

Original Research Article

Drug sensitivity pattern of the pathogenic microorganisms causing atticofacial type of chronic suppurative otitis media

Nagat M. Saeed, Mabruka S. Elashheb, Fatma M. Ben Rabha, Lamees A. Ben Saad, Samia A Hassan

Department of pharmacology, faculty of medicine, University of Tripoli

***Corresponding author**

Nagat M. Saeed

Email: lameesbensaad@gmail.com

Abstract: Chronic suppurative otitis media (CSOM) is one of the common otological problems in our community and atticofacial type is associated with increased incidence of intracranial and extracranial complications. The aim of this study is to determine the type and pattern of drug susceptibility of the pathogenic microorganisms causing atticofacial disease, which could lead to better therapeutic decisions, thereby reducing the potential risks of complications. Total 42 Patients with persistent otorrhea for more than 3 months with atticofacial type of chronic otitis media were selected. The exudates were collected under sterile conditions and inoculated onto culture media; bacterial growth and drug sensitivity pattern were studied. This study analyzes the causal organisms and their sensitivity to various antimicrobial agents. Most frequently isolated agents were *Pseudomonas aeruginosa* (25.4%) followed by *proteus mirabilis* (23.7%) and *Staphylococcus aureus* (6.8%) while other organisms such as *Providencia* species, *Escherichia coli*, *Klebsella*, *Enterobacter* and *Citrobacter* species were the less commonly involved organisms. Drug sensitivities pattern of *P. aeruginosa* showed that ciprofloxacin was active against the majority of isolates (93.9%) followed by ceftazidime 86.2% and amikacin 76.2%. Whereas the sensitivity of *P. mirabilis* was 100% to ceftazidime and ciprofloxacin, 95.2% to amoxil/clavulanic acid and amikacin. All (100%) of the *Staphylococcus* isolates were sensitive to vancomycin, 96.2% to ciprofloxacin and 93.1% were sensitive to amoxil/clavulanic acid. Continuous and periodic evaluation of microbiological pattern and drug sensitivity of atticofacial CSOM is necessary to decrease the potential risks of complications by early institution of appropriate systemic and topical antibiotic alongside mastoid exploration. We believe that our data may contribute to an effective medical management of atticofacial disease. Since the most common organisms in our clinical set up being *P. aeruginosa* and *P. mirabilis* which showed a highly percentage susceptibility to ciprofloxacin and ceftazidime, thus making it an empirical antibiotic combination therapy of choice in the recent time.

Keywords: Chronic, suppurative, otitis media, atticofacial disease, antibiotics.

INTRODUCTION

Chronic suppurative otitis media (CSOM) is a long standing purulent infection of middle ear cleft presenting as purulent ear discharge which may be associated with variable degree of hearing loss. Chronic inflammation of middle ear cleft is slow and insidious in its course, tends to be persistent and often produce irreversible local destruction of middle ear cleft mucosa and underlying bone. This local destruction sometimes leads to serious extra and intracranial complications [1, 2].

Depending on pathology CSOM may be of two types: Tubotympanic/safe type or benign type as there is no serious complication and associated with tympanic membrane perforation and recurrent or persistent ear discharge, without cholesteatoma whereas, atticofacial/unsafe type or dangerous type because of associated with intracranial and extracranial complications and may be life threatening at time and

often associated with the presence of cholesteatoma or granulations [3].

Early and appropriate antibiotic treatment may reduce the risk of the serious complications [4]. Typically the disease follows viral infections of the upper respiratory tract but soon invades middle ear with pyogenic organisms [5]. In many cases of CSOM, antibiotics are prescribed indiscriminately. The consequences are treatment failures, prolongation of disease course, and emergence of resistant organisms, increased complication rate and increased treatment cost. Knowledge of commonest organisms responsible for chronic discharging ear and their resistant patterns in the community is helpful in selecting correct antimicrobial agents [6]. This study was undertaken to identify commonest microorganisms involved in atticofacial CSOM and their sensitivity patterns to commonly prescribed drugs. Which could lead to better

therapeutic decisions, thereby reducing the potential risks of complications.

MATERIALS AND METHODS

Patients and clinical examination

The study included 42 patients with atticoantral chronic suppurative otitis media attending the Ear, Nose, Throat (ENT) OPD clinic at Central Hospital-Tripoli. Each patient was subjected to a full otologic examination. The otic secretion (purulent discharge) was collected under sterile condition. The ear swabs were immediately placed in transport media (Amis transport media) and transferred to laboratory within 20 minutes. All specimens were cultured for aerobic and anaerobic conditions as described previously in Monica in 1984 [7].

