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Antibiotic resistance in pathogens causing acute otitis media in Finnish children

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ABSTRACT

Introduction: Microbiology and susceptibility of middle ear pathogens in children change over time and antibiotic resistance is increasing globally. For the clinicians it is important to be up to date about the resistance situation when considering antibiotic treatment in acute otitis media (AOM). In this study we analysed the resistance profile of AOM pathogens in out-patient children in Finland.
Methods and materials: A total of 41 culture positive middle ear fluid (MEF) samples were analysed for bacteria and the presence of antibiotic resistant strains. The samples were obtained from children aged six – 39 months who participated in the otitis media trial during one year period.
Results: The most common pathogen was *Haemophilus influenzae* 17 (40%), followed by *Streptococcus pneumoniae* in 15 (35%) and *Moraxella catarrhalis* in 8 (19%). Other pathogens were detected in 3 (7%) of cases. Antibiotic resistance or diminished sensitivity was seen in 63% of the detected bacteria and 28% of pathogens produced beta-lactamase.
Conclusions: Antibiotic resistant bacterial strains causing AOM have increased in Finland. Nevertheless, most of the pathogens (72%) were sensitive to amoxicillin, which is still recommended as the first line antibiotic in the treatment of AOM.

1. Introduction

Acute otitis media (AOM) is one of the most frequent diagnoses in small children and is the most common reason for antimicrobial treatment in children. It is estimated that about 500000 AOMs are diagnosed in Finland every year [1]. Nowadays the major bacterial AOM pathogens in children are *Streptococcus pneumonia* (*SP*), *Haemophilus influenzae* (*HI*) and *Moraxella catarrhalis* (*MC*) [2,3], but the prevalence of these bacteria is variable and resistance patterns are changing. Over the years, bacterial resistance has become a problem in many countries. The resistant strains of AOM pathogens have been relatively rare in Finland in the late 1990s [3–5], but more recent studies about AOM pathogens in out-patient children is lacking. Particularly the information of the number of drug-resistant *SP* and beta-lactamase-producing *HI* are important, because they are common pathogens in AOM, and might not be managed with all first line antibiotics recommended in the national guidelines.

In this study we determined AOM pathogens and their resistance profile in middle ear fluid (MEF) obtained from out-patient children in the city of Tampere, Finland. We also analysed how pathogens and their resistance has changed over the years in the Finnish population.

2. Methods and materials

Altogether 91 MEF samples were obtained from children aged six to 39 months who participated in our previously published otitis media trial [6]. Pathogens and their antimicrobial resistance was analysed from all 41 (45%) culture positive MEF samples. The children were enrolled for the study from outpatient clinics in the city of Tampere between September 2010 and December 2011. All patients were examined by an otolaryngologist at Tampere University Hospital ENT-outpatient

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Table 1
Demographics and AOM risk factors of 41 study children.

	All	With resistant pathogen		
	n (%)	Yes, *n* (%)	No, *n* (%)	*p*-Value
Children	41	26 (63)	15 (37)	
Mean age (months)	19.8	21.5	15.0	0.355*
Range	6–39	6–36	6–39	
Number of previous AOM episodes				
median	4	4.5	2	0.604*
Range	0–23	0–23	0–15	
Males	22 (54)	14 (54)	8 (53)	0.975
PVC-10 vaccination	9 (22)	3 (12)	6 (40)	0.053
≥3 AOMs in history	27 (66)	20 (77)	7 (50)	0.155
Previous antibiotic < 30 days	17 (42)	11 (42)	6 (40)	0.885
First born	11 (27)	4 (15)	7 (47)	0.064
Cigarette smoke exposure	21 (51)	15 (58)	6 (40)	0.275
Breast feeding under 6 months	18 (44)	12 (46)	6 (40)	0.702
Siblings' with history of AOM	15 (37)	11 (42)	4 (27)	0.317
Attending day-care	21 (51)	14 (54)	7 (47)	0.658
Current use of pacifier	17 (42)	14 (54)	3 (20)	0.034**

* Mann–Whitney *U*-test.
** $p < 0.005$.

clinic. The definition of AOM was based on symptoms of acute respiratory infection with signs of inflammation of the tympanic membrane and presence of middle ear fluid, or alternatively otorrhea through a tympanostomy tube or a spontaneous perforation of the tympanic membrane. If AOM was diagnosed a myringotomy was performed under local anaesthesia (topical phenol solution) and MEF specimens were obtained by sterile suction tip. In children with tympanostomy tubes or spontaneous perforations the MEF specimens were also obtained from the middle ear by using suction.

