

A trial comparing cefaclor with co-trimoxazole in the treatment of acute otitis media

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SUMMARY A prospective random double-blind controlled trial comparing the efficacy of cefaclor with that of co-trimoxazole in the treatment of otitis media was undertaken. Two hundred and twenty-three children aged 12 years or younger were studied. Both drugs were effective, with clinical cure or improvement in more than 90% of the children. The level of compliance was high and side effects few. Both co-trimoxazole and cefaclor can be considered safe and effective drugs for the treatment of acute otitis media.

In paediatric practice, acute otitis media is the third most common reason for consultation with a doctor.¹ In a number of studies in which myringotomy or aspiration cultures were taken, *Haemophilus influenzae*, especially in younger children, was found not only to be a common pathogen, but also one that is developing increasing ampicillin resistance.²⁻⁴ Thus, not only is acute otitis media common, but the most frequently used drug is not as efficacious as it was.

It seemed desirable to assess the effectiveness of two drugs, which, in Canada at least, are not widely used for the treatment of acute otitis media — namely, cefaclor and co-trimoxazole. A review of the literature showed very few random, double-blind, controlled trials with large sample size designed to assess the effectiveness of antimicrobial therapy in otitis media; in particular, there have been no previous studies comparing cefaclor with co-trimoxazole.

Schwartz *et al.*³ in a small series found that clinical failures after ampicillin were due to ampicillin-resistant *H. influenzae* cultured after tympanocentesis; 93% of these children responded to co-trimoxazole.

McLinn,⁵ in a non-double-blind study found cefaclor more efficacious than amoxicillin, but the results were not statistically significant. He suggests that cefaclor is more efficacious than co-trimoxazole because it attacks not only *H. influenzae*, but also group A beta haemolytic streptococci and *Staphylococcus aureus*, less common but also important pathogens.

In another study, McLinn⁶ found the recurrence rate after amoxicillin was twice as great as after

cephradine. That study was not double-blind and the sample was small.

With this knowledge, we set out to answer the following questions; firstly, are cefaclor and co-trimoxazole effective in the treatment of acute otitis media in children, and secondly, if so, is one better than the other?

Subjects and methods

Six paediatricians in busy private primary care paediatric practices agreed to enrol their patients with acute otitis media into the study. These paediatricians were experienced in seeing many children with otitis media (mean number of years in practice = 17, range 5 to 25) and their practices ranged in location from the centre of a large industrial city to an affluent suburban area. Since Canada has universal health care and all patients are private ones, we felt our patients were representative.

All children in the 6 practices who were diagnosed as having acute otitis media, who were 12 years of age or younger, who had not received treatment with antibiotics within the previous 7 days, who had never had otic surgery, and who had had 3 episodes or less of acute otitis media in the preceding 6 months, were enrolled in the study.

Upon diagnosis, the paediatrician telephoned the research nurse and gave her details of the child's age, weight, and home address. The nurse phoned the research pharmacist who prepared either liquid co-trimoxazole or liquid cefaclor at the recommended dose per weight, in a numbered brown container, to be given to the child for 10 days. Within one hour the nurse delivered the assigned drug to the

child's home. The parent(s) was told that the child should see the paediatrician in 10–14 days and that the nurse would visit the home again at 10 days.

No instructions were given on the need for compliance. Neither the nurse, the paediatrician, nor the parent(s) knew which drug was used.

Follow-up consisted of a visit to the paediatrician's office where visual inspection showed whether the tympanic membrane was normal, better, or worse. No attempt was made to influence the judgment of the paediatrician regarding the appearance of the tympanic membrane.

In addition, at the second home visit, the nurse, who did not know the results of the follow-up assessment, did a pure-tone audiogram on any child older than 4 years. She also assessed compliance by measuring the volume of remaining drug in the bottle, and assessed side effects by means of a questionnaire.

Results

A total of 223 children was studied, with complete follow-up in 197 and partial follow-up in 26. Partial follow-up consisted of 26 children (14 in co-trimoxazole, 12 in cefaclor group) who had had home audiograms, and compliance and side effects assessments, but who did not return to the paediatrician for visual inspection of the tympanic membrane. In addition to the 223 children, 3 children were excluded from the study within 24 hours of enrolment: 1 child given cefaclor refused to take that drug, was switched by the paediatrician to co-trimoxazole (which he took), and when seen at 10 days was cured. Two children vomiting at the outset, continued vomiting with co-trimoxazole to which group they had been assigned; in each case the paediatrician changed the drug to ampicillin which they tolerated and in follow-up, one was cured and the condition of the other was improved.

