Acta Otolaryngol (Stockh) 1998; 118: 557–562

Epidemiology and Treatment of Otitis Media with Effusion in Children in the First Year of Primary School

P. MARCHISIO[1], N. PRINCIPI[1], D. PASSALI[2], D. C. SALPIETRO[3], G. BOSCHI[4], G. CHETRÌ[5], G. CARAMIA[6], R. LONGHI[7], E. REALI[8], G. MELONI[9], A. DE SANTIS[10], B. SACHER[11] and G. CUPIDO[12]

From the [1]Department of Paediatrics 4, University Hospital, Milan, Italy, [2]ENT Department, University Hospital, Siena, Italy, Departments of Paediatrics of [3]University Hospital, Messina, [4]Arcispedale S. Maria Nuova, Reggio Emilia, [5]University Hospital, Bari, [6]Ospedale G. Salesi, Ancona, [7]Ospedale S. Anna, Como, [8]Ospedale Bassini,Cinisello Balsamo, [9]University Hospital, Sassari, [10]University Hospital, Genova,[11]Ospedale Civile, S. Daniele del Friuli and the [12]ENT Department, University Hospital, Palermo, Italy

Marchisio P, Principi N, Passali D, Salpietro DC, Boschi G, Chetrì G, Caramia G, Longhi R, Reali E, Meloni G, De Santis A, Sacher B, Cupido G. *Epidemiology and treatment of otitis media with effusion in children in the first year of primary school.* Acta Otolaryngol (Stockh) 1998; 118: 557–562.

In this multicentre study we evaluated the prevalence and risk factors of otitis media with effusion (OME) in Italian school-children and the effectiveness of medical treatment of chronic OME with a new cephalosporin, ceftibuten. During two winter periods, 3413 children, aged 5 to 7 years, were examined for the presence of OME by means of pneumotoscopy and a portable, hand-held tympanometer. The prevalence of asymptomatic OME was 14.2%, with no difference as regards sex, age, month of examination or geographic area. Younger children had significantly more bilateral than unilateral effusion. A recent episode of acute otitis media and previous tonsillectomy or adenoidectomy were associated with an increased risk of OME in multivariate logistic regression models. The presence of OME was unrelated to such factors as birthweight, prematurity, sibling or parental history of allergy, duration of daycare attendance, family history of ear infections. After 12 weeks, 26.6% of children with OME still had middle-ear fluid: 52 were randomized to ceftibuten (9 mg/kg q.d. for 14 days) and 59 to no treatment (nasal saline drops allowed). Children treated with ceftibuten had a significantly better resolution of middle-ear effusion after 4 and 8 weeks. As mass screening programmes for OME in the year of school entry are questioned, a focus only on children with known risk factors seems advisable. Ceftibuten can be useful in reducing the duration of middle-ear effusion. *Key words: ceftibuten, epidemiology, otitis media with effusion.*

INTRODUCTION

Otitis media with effusion (OME) is defined as an inflammation of the middle ear accompanied by the presence of liquid in the middle-ear space without the signs and symptoms of acute infection (1). The presence of fluid in the middle ear is accompanied by a variable degree of conductive hearing loss which can be particularly disturbing in two periods of a child's life: in the first 2–3 years of age, because of the risk of speech and language delay, and in the first year of primary school, as hearing loss can cause problems with school work and impair the child's ability to cope with various stresses imposed by the school setting (2–4). Considering the potential healthcare implications of OME, various authorities have called for mass screening for asymptomatic middle-ear effusion both in young children and in children attending the first year of primary school (5, 6). However, mass screening for OME in school-children has been questioned because of the difficulty in identifying the optimal diagnostic method/s and its cost-effectiveness ratio in an era of concerns about the increasing costs of the healthcare system (7). A possible solution to the problem might be the identification of variables that predict children at high risk for OME and thus the careful monitoring of only these children.

In addition, studies have shown that in 27 to 50% of cases middle-ear aspirates from children with OME contain the same bacteria encountered in acute otitis media and that antibiotics have some efficacy in the short-term resolution of the disease (8, 9). Amoxicillin has been indicated as first choice, but its use can be questioned in areas where the emergence of resistance among the most commonly isolated pathogens is relevant (10).

