



## Effectiveness of ciprofloxacin in the treatment of Acute Otitis Media

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### Abstract

Acute otitis externa is an infection of the outer ear canal that can occur at any age and is diagnosed by symptoms and examination findings. The aims of our study were to understand the seasonal frequency of acute otitis externa and to determine the susceptibility of causative bacteria to ciprofloxacin. Discharge samples were collected from the external ear canals of 76 patients diagnosed with acute otitis externa. The samples were evaluated and culture-antibiogram results were compiled. Routine microbiological methods were used for the reproduction of clinical material as bacterial and fungal cultures. The 76 enrolled patients were 18–80 years old (mean 41.6 years). Acute otitis externa occurred most frequently during summer, especially in July. Culture results revealed *Pseudomonas aeruginosa* growth in 30 cases (39.4%), *Staphylococcus aureus* in 18 cases (23.6%), and *Serratia* spp. in 5 cases (6.5%), while fungal growth was observed in 10 cases (13.1%). The antibiogram analyses determined ciprofloxacin resistance in *P. aeruginosa* in 13 patients (43.3%) and in *S. aureus* in 6 patients (33.3%). Acute otitis externa should be treated with antibiotics in accordance with culture antibiogram results, while keeping in mind that bacterial causes could be ciprofloxacin resistant.

**Keywords:** Acute otitis externa, season, culture antibiogram, ciprofloxacin effectiveness

### 1. Introduction

Acute otitis externa (AOE) is an infection of the outer ear canal that is diagnosed based on symptoms and examination findings. It can occur in individuals of any age and can occasionally affect the tympanic membrane and the auricle. It is generally unilateral, but bilateral occurrences can account for 10% of the cases (1). The infection may develop in response to many factors, including local trauma, high humidity, use of swimming pools, excessive serumen cleansing, anatomical anomalies, and the use of hearing aids (2, 3). AOE generally responds to localized and topical treatments; however, the presence of immunodeficiency or chronic otitis media can lead to serious complications. Malignant otitis externa should be considered, especially in patients with diabetes mellitus with severe ear pain and granulation in the outer ear canal who do not respond to topical treatments.

AOE is usually seen during the summer, and it causes discharge, pain, swelling, decreased hearing capacity, and increased itching in the outer ear canal (1, 4). Bacteria are the most common causative agents of AOE infections, but viruses and fungi may sporadically play a role in the etiology (5). *Pseudomonas aeruginosa* and *Staphylococcus aureus* are the most frequently isolated bacteria from infection cultures, whereas fungal infections may occur as secondary or primary to antibiotic treatment. AOE is usually treated locally, with

treatments typically effective against the most common agents, namely *P. aeruginosa* and *S. aureus*. When aminoglycoside antibiotics are used in local treatment, chronic suppurative otitis media should be excluded (2).

Ciprofloxacin is commonly used to treat AOE. It is a broad-spectrum antibiotic of the fluoroquinolone group that works as a bactericide against gram-negative bacteria, with moderate effects on gram-positive bacteria (6). However, antibiotic treatment of AOE without identification of the etiological pathogen can prolong the treatment period and increase economic losses, complication rates, mortality, and bacterial antibiotic resistance (7). The aim of our study was to determine the age and sex distributions of the patients with AOE, the season and month when most infections occur, the frequency of causative pathogens detected in culture, and the susceptibility of causative bacteria to ciprofloxacin.

### 2. Materials and Methods

The study was approved by the Ethics Committee of University of HealthSciences- Samsun Health Practices and Research Center. This was a retrospective study of patient files of 76 individuals diagnosed with acute otitis externa and sampled for culture from the outer ear canal discharge in the otolaryngology clinic at Research Center between January and December 2019. Pediatric patients, pregnant patients, patients

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undergoing chemotherapy due to malignancy, patients with immune deficiency, patients with chronic otitis media, and patients who were already on antibiotic treatment prior to culture tests were excluded from the study.

