Martin et al found that *Candida* accounted for 67% of cases in temperate America, in contrast to *Aspergillus*, which was observed in only 13% of cases.[29] On the contrary, an overwhelming 87% of cases in tropical India yielded *Aspergillus* spp.[27] In our study, *Aspergillus* was cultured in 58% of fungal-positive cultures and *Candida* in 42%. This concurred with the study by Loh et al, which found *Aspergillus* spp. to be more common than *Candida* spp. in Singapore.[6] Topical clotrimazole is an excellent treatment option for both *Aspergillus* and *Candida*. It has not been shown to be ototoxic, and is particularly useful in concomitant mixed bacterial and fungal infections due to its antibacterial properties.[26,30]

Out of the 91 patients in our study, 55 had previously been treated in the community. The cultures from ten of these patients yielded no growth or normal skin flora, either secondary to microbiological resolution of the infection or inadequate specimen sampling. The most common reasons for failure of community-initiated therapy in the remaining 45 patients included inadequate antibiotic coverage for polymicrobial growth, failure to diagnose and treat otomycosis, and inappropriate choice of antibiotics. About 38% of community-treated patients had positive fungal cultures in contrast to only 25% of non-treated patients. While antibacterial treatment has been known to predispose to secondary fungal growth due to the lack of competitive bacterial growth or pH optimisation,[30] the possibility of misdiagnosis and incorrect treatment is considerable, given that none of the 55 community-treated patients had been given antifungal medications in the community. It is also known that otomycosis is more strongly implicated in chronic otitis externa, which would be seen more frequently in a tertiary centre.[1] In our study, only 56% of cases with fungi were diagnosed correctly on the first visit. This suggests that the clinical signs of otomycosis, such as the thick grey-white debris of *Candida* and black hyphae of *Aspergillus*, are often not readily visible, even under the microscope. The study by Saunders et al also acknowledged this diagnostic difficulty.[3] In Singapore, the persistence of otorrhoea despite antibacterial treatment should alert the clinician to the possibility of fungus as the causative agent.

Based on our study, 34 of the 55 (61.8%) patients treated in the community had been prescribed oral antibiotics. The most common empirical oral antibiotic used was amoxicillin +/– clavulanic acid, which had been given to 27 patients. While amoxicillin +/– clavulanic acid is a broad-spectrum antibiotic that many general practitioners feel comfortable prescribing, Roland et al did not find any significant difference in terms of microbial eradication or duration of otalgia with the empirical addition of an oral antibiotic to antibiotic/steroid eardrops.[31] Concomitant use of oral antibiotics is advisable in patients with severe infection or middle ear disease, or in immunocompromised or diabetic patients.[32] It should also be started if culture sensitivities suggest utility in doing so.

In view of the large percentage of patients (60.4%) who received prior treatment, our study results may not be a true reflection of the initial pathogens that caused otorrhoea. This must be taken into account when treating new patients. Nevertheless, this study is still relevant to the general practitioner dealing with recalcitrant cases. Patients whose otorrhoea does not show improvement after two weeks of treatment are considered treatment failures, and the clinician should then consider alternative antimicrobials.[33] It would then be prudent to perform an ear swab to obtain culture sensitivities. This would also be helpful in view of the 19.8% of ear cultures that are polymicrobial, albeit a lower figure than the reported 35%–44% in other studies.[2,5,34] At present, ear cultures are not routinely obtained at initial presentation in the community or ENT clinics. We are conducting a cost-benefit analysis at our institution to determine whether cultures should be obtained for all cases of otorrhoea referred to a tertiary hospital.

In conclusion, the common microorganisms involved in otorrhoea in Singapore are *P. aeruginosa*, *Aspergillus* and methicillin-sensitive *S. aureus*. MRSA is becoming more prevalent in our population, and local strains are highly sensitive to vancomycin and fusidic acid. Both aminoglycoside and fluoroquinolone-containing eardrops are suitable as first-line topical antimicrobials, but the latter is recommended only when the integrity of the tympanic membrane is uncertain. While oral antibiotics are not recommended as an empirical addition to topical agents in straightforward cases, cloxacillin may be a good choice should a concomitant oral antibiotic be warranted due to the high prevalence of *S. aureus* and its high sensitivity. Otomycosis should be considered in cases that do not improve with empirical antibiotics, in which case, clotrimazole eardrops may be commenced.

REFERENCES

1. Hawke M, Wong J, Krajden S. Clinical and microbiological features of otitis externa. J Otolaryngol 1984; 13:289-95.
2. Brook I, Frazier EH, Thompson DH. Aerobic and anaerobic microbiology of external otitis. Clin Infect Dis 1992; 15:955-8.
3. Saunders JE, Raju RP, Boone JL, Hales NW, Berryhill WE. Antibiotic resistance and otomycosis in the draining ear: culture results by diagnosis. Am J Otolaryngol 2011; 32:470-6.
4. Jadhav VJ, Pal M, Mishra GS. Etiological significance of Candida albicans in otitis externa. Mycopathologia 2003; 156:313-5.
5. Roland PS, Stroman DW. Microbiology of acute otitis externa. Laryngoscope 2002; 112 (pt 1):1166-77.
6. Loh KS, Tan KK, Kumarasinghe G, Leong HK, Yeoh KH. Otitis externa--the clinical pattern in a tertiary institution in Singapore. Ann Acad Med Singapore 1998; 27:215-8.
7. Agius AM, Pickles JM, Burch KL. A prospective study of otitis externa. Clin Otolaryngol Allied Sci 1992; 17:150-4.
8. Saunders JE, Raju RP, Boone J, Berryhill W. Current bacteriology of suppurative otitis: resistant patterns and outcomes analysis. Otol Neurotol 2009; 30:339-43.
9. Cantrell HF, Lombardy EE, Duncanson FP, Katz E, Barone JS. Declining susceptibility to neomycin and polymyxin B of pathogens recovered in otitis externa clinical trials. South Med J 2004; 97:465-71.
10. Jones RN, Milazzo J, Seidlin M. Ofloxacin otic solution for treatment of otitis externa in children and adults. Arch Otolaryngol Head Neck Surg 1997; 123:1193-200.
11. Fradis M, Brodsky A, Ben-David J, et al. Chronic otitis media treated topically with ciprofloxacin or tobramycin. Arch Otolaryngol Head Neck Surg 1997; 123:1057-60.