The epidemiology of OME in Italian children has not yet been studied at length (11). Our study had 2 aims: *(a)* to evaluate the prevalence and the risk factors of OME in Italian children in the year of school entry and *(b)* to evaluate the effectiveness of treatment of OME with a recent broad spectrum of cephalosporin, ceftibuten, active against the most common pathogens of this disease.

METHODS

Population and enrollment

The multicentre study was conducted in two winter seasons (October through January) in 1993–94 and 1994–95. Children attending the first year in 11 primary schools distributed in different regions of Italy were included. The study was approved by the local Ethics Committee in each centre and parents had to

 ISSN 0001-6489

give informed consent before enrolment. A child was excluded if he/she had any of the following conditions: craniofacial abnormality, serious underlying disease, any major congenital malformation, acute upper respiratory infection including acute otitis media, high risk of sensorineural hearing loss, chronic suppurative otitis media, perforation of tympanic membrane and previous ear surgery.

All the children in the same class were visited at the same time, at school, by a validated otoscopist from either one of the 9 Pediatric Departments or the 2 Otolaryngology Departments involved in the study (12). An ear examination including pneumatic otoscopy and tympanometry was performed; both ears were examined. Pneumatic otoscopy was performed using a Welch Allyn model 20100 otoscope. Tympanograms were obtained with a portable tympanometric system (Microtymp, Welch Allyn; proble frequency 226 Hz, SPL 85 db and air pressure range from +200 to −400 mm H_2O) (13). OME was defined as asymptomatic middle-ear effusion, demonstrated by an abnormal appearance of the tympanic membrane, diffusely opaque, with impaired mobility or presence of air-fluid levels associated with a flat, type B tympanometric curve. The otoscopic findings were noted prior to the tympanometric measurements. Ears with occluding wax underwent the tympanometric measurement after removal of the ear wax. Unilateral or bilateral OME were both considered as one episode of OME.

At time of enrollment the parents were asked to answer a questionnaire regarding the following factors: duration of breast feeding, duration of daycare attendance, the number of family members and their ages, birth rank, smoking habits (whether more or less than 10 cigarettes a day in the home), previous tonsillectomy and/or adenoidectomy, time of the last episode of acute otitis media, family history of allergy (eczema, asthma, hay-fever), family history of acute otitis media.

Ceftibuten as treatment of OME

Children with a diagnosis of unilateral or bilateral OME were re-examined after 12 weeks. A careful interval history was obtained. Those with persistent unilateral or bilateral middle-ear effusion were randomized to receive ceftibuten (9 mg/kg/day in one daily dose for 14 days) or no treatment (only nasal saline drops were allowed). Randomization was made in each centre on the basis of a local randomization list. Children were excluded if they had any of the following: hypersensitivity to a beta-lactam drug, antibiotic therapy in the previous month, concomitant upper respiratory infection that would preclude evaluation of response to study medication. Outcome was assessed at 4 and 8 weeks after entry by means of both pneumatic otoscopy and tympanometry. Investigators were blinded to treatment assignments and patients and parents were asked not to discuss medications or duration of treatment with investigators. Outcome was defined as cure if the child was effusion-free or as improvement if the child with bilateral OME at entry had unilateral effusion.

Data analysis

In order to assess the association between the presence of OME and covariates, proportions were compared using the χ^2 test and Fisher's exact test in the case of 2×2 contingency tables. Odds ratio and relative confidence intervals were provided for variables possibly related to OME. Logistic regression analysis was used as multivariate approach to evaluate the influence of prognostic factors (Link Italia, Scientific Division). All reported p-values are 2-sided and referred to the significance level of 5%.

RESULTS

During the two winter seasons, 3,413 children entered the study: 1,508 in the first year and 1,905 in the second year; 13.5% of the children in the first survey and 14.8% in the second survey had OME. A preliminary comparative evaluation of the epidemiological data obtained in the 2 surveys showed no statistically significant differences, thus the data of the 2 surveys were pooled and analysed together. Asymptomatic OME was diagnosed in 485 (14.2%) children: 219 (45.2%) had unilateral middle-ear effusion while 266 (54.8%) had bilateral effusion. Table I gives the distribution of selected subject characteristics according to the presence of middle-ear effusion. No significant differences were found in the proportion of children with OME compared with those without middle-ear effusion as regards sex, age, month of examination and geographic location of the school. When considering unilateral and bilateral OME separately, children 7 years of age had significantly less bilateral OME (120/256, 46.8%) than children 6 years of age or younger (142/227, 62.5%).