Samples taken from the discharge in the outer ear canal were sent to the microbiology laboratory within 30 minutes inside Amies transport medium with charcoal (swab RTA, Turkey). Bacteriological examinations were conducted by plating the outer ear canal samples onto blood agar, chocolate agar, and Eosin Methylene Blue (EMB) agar, whereas samples with suspected fungal growth were plated onto Sabouraud dextrose agar (SDA). A *VITEK 2 automatic bacterial identification system (bioMérieux, France)* was used for isolates that could not be identified by conventional methods. The antimicrobial susceptibilities of the isolated strains were evaluated and reported according to the criteria of *EUCAST (European Committee on Antimicrobial Susceptibility Testing)* in the microbiology laboratory of our hospital.

In the clinic, local ciprofloxacin (0.3%), rifampicin (1%), aminoglycoside, and antifungal drops were administered to the patients without waiting for culture results. The culture results were evaluated by the clinicians and the treatment given to the patient was reviewed accordingly. Recorded data included the age and sex of the patients, frequency of AOE according to season and month, type of pathogen isolated from culture samples, and ciprofloxacin susceptibility of bacteria grown in culture.

**Table 1.** Culture results and ciprofloxacin susceptibility of bacteria isolated from ear canal discharge with acute otitis externa

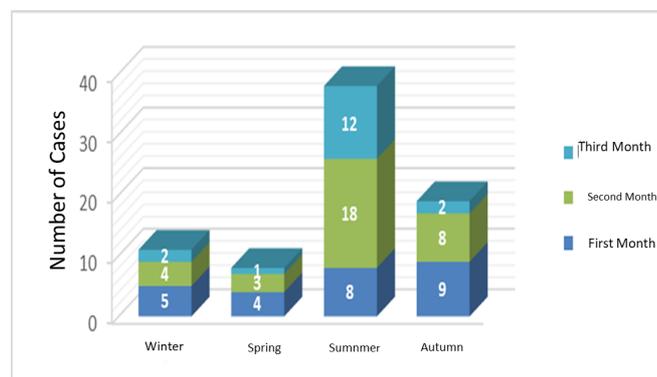
Culture results	Number (n=76) (%)	Ciprofloxacin		
		Susceptible (%)	Resistant (%)	No antibiogram
<i>Pseudomonas aeruginosa</i>	30 (39.4%)	17 (56.6%)	13 (43.3%)	-
<i>Staphylococcus aureus</i>	18 (23.6%)	12 (66.6%)	6 (33.3%)	-
<i>Serratia</i> spp.	5 (6.5%)	4 (80%)	1 (20%)	-
<i>Escherichia coli</i>	4 (5.2%)	2 (50%)	2 (50%)	-
<i>Proteus mirabilis</i>	3 (3.9%)	3 (100%)	0	-
<i>Klebsiella</i> spp.	2 (2.6%)	2 (100%)	0	-
<i>Enterobacter cloacae</i>	2 (2.6%)	2 (100%)	0	-
<i>Enterococcus faecalis</i>	1 (1.3%)	-	-	1 (100%)
<i>Comamonas testosteroni</i>	1 (1.3%)	1 (100%)	0	-
Fungi	10 (13.1%)	-	-	-

### 3. Results

The ages of patients with AOE included in the study ranged between 18 and 80 years, with an average age of 42.6 years. Overall, 41 (54%) of the patients were female and 35 (46%) were male.

The most frequent season for AOE occurrences was summer, with 38 (50%) cases; the least frequent season was

spring, with 8 (10.5%) cases. The highest diagnosis rate during the year occurred in July, with 18 cases (23.6%), while only 1 case (1.3%) was observed in May, which was the month with the least number of diagnoses (Fig 1).



