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Analysis of pathogens and antimicrobial treatment in different groups of patients with chronic otitis media

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Main Article

Dr M Nowaczewska takes responsibility for the integrity of the content of the paper

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Abstract

Objective. Microbial infection plays an important role in exacerbation of chronic otitis media. The aim of this study was to analyse the microbiota in chronic otitis media in the context of local treatment.

Method. In this prospective study, samples for microbiological examination were taken from 119 patients who underwent operation because of chronic otitis media.

Results. The results were compared between groups depending on the type of operation (none, tympanoplasty or radical), the presence of cholesteatoma or granulomatous tissue or discharge from the ear as a symptom of exacerbation. Antibiotic susceptibility of germs was analysed to define the strategy of treatment. A total of 209 samples were collected from 119 patients with chronic otitis media.

Conclusion. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were pathogens most frequently identified from the ear in the course of chronic otitis media. *Pseudomonas aeruginosa* was concerned with major pathology of the middle ear (radical surgery, cholesteatoma or granulomatous tissue, persisting discharge after treatment), whereas *Staphylococcus aureus* was obtained in dry perforations without other pathology in the middle-ear cavity. Ciprofloxacin was effective against *Staphylococcus aureus,* but *Pseudomonas aeruginosa* strains were ciprofloxacin resistant.

Introduction

Microbial infection plays a significant role in development of chronic otitis media. Despite availability of antibiotics, pathogens existing in the air-filled cavity of temporal bone still present an enormous therapeutic problem. Pathogens are responsible for exacerbation of inflammation which manifests as pain and discharge.[1] They also lead to otogenic intratemporal and intracranial complications. The matrix of cholesteatoma is an ideal substrate for colonisation and makes antibiotic penetration more difficult. Accumulation of inflammatory cytokines, lymphokines, and bacterial antigens or toxins may induce development of inflammatory granulation tissue.[1]

The aim of our study was to analyse pathogenic germs isolated from patients with chronic otitis media and antibiotic susceptibility in combination with the pathology (cholesteatoma, granulation), method of treatment (operation type) and intensity of inflammation (discharge from the ear) in order to determine antimicrobial treatment in this group of patients.

Materials and methods

This prospective study involved 119 patients recruited consecutively from the Department of Otolaryngology at University Hospital in Bydgoszcz between 2015 and 2018. Patients were diagnosed and treated because of chronic otitis media. Patients were admitted to hospital for initial management and were not treated by primary care at all before being referred to the hospital; this included not being treated with either ciprofloxacin or any other local or systemic drug. During the study, 209 smears from the ears were collected and analysed.

Inclusion criteria were: patients with chronic otitis media, patients with tympanic membrane perforation, and patients treated by two experienced surgeons with complete medical documentation. Exclusion criteria were: patients with a complete tympanic membrane, patients with secretory otitis media, acute otitis media, otogenic complication and current antibiotic use.

Samples for microbiological testing were collected by the ENT specialist using a microscope and sterile swabs, avoiding contact with skin of the external auditory canal after

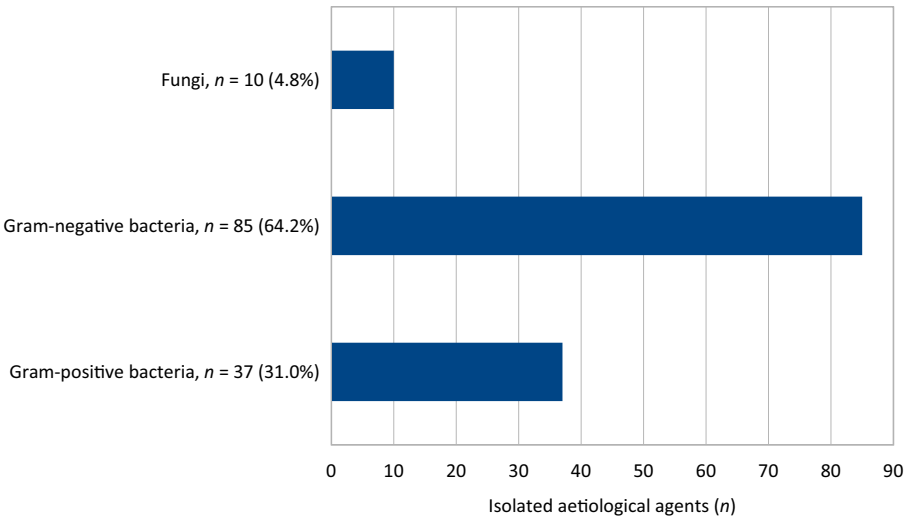

Fig. 1. Proportion of bacterial and fungal aetiological agents ($n = 132$) isolated from smears from the ear.

cleansing it with an antiseptic solution. No patient received local or general antibiotics within four weeks before hospitalisation.