Identification

The ear discharge samples were plated on blood agar, chocolate agar, gentamicin blood agar, MacConkeys agar, mannitol salt agar, neutrient agar with X and V factors, and Sabourads agar (Oxoid, UK) and then incubated aerobically and anaerobically at 37°C. All isolated organisms were identified macroscopically and microbiologically by Gram's stain and then identified biochemically by standard technique as described previously in Monica in 1984 [7] and confirmed by the API 20 E, and API 20 NE (Biomerieux-France). Slidex Strepto kit (Biomerieux-France) was used to confirm the streptococci groups.

Antibiotic susceptibility testing

Antimicrobial susceptibility patterns were done on Mueller-Hinton agar (Oxoid, UK) using disk diffusion method as described by Kirby Bauer [8]. The antimicrobial agents tested were: ampicillin (10µg), pencillin (10 units), carbenicillin (100µg), cloxacillin (5µg), amoxicillin/clavulanic acid (30µg), cephalothin (30µg), ceftazidime (30µg), tetracycline (30µg), erythromycin (15µg), chloramphenicol (30µg), amikacin (30µg), gentamicin (10µg), neomycin (30µg), polymyxin (300 units), trimethoprim sulphamethoxazole (25µg), fusidic acid and ciprofloxacin (5µg) (Oxoid, UK). Reference strains of *Pseudomonas aeruginosa* NCTC6749 and *Staphylococcus aureus* NCTC 4163 were used for quality control for antimicrobial susceptibility tests.

STATISTICAL ANALYSIS

The results obtained were analyzed statistically using the Chi-square and SPSS version 15 software wherever appropriate. P-value of <0.05 were regarded as statistically significant.

RESULTS

The present study included 42 patients with atticoantral type of disease, the granulation tissue and cholesteatoma was observed in 13 (31%). Adhesive type of otitis media was observed in only one patient. Out of 42 patients, 19 (45.2%) were females while 23 were males (54.8%) (Table 1). Males appear to have a higher risk of infection in atticoantral disease than female patients, but the relation was not found to be statistically significant. The mean age of the patients with CSOM was 28 and the peak incidence of disease was observed in the age group between the age group 15-30 years (46%). Out of the 42 swabs cultured, 4 (9.5%) were sterile, 21 (50%) were pure cultures and 17 (40.5%) mixed culture. From our results we observed that the combinations of isolates did not show any consistent pattern (Table 2). Microorganisms were recovered from 38 (90.5%) patients. A total of 59 isolates were obtained, of which 58 (98.3%) were bacterial and 1 (1.7%) was fungal. The dominant organisms isolated from patients with atticoantral disease were *Pseudomonas aeruginosa* (25.4%) followed by *Proteus mirabilis* (23.7%) and *Staphylococcus aureus* (6.8%) while other organisms were the less commonly involved (Table 3).

Drug sensitivities pattern of *P. aeruginosa* showed that ciprofloxacin was active against the majority of isolates (93.9%) followed by ceftazidime 86.2%, amikacin 76.2% and gentamicin 40.8%. Whereas the sensitivity of *P. mirabilis* was 100% to ceftazidime and ciprofloxacin, 95.2% to amoxil/clavulanic acid and amikacin. All (100%) of the *Staphylococcus* isolates were sensitive to vancomycin, 96.2% to ciprofloxacin and 93.1% were sensitive to amoxil/clavulanic acid. Other isolates *Providencia* species, *Escherichia coli*, *Klebsella*, *Enterobacter* and *Citrobacter* species) showed 100% sensitive to Amikacin and ciprofloxacin and 90.9% of isolates were sensitive to ceftazidime (Table 4).

Table 1: The distribution of patients with atticoantral CSOM according to sex

Sex	Number of case	Percentage
Female	19	45.2
Male	23	54.8
Total	42	100%

Table 2: Types of bacterial culture

Type	Number of case	Percentage
Monomicrobial (Pure culture)	21	50
Polymicrobial (Mixed culture)	17	40.5
No growth (Sterile)	4	9.5
Total	42	100

Table 3: Percentage of different organisms isolated from patient with CSOM.

Microorganisms	Total number & percentage of isolates
<i>Pseudomonas aeruginosa</i>	15 (25.4)
<i>Proteus mirabilis</i>	14 (23.7)
<i>Providencia stuartii</i>	6 (10.2)
<i>Staphylococcus aureus</i>	4 (6.8)
<i>Bacteroides melaninogenicus</i>	4 (6.8)
<i>Providencia rettgeri</i>	3 (5.1)
<i>Enterobacter cloacae</i>	2 (3.4)
<i>Klebsiella oxytoca</i>	2 (3.4)
<i>Citrobacter diversus</i>	2 (3.4)
<i>Escherichia coli</i>	1 (1.7)
<i>Klebsiella pneumonia</i>	1 (1.7)
<i>Peptococcus species</i>	1 (1.7)
<i>Pseudomonas fluorescens</i>	1 (1.7)
<i>Pseudomonas stutzeri</i>	1 (1.7)
<i>Citrobacter freundii</i>	1 (1.7)
<i>Aspergillus species</i>	1 (1.7)
Total	59

Note: The total number of isolates more than 42 due to multiple isolates from same ear.