**Fig. 1.** Frequency of acute otitis externa by season and month.

The culture samples from the outer ear canal showed bacterial growth in 66 cases (86.8%), while fungal growth was observed in 10 cases (13.1%) (*Candida* spp. in 6 cases; *Aspergillus* spp. in 4 cases). Fifty-nine patients included in the study were given ciprofloxacin (77.6%), 6 patients were given rifampicin (7.9%), and 4 were given aminoglycoside (5.2%) as local antibiotics, while 7 were given antifungals. The results of culture-antibiogram tests demonstrated that the bacteria in 37 (62.7%) patients who were given ciprofloxacin were susceptible to that drug, while the bacteria in 22 (37.2%) patients were resistant to ciprofloxacin.

The bacteria cultured from patient samples were identified as *P. aeruginosa* in 30 cases (39.4%), *S. aureus* in 18 cases (23.6%), and *Serratia* spp. in 5 cases (6.5%). The antibiogram test revealed that *P. aeruginosa* was resistant to ciprofloxacin in 13 patients (43.3%), while *S. aureus* was resistant in 6 patients (33.3%) (Table 1).

### 4. Discussion

Acute otitis externa is an infection of the skin and subcutaneous tissue of the outer ear canal. It is an otology emergency that affects one in every 10 individuals. Most symptoms are mild, but they can cause necrosis, osteomyelitis, and facial nerve paralysis, and even death on rare occasions (8). Treatment of uncomplicated cases of AOE consists of cleaning the ear canal and administering analgesia, topical antiseptics, and antibiotics. The chosen topical antibiotics generally target the most common pathogens, namely *P. aeruginosa*, and *S. aureus*. The usual topical antibiotics are quinolones (ciprofloxacin), aminoglycosides (neomycin), and polymyxins (polymyxin B). Oral antibiotics should be administered to patients with diabetes, immunosuppression, or no response to local treatment (9).

The development of AOE infection is correlated with an alkaline shift of the normal acidic pH of the outer ear canal (10). The incidence of AOE also increases significantly during the summer, due to high temperatures and humidity (11). For example, Villedieu et al., in their study of 7770 patients with

otitis externa, reported that infection was seen most frequently in August and September and least frequently in April and May (12). In our study, our cases of AOE occurred most frequently during the summer and least frequently during the spring, with July being the month with the highest number of AOE diagnoses (18 cases; 23.6%) and May being the month with the fewest (1 case; 1.3%).

In addition to these seasonal differences in AOE occurrence, the bacterial pathogens associated with acute otitis externa can also show geographic variations. Overall, *P. aeruginosa* is generally considered responsible for 20–71.3% of cases, while *S. aureus* accounts for about 40% of cases (8, 13). Bacterial pathogens cause 98% of the AOE cases in North America, fungi such as *Aspergillus* and *Candida* are frequently causes of AOE in tropical or subtropical environments and in patients previously treated with antibiotics (13, 14). For example, Heward et al. reported *P. aeruginosa* growth in 31.1%, *Candida* growth in 22.9%, and *S. aureus* growth in 11.7% of the cultures produced from ear discharge samples of 217 patients (15). By contrast, Pino Rivero et al. found *P. aeruginosa* in 46.83% of the cultures from their patient samples, *S. aureus* in 18.98%, and fungal growth in 25% (16). Borsa et al. isolated *P. aeruginosa* in 59%, *S. aureus* in 14%, and fungal strains in 19% of their 76 individuals with otitis externa (17). In the current study, we detected *P. aeruginosa* growth in 39.4%, *S. aureus* growth in 23.6%, fungal growth in 13.1%, and *Serratia* spp. growth in 5.6% of the cultures from the ear discharge samples of our patients.