Univariate analysis of factors potentially associated with risk of middle-ear effusion (considering unilateral and bilateral effusion both as a whole and separately) indicated as significant: having been breast-fed for less than 6 months, previous tonsillectomy or adenoidectomy, recent episode of acute otitis media and passive smoking. Variables not significantly associated with the presence of OME included having an older sibling, birthweight, sibling or parental history of allergy, duration of daycare attendance, family history of ear infections, presence of house pets (Table II).

Table I. *Characteristics of school-children according to the presence of otitis media with effusion*

Characteristic	OME no. (%)	No OME no. (%)	Total no. (%)
No. of children	485	2,928	3,413
Month of examination			
October–November	296 (61.0)	2,024 (69.1)	2,320 (67.9)
December–January	189 (39.0)	904 (30.2)	1,093 (32.1)
Age (years)			
5	16 (3.3)	92 (3.1)	108 (3.2)
6	211 (43.5)	1,452 (49.6)	1,663 (48.7)
7	258 (53.2)	1,384 (47.3)	1,642 (48.1)
Sex			
Male	248 (51.1)	1,562 (53.3)	1,810 (53.0)
Female	237 (48.9)	1,366 (46.7)	1,603 (47.0)
Laterality of OME			
Unilateral	219 (45.2)	–	219 (45.2)
Bilateral	262 (54.0)	–	262 (54.0)
Geographic area			
Northern Italy	291 (60.0)	1,656 (56.6)	1,947 (57.0)
Southern Italy	194 (40.0)	1,272 (43.4)	1,466 (43.0)

Multivariate logistic regression analysis of factors associated with risk of OME identified as significant factors only having a recent episode of acute otitis media and a history of adenoidectomy or tonsillectomy.

Persistence of OME

Four-hundred-and-fifty-one children out of the initially identified 485 with OME were re-examined after 12 weeks. One-hundred-and-twenty (26.6%) children still had middle-ear effusion. Most of the children were males; one-third had had one episode of acute otitis media in the previous 90 days and about 70% had bilateral effusion. Factors associated with risk of persistence of effusion for 12 weeks were identical to those already demonstrated significantly related to the presence of OME.

Treatment of OME with ceftibuten

One-hundred-and-twenty (26.6%) children were randomized to receive ceftibuten (58 patients) or no treatment (only nasal saline drops allowed) (62 children). Because of protocol violations, 9 children (6 in the ceftibuten and 3 in the saline drops group) were excluded from analysis. Thus 111 children were evaluated: 52 treated with ceftibuten and 59 who received only nasal saline drops. The baseline characteristics of children were similar in the two groups as regards sex, occurrence of acute otitis media in the interval period, laterality of effusion and presence of risk factors (Table III). As far as outcome is concerned, all children returned to scheduled follow-up visits. At both the 4-week and 8-week assessment subjects treated with ceftibuten had a significantly better outcome compared with children receiving no treatment or treated with only nasal saline drops. No medication side effects were reported in any subject.

DISCUSSION

The prevalence of OME in Italian children at the age of 6–7 years, in the year of school entry, is about 14%. This figure is a little higher than that demonstrated in most European studies, in which the prevalence has ranged from 3 to 10% (14, 15). We believe that these data do not result from an overdiagnosis but that they reflect the real Italian situation: in fact the diagnosis of otitis media with effusion was made on very strict criteria, that is on the combination of otoscopic findings obtained by a validated pneumatic otoscopist plus a type B tympanogram. Tympanograms were obtained by means of a portable, hand-held tympanometer, which provided printed curves, easy to be retained for documentation and future comparisons, and which has been recently found accurate in predicting middle-ear fluid (13). Planning this study, we knew that the use of both pneumatic otoscopy and tympanometry is usually not recommended for screening purposes, as the use of otoscopy needs an otoscopist with extensive training, but, on the other hand, we were aware that total reliance on tympanometry for the diagnosis of OME can be inappropriate, because other conditions can produce tympanometric findings similar to effusion (6). Moreover, we decided to use only a type B tympanogram to define the presence of effusion and not to take into account tympanograms of the type C curve, even if some of the ears with these tympanometric types, especially type C2, probably have some