The microbiological examination of material was performed at Clinical Microbiology Division of The University Hospital No. 1 in Bydgoszcz. Samples were prepared in line with standard microbiological procedures. Materials were inoculated in blood agar, chocolate agar, MacConkey agar, cetrimide agar and Sabouraud dextrose agar (bioMérieux, Marcy l'Étoile, France), then incubated for 24 hours at 37 degrees either aerobically or under 5 per cent CO_2 atmosphere. For obligatory anaerobes, samples were collected only from selected patients (not routinely), so they were not taken into consideration in this study.

Species were identified in 2015 using VITEK 2 compact automated system tests (bioMérieux) and in 2016–2018 were identified using matrix-assisted laser desorption ionisation-time of flight mass spectrometry (Bruker, Germany). The VITEK 2 compact system was used for the susceptibility testing of isolated microorganisms. Results were interpreted in accordance with recommendations of the European Committee on Antimicrobial Susceptibility Testing ('EUCAST').[2]

The results of cultures were grouped depending on the clinical picture. We compared patients who had not been operated on so far, patients who had undergone tympanoplasty and patients who had undergone radical surgery in terms of microbiological examination results. Radical surgery was defined as the canal wall down technique without tympanoplasty or ossiculoplasty (due to extensive damage of the ossicles or other co-indications to reconstructive procedures).

Afterwards, the results of cultures obtained in patients with chronic simple otitis media or with granulomatous infection or cholesteatoma were compared. The classification of the patients was based on intra-operative findings after the culture swab was taken. Cultures were also assessed in patients with discharge that subsided or persisted after treatment, (i.e. with or without persistent inflammation in the middle-ear spaces).

All the procedures were approved by the Local Ethics Committee of the Ludwik Rydygier Collegium Medicum in Bydgoszcz. The patients gave their informed consent before the start of any procedure.

Statistical analysis was performed to compare groups of patients using the chi-square test. Data were statistically significant if the p-value was equal to or less than 0.05.

Results

A total of 209 samples were collected from 119 patients with chronic otitis media. In a few patients, samples were taken for analysis several times during the study period, resulting in different pathogens from the same ear. Swabs from both ears were collected in 12 patients.

The study group consisted of 86 men (72.3 per cent) and 33 women (27.7 per cent) aged between 18 and 76 (average age, 53 years). A total of 88 cultures (42.1 per cent) were positive for pathogenic germs and 123 cultures (57.9 per cent) were negative for pathogenic germs. Negative samples were excluded from the study.

In total, 132 potential aetiological agents were isolated, including 37 (31.0 per cent) gram-positive bacteria, 85 gram-negative bacteria (64.2 per cent) and 10 fungi (4.8 per cent) (Figure 1).

In 49 cultures (55.7 per cent), only one aetiological factor of infection was shown, while a mixed culture was obtained in 39 cultures (44.3 per cent). *Staphylococcus aureus* was more often isolated in monocultures than in a mixed culture (16 (64 per cent) *vs* 9 (36 per cent) of samples), while a higher proportion of *Pseudomonas aeruginosa* was more frequently grown in cases of mixed infections (20 (58.8 per cent) *vs* 14 (41.2 per cent) of samples). Generally, *P aeruginosa* and *S aureus* were isolated most frequently (Table 1).

Afterwards, culture results were compared in the three groups of patients: those who had not been operated on so far, those who had undergone tympanoplasty and those who had undergone radical surgery. *S aureus* (13 samples; 27.7 per cent) was cultured most often in patients from the first group. No single prevailing germ was found in patients who underwent tympanoplasty. *P aeruginosa* (25 samples; 38.5 per cent) was most often identified in patients who underwent radical surgical procedures.

Samples collected from patients without abnormalities within the middle-ear cavity were compared with the ones from patients with granulomatous infection or cholesteatoma. *P aeruginosa* (27 samples; 28.1 per cent) and *Proteus mirabilis* (8 samples; 8.3 per cent) were most frequently identified in patients suffering from chronic otitis media with cholesteatoma or granulation, whereas *S aureus* (9 samples; 27.3 per cent) prevailed in the study group without additional abnormalities.