Ear infections like AOE are also among the most common diseases associated with the excessive antibiotic use that generates antibiotic-resistant bacteria (18). In several studies, quinolone group ear drops were more effective at bacterial eradication and ear discharge reduction when compared to non-quinolone medications (19). In addition, no quinolone toxicity was encountered in human and animal studies (20). Pane et al. presented culture antibiograms of patients with otitis externa showing that *P. aeruginosa* is 100% and *S. aureus* is 66.6% sensitive to ciprofloxacin (21). Duarte et al. isolated *S. aureus* from 30.6% of their 173 patients with AOE and found 38.8% ciprofloxacin resistance in the antibiogram tests (22). Berenholz et al. studied culture antibiogram of 28 patients with malignant otitis externa and detected ciprofloxacin-resistant *Pseudomonas* in seven of those patients, suggesting that *Pseudomonas* could develop antibiotic resistance over time (23). Conversely, El-Nasr et al. detected *P. aeruginosa* growth in 65% of the culture samples from 60 patients with malignant otitis externa and found 77% antibiotic resistance in the antibiogram (24). The antibiogram analyses in the current study revealed that 43.3% of the *P. aeruginosa* and 33.3% of the *S. aureus* were ciprofloxacin resistant. In addition, evaluation of the culture antibiogram results of patients with empirical use of local ciprofloxacin revealed that the pathogens in 37.2% of the patients were resistant to ciprofloxacin.

Ciprofloxacin is frequently used locally or systemically to treat acute cases of otitis externa. However, the reported rate of occurrence of ciprofloxacin-resistant bacteria commonly isolated from patient cultures is concerning. This issue should be taken into consideration when treatments are administered prior to culturing patient samples. Treatment of AOE must be planned according to culture antibiogram results to decrease the treatment duration, to reduce morbidity, to prevent economic losses, and, most importantly, to diminish the generation of antibiotic-resistant bacteria. The retrospective nature and the low number of cases are limitations of our study; therefore, we suggest that large-scale prospective randomized studies are needed.

#### Conflict of interest

None to declare.

#### Acknowledgments

None to declare.

#### Ethical Approval

The study was approved by the Ethics Committee of University of HealthSciences- Samsun Health Practices and Research Center. The study was conducted in accordance with the principles of the Declaration of Helsinki.

#### References

- Hui CP; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Acute otitis externa. Paediatr Child Health. 2013 Feb;18(2):96-101. doi: 10.1093/pch/18.2.96
- Osguthorpe JD, Nielsen DR. Otitis externa: Review and clinical update. Am Fam Physician. 2006 Nov 1;74(9):1510-6.
- Neher A, Nagl M, Scholtz AW. Otitis externa: Aetiologie, Diagnostik und Therapie [Otitis externa: etiology, diagnostic and therapy]. HNO. 2008 Oct;56(10):1067-79; quiz 1080. German. doi: 10.1007/s00106-008-1830-y.
- Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD004740. doi: 10.1002/14651858.CD004740
- Mösges R, Nematian-Samani M, Eichel A. Treatment of acute otitis externa with ciprofloxacin otic 0.2% antibiotic ear solution. Ther Clin Risk Manag. 2011; 7:325-36. doi: 10.2147/TCRM.S6769
- Scholz H, Schwabe U. (Hrsg.). Taschenbuch der arzneibehandlung – angewandte pharmakologie. Berlin Heidelberg: Springer Verlag; 2005.
- Edwin B, Prasanna V, Kannan I, Katiyar VH, Dhanapal E. Incidence of bacterial colonization in the oropharynx of patients with ear, nose and throat infections. International Journal of Medical Science and Public Health. 2014;3(8):931-4.
- Centers for Disease Control and Prevention (CDC). Estimated burden of acute otitis externa--United States, 2003-2007. MMWR Morb Mortal Wkly Rep. 2011 May 20;60(19):605-9.
- Rosenfeld RM, Singer M, Wasserman JM, Stinnett SS. Systematic review of topical antimicrobial therapy for acute otitis externa. Otolaryngol Head Neck Surg. 2006 Apr;134(4 Suppl): S24-48. doi: 10.1016/j.otohns.2006.02.013
- Martinez Devesa P, Willis CM, Capper JW. External auditory canal pH in chronic otitis externa. Clin Otolaryngol Allied Sci.