Table II. *Analysis of variables potentially associated with the presence of otitis media with effusion in school-children*

Variable	Odds ratio	95% CI	p
Breast-feeding ≤ 6 months	1.319	1.019–1.707	0.036
Passive smoking	1.269	1.043–1.544	0.018
Recent (<90 days) acute otitis media	5.356	3.786–7.578	<0.001
Adenoidectomy	1.596	1.170–2.178	0.004
Tonsillectomy	1.589	1.037–2.434	0.044
Prematurity	1.231	0.876–1.73	0.232
Documented allergy	0.998	0.692–1.440	1.000
Older sibling/s	1.240	0.989–1.466	0.071
Daycare attendance for ≥1 year	1.190	0.866–1.636	0.309
Family history of ear disease	1.065	0.863–1.314	0.553
Family history of allergy	1.189	0.965–1.465	0.103
House pets	1.037	0.804–1.337	0.794

fluid in the middle ear (16). It is likely that if we had also included type C tympanometric curves the point prevalence of OME in our population would have been a little bit higher. Using both type B and type C tympanograms, Portoian-Shuhaiber and Cullinan (17) reported that 41% of children aged 5–6 years in South London had middle-ear disease, and Holmquist et al. (18) in Kuwait demonstrated that 31.3% of school-children (aged 7–9.5 years) had OME.

A criticism to our study might be that we did not evaluate the acoustic reflex and we did not perform a hearing test, so we could not evaluate the degree of hearing loss in children with OME and the possible impact of treatment on it. However, the main purpose of our study was not to assess the prevalence of hearing loss in primary school but to evaluate risk factors for the presence and persistence of OME in order to select those children who require a more accurate otologic and hearing examination and thus save on healthcare costs.

Table III. *Ceftibuten compared with no treatment in children with persistent otitis media with effusion*

	Ceftibuten no. (%)	No treatment no. (%)
No. of children	52	59
Males	31 (59.6)	33 (55.9)
Recent (<90 days) acute otitis media	19 (36.5)	23 (39.0)
Bilateral effusion	37 (71.1)	41 (69.5)
Unilateral effusion	15 (28.9)	18 (30.5)
STATUS BY 4-WEEK VISIT		
Effusion-free	15 (28.8)	7 (11.9)
Bilateral to unilateral effusion	15 (28.8)	13 (22.0)
Persisting bilateral effusion	22 (42.4)	39 (66.1)
STATUS BY 8-WEEK VISIT		
Effusion-free	19 (36.5)	11 (18.6)
Bilateral to unilateral effusion	17 (32.7)	17 (28.8)
Persisting bilateral effusion	16 (30.8)	31 (52.6)

By 4-week visit: ceftibuten vs no treatment: $p = 0.02$.
By 8-week visit: ceftibuten vs no treatment: $p = 0.03$.

In epidemiological studies on OME in 6–7-year-old children in industrialized countries the role of possible risk factors for the presence of ear effusion has not yet been studied extensively. Teele et al. (19) were able to identify a sibling or parental history of ear infection and not being breast-fed as the only factors significantly associated with the duration of middle-ear effusion in a 7-year-old cohort, while Strachan et al. (20) found a strict correlation between passive smoking and middle-ear effusion in 7-year-old children. Our data are only partially in agreement with these studies, because in our study several factors (duration of breast-feeding less than 6 months, a previous history of tonsillectomy and adenoidectomy, exposure to passive smoking together with a recent episode of acute otitis media) were of major importance.

In our study, a duration of daycare attendance longer than 1 year between the age of 3 and 5 years was not associated with the presence of middle-ear effusion in the year of school entry: this seems difficult to explain, considering that children in daycare have middle-ear problems 2–4 times more frequently than children cared for at home and thus should be more likely to have long-term ear problems (21). However, the high number of children in our population attending daycare for more than 1 year

probably precluded a definitive evaluation of this variable.