Bacterial culturing from MEF samples was performed by an accredited laboratory (Department of Microbiology, Fimlab Laboratories, Tampere, Finland) using standard protocols. Briefly, samples were streaked on chocolate and 5% horse blood agar plates. The plates were incubated at 35 °C for 24 h (−48 h chocolate agar plate for *HI*) in aerobic conditions. Species identification was performed by conventional methods including specific identification tests and API tests, and antimicrobial susceptibility testing by EUCAST disk diffusion and – if needed – by gradient MIC (E-test) methods according to the standard procedure. The MIC breakpoints were classified according to EUCAST guidelines, e.g. *SP* isolates were considered penicillin-susceptible if penicillin MIC values were <0.06 μg/ml, intermediately susceptible if MIC values were between 0.06 and 2.0 μg/ml and fully resistant if MIC values were >2.0 μg/ml [7]. Antibiotic treatment was based on the results from bacterial culture and susceptibility testing of detected bacteria and on the recommendations of the Finnish Current Care Guidelines for AOM [8]. Antibiotic treatments included amoxicillin or penicillin as first line, and for those allergic to penicillin trimethoprim-sulphamethoxazole (TMP-SMX) or macrolides. In case of treatment failure, second line recommendations were amoxicillin-clavulanate, cefaclor or cefuroxime.

The study was approved by the ethical committee of Tampere University Hospital (grant number R10026) and a written consent was obtained from all participating families.

3. Results

The demographics and AOM risk factors of the patients with or without resistant bacteria is seen in Table 1. 41 culture positive MEF samples were analysed, and altogether 43 bacterial pathogens were detected. Seven (17%) of the samples were taken from a child with tympanostomy tubes and two with spontaneous perforations. The most frequently isolated pathogen was *HI*, and it was detected in 17 (40%) cases, followed by *SP* 15 (35%) and *MC* 8 (19%). Other pathogens were detected in 3 (7%) cases. Other pathogens included *Staphylococcus aureus* and mixed flora. Culture results are shown in Table 2. In two MEFs two different pathogens were detected and the combinations were *HI* + *MC* and *SP* + *MC*.

Antimicrobial susceptibility tests were performed and diminished susceptibility was documented in 27 (63%) of all detected bacteria. Twelve (80%) *SP* isolates were totally susceptible for penicillin, while three (20%) cases were intermediately resistant to penicillin. All of these strains were also non-susceptible for TMP-SMX and erythromycin. Overall, 27% of all *SP* strains were fully resistant to TMP-SMX and 40% were fully resistant to erythromycin. Similarly, 29% of all *HI* strains were fully resistant to TMP-SMX and 47% of strains were intermediately resistant to erythromycin. Of *HI* strains 24% produced beta-lactamase and were resistant to ampicillin. All *MC* strains produced beta-lactamase and were resistant to ampicillin, but *MC* strains were susceptible for all other antibiotics. One third (37%) of the detected bacteria showed no resistance, and 10 (37%) of the 27 resistant strains were resistant to more than one antibiotic. Susceptibility of *HI*, *SP* and *MC* to different antibiotics is seen in Table 3.

Table 2
Distribution of the 43 detected pathogens.

Pathogen	Total	Sample obtained by myringotomy	Sample obtained via tympanostomy tube	Sample obtained via perforated tympanic membrane
HI	17	14	3	0
SP	15	12	2	1
MC	8	6	2	0
SA	1	0	0	1
Mixed flora	2	1	1	0