Table 4: Drug sensitivity pattern

Antimicrobial agents	<i>Pseudomonas aeruginosa</i>	<i>Proteus mirabilis</i>	<i>Staphylococcus aureus</i>	Others*
Pencillin G	NT	NT	27.3	NT
Ampicillin	NT	44.4	27.6	27.8
Cloxacillin	NT	NT	91.7	NT
Carbencillin	64.1	52.9	NT	63.2
Amoxil/ clavulanic acid	NT	95.2	93.1	51.9
Cephalothin	NT	70.6	81.8	76.9
Ceftazidime	86.2	100	NT	90.9
Gentamicin	40.8	85.7	82.8	82.1
Amikacin	76.2	95.2	NT	100
Neomycin	36.7	85.7	80.9	85.7
Polymyxin	97.9	NT	48.3	87.5
Chloramphenicol	NT	71.4	80.8	55.6
Ciprofloxacin	93.9	100	96.2	100
Trimethoprim- sulphamethoxazole	NT	93.3	NT	85
Fusidic acid	NT	NT	72.4	NT
Tetracycline	NT	NT	71.4	34.6
Erythromycin	NT	NT	71.4	NT
Vancomycin	NT	NT	100	NT

* Include: *Providencia species*, *klebsiella species*, *Escherichia coli*, *Enterobacter cloacae* and *Citrobacter species* (NT= Not tested)

Note: *Providencia species* were not tested by (polymyxin, cephalothin), *Klebsiella species* were not tested by (ampicillin and carbencillin).

DISCUSSION

Chronic Suppurative Otitis Media and its complications are among the most common conditions seen by the Otologist, paediatrician and the general practitioner. It is a persistent disease with great risk of irreversible complications [9]. Early accurate and appropriate effective therapy needs bacteriological diagnoses in all cases. A wide range of organisms both

aerobic and anaerobic isolated from cases of CSOM. Knowledge of pathogens responsible for otitis media can assist in the selection of most appropriate treatment regimen and can minimize complications that require surgery.

Microbiological analysis of chronic otitis media shows an interaction between local infection and

the disease. In our study the predominant organisms are *Pseudomonas aeruginosa*. This correlates well with many other studies [10-12], followed by *proteus mirabilis* and this is agreement with previous study [11, 12] and in agreement with previous study by Naveen *et al.*; in 2014 [13] have reported that *Staphylococcus aureus* was the second most common organism isolated.

Regarding drug sensitivity test, all the pathogenic (59) isolates from atticofur type of disease were tested against various drugs. Ciprofloxacin was found to be the most effective drug against majority 93.9%, *Pseudomonas* isolates this is supported by many other studies [14, 15, 12] followed by ceftazidime 86.2% and amikacin 76.2%. All *Proteus* isolates (100%) were sensitive to ciprofloxacin and ceftazidim and 95.2% amikacin. In general, gram negative organisms showed increased sensitivity to ceftazidime, ciprofloxacin and amikacin. This result correlated well with other investigator [14]. All (100%) of the *Staphylococcus* isolates were sensitive to vancomycin, 96.2% to ciprofloxacin and 93.1% were sensitive to amoxil/clavulanic acid, whereas only 27.3% and 27.6% isolates showed sensitivity to penicillin G and ampicillin respectively. In similar study, different investigators reported different sensitivity patterns [10, 16, 12]. Other isolates in this study *Providencia* species, *Escherichia coli*, and *Klebsella*, *Enterobacter* and *Citrobacter* species showed 100% sensitive to Amikacin and ciprofloxacin and 90.9% of isolates sensitive to ceftazidime.

