Three-day and seven-day treatment in acute otitis media: a double-blind antibiotic trial

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SUMMARY. Ninety-six children with acute otitis media were randomized into a double-blind general practice trial of three-day and seven-day courses of cefaclor 125 mg tds. These regimens were equally effective in terms of resolution of symptoms and signs of otitis media, even in children presenting with bulging of the tympanic membrane. There was no difference between the groups in the recurrence of middle-ear infection during the six weeks after entry to the trial. The results provide further evidence about the effectiveness of short courses of antibiotics for children with presumed middle-ear infection.

Introduction

IN England and Wales about 1.5 million episodes of acute otitis media occur annually[1] and most children are treated with antibiotics. There is, however, general uncertainty about the optimum length of courses of antibiotics to treat infection; for example, lower urinary tract infections may be treated as effectively with a single dose of an antibiotic as with a seven-day course of treatment.[2] There have been suggestions that the clinical syndrome of otitis media, traditionally treated with seven- to 10-day courses of broad-spectrum antibiotics, may be managed with shorter courses of antibiotics[3,4] or without antibiotics at all.[5-7] Reasons for not adopting shorter antibiotic regimens may be based on concerns that infection is not completely eradicated, symptoms will persist and recurrence of infection may occur. This study was designed to investigate the relative efficacy of a three-day course of antibiotic at conventional doses compared with the traditional seven-day course of antibiotic in children with acute otitis media, using symptom diaries to record resolution of symptoms and review at six weeks to check for recurrence of middle-ear infection.

Method

Fourteen general practitioners working in four health centres admitted children aged three to 10 years to this trial during the winters of 1983/4 and 1984/5. Entry criteria were that the child presented with a clinical syndrome recognized as otitis media by the general practitioner concerned, for which antibiotic treatment was considered appropriate. Children who had received an antibiotic within the last two weeks or who were known to be sensitive to penicillins or cephalosporins were excluded from the study. Details of the child's medical history, symptoms and signs were noted on a record card which has been used for previous studies of otitis media.[8]

Parental consent was obtained and the children were randomized into two groups. Group A was given cefaclor 125 mg tds for three days and group B cefaclor 125 mg tds for seven days. The parents were given two bottles of medicine, the first containing a three-day supply of cefaclor 125 mg per 5 ml and the second a four-day supply of either placebo or cefaclor 125 mg per 5 ml, the placebo being identical in appearance and taste to the active drug. The parents were also given symptom diary cards to fill in during the week; during this time they were visited by a research assistant who ensured that the card was being kept adequately. The child's eardrum signs were reviewed by the same general practitioner at the end of the week. The case notes were reviewed after a further six weeks to check for further consultations for ear, nose and throat symptoms.

Student's t-test, the chi-square test, using Yates' correction when necessary, and Fisher's exact test were used to test the differences between groups.

Results

One hundred children were admitted to the trial and 96 completed follow up — 45 in group A and 51 in group B. Follow up was not completed in two cases because earache recurred on the fifth day, the code was broken and another antibiotic was prescribed (both children were in group A) and in two other children who failed to attend their follow-up appointments. There were no withdrawals because of side-effects. The sex distribution, age and medical history of ear, nose and throat or respiratory disorders were almost identical in the two groups (Table 1). A total of 594 symptoms was recorded — a mean of 6.2 symptoms per child, with no significant differences either in the range of symptoms recorded in the treatment groups or in the distribution of five major symptoms present at the first consultation (Table 1). Other symptoms included abdominal pain, loss of apetite, fever, sore throat, vomiting, diarrhoea and discharge from the ear. Sixty-nine children had unilateral and 27 bilateral eardrum signs and these signs were distributed equally between the two treatment groups except that 24 children in group A had bulging of the tympanic membrane compared with 17 in group B ($\chi^2 = 2.25$, not significant) and there were six perforated eardrums in group A compared with two in group B (not significant).

Table 1. Comparison of characteristics of the two groups of children with acute otitis media before the start of treatment with cefaclor 125 mg tds.

	Group A 3-day treatment ($n = 45$)	Group B 7-day treatment ($n = 51$)
Mean age ±SD (years)	5.5 ± 2.1	5.9 ± 2.1
Sex (male:female)	26:19	27:24
Medical history		
Otitis media (%)	*74*	*79*
Croup (%)	*13*	*11*
Wheezy bronchitis (%)	*15*	*13*
Asthma (%)	*13*	*13*
Symptoms at entry		
Earache (%)	*89*	*90*
Nasal discharge (%)	*79*	*68*
Earache at night (%)	*70*	*74*
Cough (%)	*68*	*68*
Crying (%)	*55*	*55*

During the treatment week there was no significant difference between the two groups in the number of days on which symptoms of earache, nasal discharge, cough or waking up crying were recorded on the diary cards or in the number of occasions that analgesia was administered to the children (Table 2). There was also no difference in the number of children with earache persisting beyond the fourth day of treatment — 14 children (31%) in group A and 12 children (24%) in group B — although two children in group A had recurrence of earache on day five and required further antibiotic treatment.