12. Miró N. Controlled multicenter study on chronic suppurative otitis media treated with topical applications of ciprofloxacin 0.2% solution in single-dose containers or combination of polymyxin B, neomycin, and hydrocortisone suspension. Otolaryngol Head Neck Surg 2000; 23:617-23.
13. Sabater F, Maristany M, Mensa J, Villar E, Traserra J. [Prospective double-blind randomized study of the efficacy and tolerance of topical ciprofloxacin vs topical gentamicin in the treatment of simple chronic otitis media and diffuse external otitis]. Acta Otorrinolaringol Esp 1996; 47:217-20. Spanish.
14. Ruben RJ. Efficacy of ofloxacin and other otic preparations for otitis externa. Pediatr Infect Dis J 2001; 20:108-10; discussion 120-2.
15. Schwartz RH. Once-daily ofloxacin otic solution versus neomycin sulfate/polymyxin B sulfate/hydrocortisone otic suspension four times a day: a multicenter, randomized, evaluator-blinded trial to compare the efficacy, safety, and pain relief in pediatric patients with otitis externa. Curr Med Res Opin 2006; 22:1725-36.
16. Jevons MP, Coe AW, Parker MT. Methicillin resistance in staphylococci. Lancet 1963; 1:904-7.
17. Hwang JH, Chu CK, Liu TC. Changes in bacteriology of discharging ears. J Laryngol Otol 2002; 116:686-9.
18. MacNeil SD, Westerberg BD, Romney MG. Toward the development of evidence-based guidelines for the management of methicillin-resistant Staphylococcus aureus otitis. J Otolaryngol Head Neck Surg 2009; 38:483-94.
19. Park DC, Lee SK, Cha CI, et al. Antimicrobial resistance of Staphylococcus from otorrhea in chronic suppurative otitis media and comparison with results of all isolated Staphylococci. Eur J Clin Microbiol Infect Dis 2008; 27:571-7.
20. Hwang JH, Tsai HY, Liu TC. Community-acquired methicillin-resistant Staphylococcus aureus infections in discharging ears. Acta Otolaryngol 2002; 122:827-30.
21. Jang CH, Song CH, Wang PC. Topical vancomycin for chronic suppurative otitis media with methicillin-resistant Staphylococcus aureus otorrhoea. J Laryngol Otol 2004; 118:645-7.
22. Park MK, Jung MH, Kang HJ, et al. The changes of MRSA infections in chronic suppurative otitis media. Otolaryngol Head Neck Surg 2008; 139:395-8.
23. Nassif RG, Soliman R, Edwards DH, Kara N, Hussain SS. Molecular and epidemiological analysis of methicillin-resistant Staphylococcus aureus otorrhoea: hospital- or community-acquired? J Laryngol Otol 2010; 124:1247-50.
24. Baugher KM, Hemme TS, Hawkshaw M, Sataloff RT. MRSA otorrhea: A case series and review of the literature. Ear Nose Throat J 2011; 90:60-79.
25. Micek ST. Alternatives to vancomycin for the treatment of methicillin-resistant Staphylococcus aureus infections. Clin Infect Dis 2007; 45 Suppl 3:S184-90.
26. Munguia R, Daniel SJ. Ototopical antifungals and otomycosis: a review. Int J Pediatr Otorhinolaryngol 2008; 72:453-9.
27. Aneja KR, Sharma C, Joshi R. Fungal infection of the ear: a common problem in the north eastern part of Haryana. Int J Pediatr Otorhinolaryngol 2010; 74:604-7.
28. Vennewald I, Klemm E. Otomycosis: Diagnosis and treatment. Clin Dermatol 2010; 28:202-11.
29. Martin TJ, Kerschner JE, Flanary VA. Fungal causes of otitis externa and tympanostomy tube otorrhea. Int J Pediatr Otorhinolaryngol 2005; 69:1503-8.
30. Jackman A, Ward R, April M, Bent J. Topical antibiotic induced otomycosis. Int J Pediatr Otorhinolaryngol 2005; 69:857-60.
31. Roland PS, Belcher BP, Bettis R, et al. A single topical agent is clinically equivalent to the combination of topical and oral antibiotic treatment for otitis externa. Am J Otolaryngol 2008; 29:255-61.
32. Osguthorpe JD, Nielsen DR. Otitis externa: Review and clinical update. Am Fam Physician 2006; 74:1510-6.
33. Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. Cochrane Database Syst Rev 2010; CD004740.
34. Clark WB, Brook I, Bianki D, Thompson DH. Microbiology of otitis externa. Otolaryngol Head Neck Surg 1997; 116:23-5.