CONCLUSION

Microbial organisms are one of the supporting factors in developing of the chronic otitis media. Clinical manifestations, treatment, course and prognosis of chronic otitis media depends on local infection and its treatment. From our results of drug sensitivity test, we concluded that; firstly, the ototoxic topical aminoglycoside (gentamicin, neomycin) were active *in vitro* against the *Staphylococcus aureus*, *proteus mirabilis*, and other Gram-negative bacilli, while they were inactive against *Pseudomonas aeruginosa*. Secondly, the aminoglycoside (polymyxin) was active against *Pseudomonas aeruginosa* and other gram-negative bacilli except *Proteus mirabilis* and *Providencia* species were intrinsically resistant to this drug. The side effects of aminoglycosides limit their usage. Next, chloramphenicol which is often used topically, and the systemic antibiotic cephalexin, cloxacillin, amoxil/clavulanic acid appear to be effective *in vitro* against *Staphylococcus aureus*. On the other hand, the systemic antibiotics ampicillin and penicillin G were inactive against *Staphylococcus aureus* as might be expected because the majority of these strains are beta-lactamase producers. This observation necessitates the choice of beta lactamase stable antibiotics as first line treatment. Finally, Quinolones, especially ciprofloxacin which can be used topically or systemically, found to be effective in

eradicating majority of Gram positive and Gram negative bacteria. Since the most common organisms in our clinical set up being *Pseudomonas aeruginosa* and *Proteus mirabilis* which showed a high percentage susceptibility of to ceftazidime and ciprofloxacin, thus making it an empirical antibiotic combination therapy of choice in the recent times. The side effects of ciprofloxacin are less as compared to aminoglycosides. Ciprofloxacin should be avoided in children due to damaging effects on developing cartilage and bones. Third generation cephalosporin is a suitable alternative in children.

REFERENCES

1. Matsuda Y, Kurita T, Ueda Y, Ito S, Nakashima T. Effect of tympanic membrane perforation on middle-ear sound transmission. *The Journal of Laryngology & Otology*. 2009 May; 123(S31):81-9.
2. Wright D, Safranek S. Treatment of otitis media with perforated tympanic membrane. *Clinical Inquiries*, 2009 (MU). 2009.
3. Prakash R, Juyal D, Negi V, Pal S, Adekhandi S, Sharma M, Sharma N. Microbiology of chronic suppurative otitis media in a tertiary care setup of Uttarakhand state, India. *North American journal of medical Sciences*. 2013 Apr; 5(4):282.
4. Browning GG, Gatehouse S, Calder IT. Medical management of active chronic otitis media: a controlled study. *The Journal of Laryngology & Otology*. 1988 Jun; 102(6):491-5.
5. Fliss DM, Meidan N, Dagan R, Leiberman A. Aerobic bacteriology of chronic suppurative otitis media without cholesteatoma in children. *Annals of Otology, Rhinology & Laryngology*. 1992 Oct; 101(10):866-9.
6. Vartiainen E, Vartiainen J. Effect of aerobic bacteriology on the clinical presentation and treatment results of chronic suppurative otitis media. *The Journal of Laryngology & Otology*. 1996 Apr; 110(4):315-8.
7. Cheesbrough M. Medical laboratory manual for tropical countries. M. Cheesbrough, 14 Beville's Close, Doddington, Cambridgeshire, PE15 0TT; 1981.
8. Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disk method. *American journal of clinical pathology*. 1966 Apr; 45(4):493.
9. Jang CH, Park SY. Emergence of ciprofloxacin-resistant *Pseudomonas* in chronic suppurative otitis media. *Clinical Otolaryngology*. 2004 Aug 1; 29(4):321-3.
10. Mansoor T, Musani MA, Khalid G, Kamal M. *Pseudomonas aeruginosa* in chronic suppurative otitis media: sensitivity spectrum against various antibiotics in Karachi. *J Ayub Med Coll Abbottabad*. 2009; 21(2):120-3.
11. Viswanatha B, Durganna S, Ravikumar R, Vijaya MS, Vincent P. Bacteriology of Active Squamous

- Type of Chronic Otitis Media with Complications. Research in Otolaryngology. 2014; 3(2):9-15.
12. Mohammad Hiari. Chronic suppurative otitis media: Microbial and antimicrobial findings. *International journal of advanced research*, 2016,4:1:1315-1320
 13. Naveen k, Ramagiri V, RadhaKrishna and Rama P. CSOM: Atticoantral disease-role of microbes. *Scholars Journal of Applied Medical Sciences (SJAMS)*, 2014, 2:4C:1315-1319
 14. 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. *Otolaryngology—Head and Neck Surgery*. 2000 Nov; 123(5):617-23.
 15. Madana J, Yolmo D, Kalaiarasi R, Gopalakrishnan S, Sujatha S. Microbiological profile with antibiotic sensitivity pattern of cholesteatomatous chronic suppurative otitis media among children. *International journal of pediatric otorhinolaryngology*. 2011 Sep 30; 75(9):1104-8.
 16. Jagdish K, Sunkum A and Hima P. Bacteriological study of chronic suppurative otitis media by aerobic methods in a teaching hospital. *Journal for Oto-Rhino-Laryngology* , 2012, 2:3: 1-6.