- 2003 Aug;28(4):320-4. doi: 10.1046/j.1365-2273.2003.00713.x.
11. Lee H, Kim J, Nguyen V. Ear infections: otitis externa and otitis media. *Prim Care*. 2013 Sep;40(3):671-86. doi: 10.1016/j.pop.2013.05.005.
  12. Villedieu A, Papesh E, Weinberg SE, Teare L, Radhakrishnan J, Elamin WF. Seasonal variation of *Pseudomonas aeruginosa* in culture positive otitis externa in Southeast England. *Epidemiol Infect*. 2018 Oct;146(14):1811-1812. doi: 10.1017/S0950268818001899.
  13. Rosenfeld RM, Schwartz SR, Cannon CR, Roland PS, Simon GR, Kumar KA, Huang WW, Haskell HW, Robertson PJ. Clinical practice guideline: acute otitis externa. *Otolaryngol Head Neck Surg*. 2014 Feb;150(1 Suppl): S1-S24. doi: 10.1177/0194599813517083.
  14. Ahmad N, Etheridge C, Farrington M, Baguley DM. Prospective study of the microbiological flora of hearing aid moulds and the efficacy of current cleaning techniques. *J Laryngol Otol*. 2007 Feb;121(2):110-3. doi: 10.1017/S0022215106002222.
  15. Heward E, Cullen M, Hobson J. Microbiology, and antimicrobial susceptibility of otitis externa: a changing pattern of antimicrobial resistance. *J Laryngol Otol*. 2018 Apr;132(4):314-317. doi: 10.1017/S0022215118000191.
  16. Pino Rivero V, Pantoja Hernandez CG, Gonzalez Palomino G, Santos ME, Pardo Romero G, Blasco Huelva A. *Pseudomonas* and acute external otitis. Results of amicrobial study in patient without previous antibiotic treatment. *An Otorinolaringol İbero Am*. 2007;34(1)45-51.
  17. Borsa BA, Kaplan HH, Aldağ ME, Dengiz Y, Hanay A, Tandoğan B. Otitis eksterna ve otitis media hastalarında etken mikroorganizmaların ve antibiyotik duyarlılıklarının belirlenmesi. *Ankem Derg*. 2016;30(2):48-52.
  18. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014 Dec;5(6):229-41. doi: 10.1177/2042098614554919.
  19. Bath AP, Walsh RM, Bance ML, Rutka JA. Ototoxicity of topical gentamicin preparations. *Laryngoscope*. 1999 Jul;109(7 Pt 1):1088-93. doi: 10.1097/00005537-199907000-00015
  20. Dohar JE, Alper CM, Rose EA, Doyle WJ, Casselbrant ML, Kenna MA, Bluestone CD. Treatment of chronic suppurative otitis media with topical ciprofloxacin. *Ann Otol Rhinol Laryngol*. 1998 Oct;107(10 Pt 1):865-71. doi: 10.1177/000348949810701010.
  21. Berenholz L, Katzenell U, Harell M. Evolving resistant *pseudomonas* to ciprofloxacin in malignant otitis externa. *Laryngoscope*. 2002 Sep;112(9):1619-22. doi: 10.1097/00005537-200209000-00017.
  22. Duarte MJ, Kozin ED, Bispo PJM, Mitchell AH, Gilmore MS, Remenschneider AK. Methicillin-resistant *Staphylococcus aureus* in acute otitis externa. *World J Otorhinolaryngol Head Neck Surg*. 2017 Nov 23;4(4):246-252. doi: 10.1016/j.wjorl.2017.09.003.
  23. Pane G, Cacciola G, Giacco E, Mariottini GL, Coppo E. Assessment of the Antimicrobial Activity of Algae Extracts on Bacteria Responsible of External Otitis. *Mar Drugs*. 2015 Oct 20;13(10):6440-52. doi: 10.3390/md13106440.
  24. Di Lullo AM, Russo C, Piroli P, Petti A, Capriglione P, Cantone E, Motta G, Iengo M, Elefante A, Cavaliere M. Malignant Otitis External: Our Experience and Literature Review. *Am J Case Rep*. 2020 Aug 18;21: e925060. doi: 10.12659/AJCR.925060