At the end of the treatment week resolution of ear signs was comparable in both groups and the percentage resolution of the eardrum signs — uniform redness, bulging, indrawing, loss of light reflex, pink blush, red rim, perforation — and of discharge from the ear are shown in Table 3.

Within the six-week period after treatment, eight new episodes of otitis media occurred in each treatment group with three further consultations for ear, nose and throat symptoms in group A and five in group B.

Finally, when the outcome for children with bulging of the tympanic membrane, who might be considered to have had more severe infection,[9] was examined, no difference was found in the number of children with earache persisting beyond four days or in the number with recurrent otitis media in the six-week follow-up period.

Discussion

It should be noted that doctors diagnosed acute otitis media from a cluster of symptoms and signs, with each child having a mean of six symptoms at entry; disturbed sleep, cough and gastrointestinal upset were often present in addition to upper respiratory tract symptoms. Findings on examination of the ears revealed a range of ear signs that doctors defined as otitis media. Almost half of the children in the study had bulging of the tympanic membrane, a sign frequently taken to reflect bacterial middle-ear infection,[9] but uniform redness of the membrane and varying degrees of vascular injection in conjunction with certain symptom clusters were also taken as evidence of acute otitis media by some participants.

This double-blind study shows that a short course of a broad spectrum antibiotic, in this case cefaclor, is as effective as a more traditional seven-day course, both in terms of resolution of symptoms and signs and prevention of recurrence of middle-ear infection. Presumably these findings are applicable to other broad-spectrum bactericidal agents: amoxycillin is as effective as cefaclor in the treatment of acute otitis media[10] and our study confirms the findings of Chaput de Saintonge,[3] who compared three- and 10-day courses of amoxycillin. However, in that study children over the age of five years received 250 mg of amoxycillin thrice daily; in the present study 72 of the 100 children were aged five years or over and all received cefaclor 125 mg tds. Bain and colleagues[8] have recently reported the use of a high dose, short duration course of amoxycillin in acute otitis media, showing that a two-day course of amoxycillin 750 mg bd is as effective as a conventional seven-day course of amoxycillin 125 mg tds. It is worth noting that in studies of short course therapy withdrawals because of side-effects have been few and in this present study there were no recorded side-effects leading to withdrawal.

The results of the present study and other studies of short-course antibiotic treatment show that there are no absolute rules for optimum dosage levels of antibiotic but short courses at conventional or high dose are as effective as the usual seven- to 10-day courses of treatment. Chaput de Saintonge[3] has drawn attention to the potential savings in cost from this approach to the use of antibiotics in acute otitis media. We have no evidence to suggest which antibiotic may be the most effective and cost may also be a determining factor in the choice. There is no doubt that in many children with presumed middle-ear infection recovery will occur without antibiotic treatment. Perhaps insufficient research has been conducted on relief of pain in acute otitis media and we can only stress that clinical experience indicates that adequate analgesia is an important component of overall treatment. In the absence of further investigations of natural history and additional placebo versus antibiotic trials in general practice, we can only rely on 'clinical judgement' when deciding whether to treat or not to treat children with an antibiotic.

Table 2. Comparison of number of days on which symptoms were recorded during treatment week per child, and number of occasions when analgesia was administered for the two groups of children with acute otitis media treated with cefaclor.

Treatment with cefaclor 125 mg tds	Mean (±SD) no. of days				Mean (±SD) no. of times analgesia administered
	Earache	Nasal discharge	Cough	Wakened crying	
Group A — 3 days ($n=45$)	1.89 ± 1.68	3.57 ± 2.60	2.87 ± 2.54	0.67 ± 1.16	1.64 ± 1.97
Group B — 7 days ($n=51$)	2.49 ± 1.89	3.73 ± 2.46	3.23 ± 2.83	0.53 ± 0.83	1.50 ± 1.71

SD = standard deviation. n = total number of cases.

Table 3. Comparison between percentage resolution of ear signs after one week for the two groups of children with acute otitis media treated with cefaclor.

Treatment with cefaclor 125 mg tds	Percentage of cases resolved (no. of cases before treatment)							
	Uniform redness of drum	Bulging drum	Indrawn drum/fluid	Loss of light reflex	Pink blush	Red rim	Perforation	Discharge
Group A — 3 days ($n=45$)	*97* (26)	*100* (21)	*63* (9)	*65* (33)	*29* (15)	*65* (15)	*83* (6)	*100* (6)
Group B — 7 days ($n=51$)	*79* (27)	*94* (19)	*50* (5)	*60* (34)	*45* (12)	*0* (11)	*100* (2)	*57* (7)

n = total number of cases.

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