A previous history of tonsillectomy or adenoidectomy was highly predictive of OME: this can be explained considering that this variable is a reliable indicator of a previous history of recurrent upper respiratory tract infections, including middle-ear diseases, as these are the most common indications for this type of surgery.Our data corroborate those of Virolainen et al. (15), who showed that 7–8-year-old children who had been reported by their parents to have had many respiratory illnesses had OME significantly more frequently than the rest of the studied population.

Bilateral middle-ear effusion was detected in about half of the children with OME. No single variable was predictive of bilateral compared with unilateral effusion, except age, as bilateral middle-ear effusion was significantly more prevalent in younger children.

In the first year of school a high resolution rate of middle-ear effusion is very common: only one-quarter of the children diagnosed as having OME still had middle-ear fluid after 12 weeks and, among them, about one-third had had a new episode of acute otitis media. The risk factors for persisting effusion were the same demonstrated in the baseline, larger, population. Our findings are in agreement with the data of Lous and Fiellau-Nikolajsen, who showed that only one-quarter of the children 7 years old still had OME after 3 months (14).

Even if small, the population of children with persisting middle-ear effusion in the first year of school deserve special attention because long-lasting hearing loss could impair their school performances. Antibiotic treatment has been indicated as a beneficial medical option: amoxicillin, given 50 mg/kg/day in 3 doses for 14 days, has so far been considered the first choice, because this was demonstrated to be superior to placebo in resolving middle-ear effusion (10). Other antibiotics, such as erythromycin-sulfisoxazole, cefaclor and trimethoprim-sulfamethoxazole have not shown a significantly different effectiveness compared with placebo or no treatment (22). The rising importance of resistance among strains of *Haemophilus influenzae*, one of the most common pathogens isolated in middle-ear fluid, and the knowledge that the compliance with multiple daily doses of a drug given for a relatively long period (such as 2 weeks) makes compliance difficult, prompted us to evaluate the use of ceftibuten (23). This antibiotic, together with a good activity against amoxicillin-resistant strains of *H. influenzae*, assures a good compliance, as it can be given only once daily and has a good palatability (24). In our study, children treated with ceftibuten had a better outcome than those receiving no treatment or only nasal saline drops: almost 30% were effusion-free at the 4-week visit compared with only 12% of those not receiving medical treatment. The better outcome was confirmed at the 8-week assessment. This finding concurs with the recent data of Mandel et al. (25), who, comparing the efficacy of ceftibuten with amoxicillin for OME in children, found that after 2 weeks of treatment 29.8% of the children treated with ceftibuten and 27.2% of those given amoxicillin were effusion-free.

The results of this large epidemiological survey could be useful in suggesting strategies for the problem of OME in children in primary school. Considering that only a small proportion of children have middle-ear effusion in winter months, and that there is a high spontaneous improvement and normalization of ears with effusion, it would seem advisable to focus attention only on the children with a history of recent acute otitis media and previous tonsillectomy or adenoidectomy while excluding from extensive and expensive screening programmes the children who are not potentially prone to have OME. Moreover, when medical treatment for OME is considered desirable (such as before considering surgical treatment for long-lasting middle-ear effusion), the use of a broad spectrum antimicrobial drug such as ceftibuten can be suggested, as it can reduce the duration of middle-ear effusion, thus preventing or minimizing possible cognitive impairments.

ACKNOWLEDGEMENT

This work was supported in part by Recordati SpA, Italy which supplied Ceftibuten Isocef®.

REFERENCES

1. Paradise JL. Otitis media in infants and children. Pediatrics 1980; 65: 917–43.
2. Paradise JL. Otitis media during early life: how hazardous to development? A critical review of the evidence. Pediatrics 1981; 68: 869–73.
3. Fria TJ, Cantekin EI, Eichler JA. Hearing acuity of children with otitis media with effusion. Arch Otolaryngol Head Neck Surg 1985; 111: 10–6.
4. Lous J. Silent reading and secretory otitis media in school-children. Int J Ped Otorhinolaryngol 1993; 25: 25–38.
5. American Speech-Language-Hearing Association. Guidelines for acoustic immittance screening of middle ear-function. ASHA 1979; 21: 283–8.
6. Gates GA, Stewart IA, Northern JL, et al. Diagnosis and screening of otitis media. Ann Otol Rhinol Laryngol 1994; 103 (Suppl 4): 53–7.
7. Lous J. Secretory otitis media in schoolchildren. Dan Med Bull 1995; 42: 71–99.