Subsequently, microbiological results were compared in patients with discharge that subsided or persisted after

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Table 1. Micro-organisms isolated from ears with chronic otitis media

Micro-organism	Isolates (*n*)	Isolates (%)
Pseudomonas aeruginosa	34	25.8
Staphylococcus aureus	25	18.9
Proteus mirabilis	10	7.6
Escherichia coli	9	6.8
Enterococcus faecalis	6	4.5
Klebsiella oxytoca	4	3
Candida albicans	4	3
Morganella morgani	3	2.3
Serratia marcescens	3	2.3
Enterobacter cloacae	3	2.3
Citrobacter koseri	3	2.3
Achromobacter xylosoxidans	3	2.3
Coagulase negative staphylococci	2	1.5
Providencia stuartii	2	1.5
Alcaligenes faecalis	2	1.5
Candida parapsilosis	2	1.5
Other species*	17	12.9
Total	132	100

*Other species (n = 1 for each of the micro-organisms): *Streptococcus pyogenes*, *Enterococcus faecium*, *Proteus vulgaris*, *Enterobacter asburiae*, *Raoultella ornithinolytica*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Citrobacter freundii*, *Acinetobacter haemolyticus*, *Haemophilus influenzae*, *Pseudomonas fluorescens*, *Achromobacter denitrificans*, *Bordetella trematum*, *Candida glabrata*, *Aspergillus niger*, *Aspergillus fumigatus,* aspergillus spp.

treatment. *P aeruginosa* (27 samples; 33.8 per cent) was most frequently identified if discharge from the ear persisted. On the other hand, *S aureus* (12 samples; 24.5 per cent) was grown if excretion subsided after treatment. All data described above were statistically significant except for *P mirabilis*. The results are summarised in Table 2.

Afterwards, antibiotic susceptibility was analysed. All *S aureus* strains were methicillin-sensitive (methicillin sensitive *S aureus*). Four of these (14.8 per cent) were resistant to ciprofloxacin. Among enterobacterales, 6 strains showed resistance to ciprofloxacin (15.4 per cent). One *P mirabilis* strain produced extended-spectrum β-lactamase, and three *P mirabilis* strains were multidrug resistant (resistant to, among other things, ciprofloxacin).

A high percentage of *P aeruginosa* strains were not susceptible to ciprofloxacin and levofloxacin (13 (40.6 per cent) and 14 (43.9 per cent) strains, respectively). Two multidrug resistant strains were identified. *P aeruginosa* strains that were not multidrug resistant were susceptible to piperacillin with tazobactam, ceftazidime, cefepime, imipenem and meropenem (except one strain), tobramycin, amikacin, and colistin.

Discussion

In this study, *P aeruginosa* and *S aureus* were most frequently grown in cultures collected from patients with chronic otitis media, which is in agreement with the literature.[1–5] In the above comparison, presence of *P aeruginosa* was correlated with greater severity of inflammation (discharge from the ear, cholesteatoma and granulomatous infection), while *S aureus* was grown in stable cases (no discharge, dry tympanic membrane perforation).

Analysis of antibiotic susceptibility showed that three *S aureus* and 5 enterobacterales strains were resistant to ciprofloxacin, and three *P mirabilis* strains exhibited multidrug resistance. Over 40 per cent of *P aeruginosa* strains were not susceptible to ciprofloxacin and levofloxacin; two multidrug resistant strains were identified.

Microbial resistance to antibiotics is a highly disturbing phenomenon, particularly in the context of topical treatment administered to patients with chronic otitis media. The majority of antibiotic ear drops available at pharmacies should not be used if the tympanic membrane is perforated because their ingredients are toxic to the ear. Neomycin, bacitracin, gramicidin, polymyxin are broad spectrum antimicrobials but are also highly toxic to the hearing organ, nervous system and kidneys.[3,6] Therefore, they are indicated only to treat otitis externa with intact tympanic membrane.