The results in the children with incomplete follow-up showed normal audiograms in both groups, and compliance above 70% in 12 of 14 co-trimoxazole-treated and in 9 of 12 cefaclor-treated children. In the partially studied group, neither gastrointestinal nor skin side effect occurred.

The results in the children who were fully followed up are shown on Tables 1 and 2. The condition of more than 90% children in both groups was found both by visual inspection of the tympanic membrane and (if old enough) by pure-tone audiogram to have been cured or improved. Of particular importance is the observation that children under 4 years, at particular risk of having ampicillin-resistant *H. influenzae* as the causative organism, did almost as well, with 90% in the co-trimoxazole

Table 1 Results on follow-up (n=197)

	Co-trimoxazole (n=96)		Cefaclor (n=101)	
	No	(%)	No	(%)
Cured or improved	92	(96)	92	(91)
Age <4 years	40	(42)	42	(42)*
Cured or improved <4 years	36	(90)	36	(86)*
Hearing better than 25 decibels	51/55	(93)	56/59	(95)*

*No statistically significant difference.

Table 2 Results on follow-up (n=197)

	Co-trimoxazole (n=96)		Cefaclor (n=101)	
	No	(%)	No	(%)
Compliance greater than 70%	85	(88)	90	(89)*
Gastrointestinal side effects	0		4	(4)*
Skin rashes	3	(3)	2	(2)*

*No statistically significant difference.

and 86% in the cefaclor group being cured or improved.

Both groups appeared to be compliant with at least 70% medication having been taken by 88% of the co-trimoxazole group and by 89% of the cefaclor group.

Neither effectiveness, compliance, nor side effects was found to be statistically different in the two groups. The sample size selected was sufficient to determine that the likelihood of missing a difference of 10% or more was less than 2%.

Discussion

Several methodological issues arise from this study. The first is that of diagnosis. Although tympanocentesis has been done on at least 2500 children,³ it is painful and is not necessary for routine clinical practice. Without tympanocentesis and the isolation of bacteria, the diagnosis of acute otitis media is subjective. We hoped to be able to do this study under normal conditions in the community; since most paediatricians do not require tympanocentesis to make a diagnosis, and since it may be assumed that practice, whereas not making perfect at least makes less imperfect, we chose experienced primary care paediatric practitioners rather than paediatric interns or residents in a paediatric outpatient clinic. In addition, observer variation was the same for both groups of children, since it was the children who were randomly allocated to treatment groups, and not the doctors. Since the physicians did not know to which group the children would be assigned,

it is safe to assume that the same number of false-positive diagnoses was assigned to both groups.

The second issue has to do with the use of the pure-tone audiogram as opposed to impedance audiometry as one of the outcome measures. We feel that impedance audiometry is too sensitive and does not really tell us what we want to know—namely, can the child hear? Undoubtedly, had we used impedance audiometry we would have found many more children with evidence of residual serous otitis media, but since there is no evidence that treating children with serous otitis who hear normally is of long-lasting value, we chose pure-tone audiometry.

The third issue is the absence of a placebo group. We felt this would have been unethical, since the whole course of children with otitis media has changed greatly since effective antibiotic therapy. Mastoid disease and the chronic perforated drum are rare among well-nourished children who have easy access to health care, perhaps owing to early and effective antimicrobial therapy. Although a recent Dutch study suggests that antibiotics are not necessary in acute otitis media,⁷ that work has been seriously questioned by others.^{8,9}

The fourth issue is the absence of ampicillin or amoxicillin as a control group. We considered the sample size to include this treatment group would have to be so large as to make the study impractical.

Conclusions

In the first random, double-blind, controlled trial comparing co-trimoxazole with cefaclor in the treatment of acute otitis media in children, both

drugs were found to be effective and with few side effects. Compliance was high in both treatment groups. Both drugs can be recommended as effective and safe in the treatment of childhood otitis media.

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