8. Stool SE, Berg AO, Berman S, Carney CJ, Cooley JR, Culpepper L. Otitis media with effusion in young children. Clinical Practice Guideline, No. 12. AHCPR Publication No. 94- 0622. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services, July 1994.
9. Rosenfeld RM, Post JC. Meta-analysis of antibiotics for the treatment of otitis media with effusion. Otolaryngol Head Neck Surg 1992; 106: 378–86.
10. Mandel EM, Rockette HE, Bluestone CD, Paradise JL, Nozza RJ. Efficacy of amoxicillin with and without decongestant. Antihistamine for otitis media with effusion in children: results of a double blind, randomized trial. N Engl J Med 1987; 316: 432–7.
11. Calearo C, Passali D, Pestalozza G, Zavattini G. Indagine epidemiologica sulla patologia dell'orecchio medio in età evolutiva in Italia. Orl Ped 1994; 5: 3–16.
12. Stool SE, Flaherty MR. Validation of diagnosis of otitis media with effusion. Ann Otol Rhinol Laryngol 1983; 92 (Suppl 107): 5–6.
13. Babonis TR, Wier MR, Kelly PC. Impedance tympanometry and acoustic reflectometry at myringotomy. Pediatrics 1991; 87: 475–80.
14. Lous J, Fiellau-Nikolajsen M. Epidemiology of middle ear effusion and tubal dysfunction. A one-year prospective study comprising monthly tympanometry in 387 non-selected 7-year-old children. Int J Pediatr Otorhinolaryngol 1981; 3: 303–17.
15. Virolainen E, Puhakka H, Aantaa E, Tuohimaa P, Ruuskanen O, Meruman OH. Prevalence of secretory otitis media in seven to eight year old school-children. Ann Otol Rhinol Laryngol 1980; 89 (Suppl 68): 7–10.
16. Paradise JL, Smith CG, Bluestone CD. Tympanometric detection of middle ear effusion in infants and young children. Pediatrics 1976; 58: 198–210.
17. Portoian-Shuhaiber S, Cullinan TR. Middle ear disease assessed by impedance in primary school-children in South London. Lancet 1984; i: 1111–3.
18. Holmquist J, Al Fadala S, Qattan Y. Prevalence of secretory otitis media among school-children in Kuwait. J Laryngol Otol 1987; 101: 116–9.
19. Teele DW, Klein JO, Rosner B and the Greater Boston Otitis Media Study Group. Epidemiology of otitis media during the first seven years of life in children in Greater Boston: a prospective, cohort study. J Infect Dis 1989; 160: 83–94.
20. Strachan DP, Jarvis MJ, Feyerabend C. Passive smoking, salivary cotinine concentrations, and middle ear effusion in 7-year-old children. BMJ 1989; 298: 1549–52.
21. Rasmussen F. Protracted secretory otitis media. The impact of familial factors and day care center attendance. Int J Pediatr Otorhinolaryngol 1993; 26: 29–37.
22. Mandel EM, Rockette HE, Paradise JL, Bluestone CD, Nozza RJ. Comparative efficacy of erythromycin-sulfisoxazole, cefaclor, amoxicillin or placebo for otitis media with effusion in children. Pediatr Infect Dis J 1991; 10: 899–906.
23. Nelson JD. Clinical importance of compliance and patients tolerance. Infect Dis Clin Pract 1994; 3: 158–60.
24. Jones RN. Ceftibuten: a review of antimicrobial activity, spectrum and other microbiologic features. Pediatr Infect Dis J 1995; 14: 77–83.
25. Mandel E, Casselbrant ML, Kurs-Lasky M, Bluestone C. Efficacy of ceftibuten compared with amoxicillin for OME in infants and children. Pediatr Infect Dis J 1996; 15: 409–14.

Submitted July 25, 1997; accepted December 17, 1997

Address for correspondence:
Paola Marchisio, MD
Pediatric Department 4
University of Milan
Via GB Grassi 74
I-20157 Milan
Italy
Fax: +39 2 3567346