Few reports suggest that the ototoxic effect of topical drugs used to treat chronic otitis media can be ignored.[7] Ciprofloxacin 2 per cent is a drug that can be safely administered in cases of tympanic membrane perforation. Literature reports indicate high efficacy of ciprofloxacin against *P aeruginosa* and *S aureus* (95 per cent and 85 per cent, respectively); therefore, this drug is recommended as a first-line treatment of infections with these strains.[1,3,8,9] Ciprofloxacin is also effective against *Streptococcus pneumoniae,* enterobacter spp., *Klebsiella pneumoniae, P mirabilis, Escherichia coli and Haemophilus influenzae.* In this study, it is worth noting there were a large percentage (40.6 per cent) of *P aeruginosa* strains that are resistant to ciprofloxacin. High drug resistance could result from antibiotic therapy that is too long at an outpatient clinic without testing susceptibility and a very broad administration of ciprofloxacin, which consequently led to selection of insensitive strains.[10] Antibiotic resistance of *P aeruginosa* in chronic suppurative otitis media may increase with recurrent infection.[11] Ciprofloxacin resistance was noted in 18.8 per cent of *S aureus* strains, which is similar to the literature.[1,3,4] Ciprofloxacin in children is recommended by many authors, especially in the case of tympanostomy because of chronic otitis media with effusion.[3,12] Only a single report suggests that this drug can be absorbed and thus damage juvenile articular cartilage.[1]

- *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the pathogens most frequently identified from the ear in the course of chronic otitis media
- *Pseudomonas aeruginosa* was concerned with major pathology of the middle ear and presented high resistance to ciprofloxacin

With regard to antifungals, clotrimazole is indicated in treatment of otitis externa and otitis media is available without a prescription. As suggested in the literature, clotrimazole is not ototoxic and exhibits broad spectrum activity against a large group of micro-organisms (among other things *Candida albicans,* Aspergillus spp.).[3,12–14] Percentage of fungal infections was 4.8 per cent in the study material, whereas the literature reports that its incidence ranges from 1.4 per cent to even 24.6 per cent.[1,4,5,7] Fungal infections may be associated with excessive use of otic corticosteroids.[1]

Topical antiseptics can be used instead of the above-mentioned drugs as an alternative treatment. To acidify the environment, aqueous or alcoholic solutions of boric or acetic acid can be used and are an effective measure against germs,

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Table 2. Culture results in correlation with clinical symptoms of patients with chronic otitis media

Clinical group	Culture results	Value (*n*)	Value (%)	*P*-value
No prior surgery	*Staphylococcus aureus*	13	27.7	<0.001
Tympanoplasty	No predominant species	–	–	0.957
Radical surgery	*Pseudomonas aeruginosa*	25	38.5	<0.001
No cholesteatoma/granulomatous infection	*Staphylococcus aureus*	9	27.3	<0.001
Cholesteatoma/granulomatous infection	*Pseudomonas aeruginosa*	27	28.1	<0.001
	Proteus mirabilis	8	8.3	>0.05
Ear discharge subsided after treatment	*Staphylococcus aureus*	12	24.5	<0.001
Ear discharge persisted after treatment	*Pseudomonas aeruginosa*	27	33.8	<0.001

making it easier to remove the discharge and dead epithelial cells. Alcoholic solutions may irritate the mucous membrane of the middle ear and they are ototoxic. That is why aqueous solutions are recommended (e.g. a 3 per cent solution of boric acid).[1,3] Cleaning of the post-operative cavity under the microscope after canal wall down procedures using suction is an elementary procedure that not only removes deposits but also improves drug penetration.[1,3,6]

If inflammation of the middle or external ear becomes exacerbated, an otic steroid (e.g. fluocinolone) may be used. Topical administration of steroids contributes to faster pain relief[3] but may also lead to fungal superinfection that would require initiation of antifungals.[1]

Systemic antimicrobial drugs should not be used to treat chronic otitis media because of low penetration into the tympanic cavity, selection of drug-resistant strains and masking of otogenic complications. It is advisable to always collect material for microbiological testing and perform an antibiotic susceptibility test before any treatment.[1,4–7]

Conclusion

P aeruginosa and *S aureus* were the pathogens most frequently identified from the ear in the course of chronic otitis media. *P aeruginosa* found in middle-ear cavities was associated with exacerbated inflammation, discharge, cholesteatoma or granulomatous tissue, whereas *S aureus* was more common in patients with chronic otitis media without additional pathology. Ciprofloxacin appeared to be effective against *S aureus*, and these strains are highly sensitive to fluoroquinolones. In cases of *P aeruginosa* strains, attention should be drawn to the high percentage (40.6 per cent) of stains resistant to these drugs. A smear should always be collected for microbiological testing. It is crucial to identify a pathogen, complete an antibiotic susceptibility test and initiate topical targeted treatment of chronic otitis media, both before and after surgery. Cleaning of the post-operative cavity under a microscope using a suction device is of particular importance after canal wall down procedures. Systemic antibiotics should not be administered in treatment of chronic otitis media.

Competing interests. None declared

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