PRACTICE OBSERVED

Practice Research

Acute otitis media: clinical course among children who received a short course of high dose antibiotic

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Abstract

A prospective study was carried out in 274 children aged 3 to 10 years with acute otitis media. They were randomly allocated to one of two treatment regimens: (*a*) a seven day course of amoxycillin 125 mg three times a day, and (*b*) a two day course of amoxycillin 750 mg twice a day. They were followed up by symptom diaries and clinical examination.

The findings in the 243 children who completed the trial showed that the short course of treatment was as effective as the seven day course in the speed of resolution of symptoms and signs, irrespective of previous history of otitis media or of episodes in which bulging of the eardrums was observed at presentation.

A subgroup of 185 children was followed up for one year after entry to the trial. During this period no appreciable differences emerged between the two antibiotic regimens, either in recurrence rate of otitis media or in the frequency of hearing loss at one month and six months after entry to the study. Side effects of treatment were few, and those that could be attributed to antibiotic use occurred with equal frequency in the two treatment groups.

Introduction

Acute otitis media is usually defined mainly in relation to the physical appearance of the eardrum,[1] but clinical experience indicates that parents and doctors respond to symptoms as much as signs in managing children with presumed middle ear infection. It is common practice to prescribe an antibiotic for acute otitis media on the assumption that the pathogenesis includes bacterial infection in most cases. This assumption is based on the findings that bacteria can be isolated in aspirations from the middle ear of children with acute otitis media.[2,3] Because *Haemophilus influenzae* has been isolated in up to a quarter of cases, especially in children under the age of 5, a broad spectrum antibiotic such as ampicillin or amoxycillin is usually recommended.[3,4] It is widely believed that such antibiotic treatment will not only shorten an episode and prevent complications, such as mastoiditis, but may reduce the likelihood of recurrent episodes.

A leading article in the *BMJ* in 1979 suggested that traditional regimens for common conditions should be scrutinised.[5] In the case of otitis media antibiotics are usually prescribed for between five and seven days,[6] and most suspensions of antibiotics are produced in packages sufficient for either a five or a 10 day course. There is little certainty concerning the optimal duration of treatment, but the findings of two recent small studies suggest that two to three day courses of either penicillin or amoxycillin at conventional doses may be as effective as the same dose given over 10 days.[7,8]

The aims of our study were (*a*) to describe the syndrome of acute otitis media in terms of symptoms and signs and (*b*) to compare the clinical outcome in children who presented with acute otitis media aged 3 to 10, who received either a two day course of amoxycillin 750 mg twice daily or a seven day course of amoxycillin 125 mg three times a day. A subgroup of the children who were studied was followed up for a year to compare the rates of recurrence and hearing loss in the two treatment regimens.

Methods

The study was conducted in the winter months of 1982-3 and 1983-4 in four practices. The 16 participating general practitioners were asked to recruit 10 consecutive children with acute otitis media each winter, with a target of 20 cases per doctor. Entry to the trial was confined to (*a*) children aged 3 to 10 years, (*b*) those with symptoms and signs of acute otitis media, which in the general practitioners' opinion warranted treatment with an antibiotic, and (*c*) children whose parents gave their informed consent.

Children were excluded who (*a*) were under age 3 because they present difficulties in communication, and different drug dosages are often recommended for younger children, (*b*) had had an episode of acute otitis media that required medical attention in the previous month, (*c*) were currently on antibiotics or had received an antibiotic for any reason in the previous 14 days, (*d*) were known or suspected of being hypersensitive to antibiotics, and (*e*) were on other drugs (short or long term) for other conditions such as asthma, epilepsy, and diabetes.

Children were entered into the trial on one occasion only. At entry to the trial doctors completed a medical and social history and recorded information about presenting symptoms and eardrum signs as described in a previous study of the treatment of acute otitis media.[9] The record card was retained in the patient's notes and arrangements made for the child to attend the same general practitioner one week later when a follow up record of eardrum signs was completed. The follow up of symptoms was measured by using a symptom diary which was issued at the initial consultation and completed by mothers during a 20 day follow up period.

Children were then randomly allocated to long (seven days, group A) or short (two days, group B) treatments with amoxycillin using a computerised allocation schedule, which was placed with bottles containing the two treatments labelled A or B in each general practitioner's consulting room. Amoxycillin powder was reconstituted by the general practitioner by adding the appropriate amount of water to bottle A and bottle B. Parents were advised to use analgesics as they considered necessary and to record the use of drugs for pain relief in the symptom diaries.

Within 24 hours of entry to the trial a research assistant visited the child's parents at home to answer queries and ensure that the method of completing the symptom diaries was understood. The research assistant visited each family again at roughly seven to 10 days and at three weeks after entry to encourage cooperation, answer queries, and collect the diary cards.

Children who attended one health centre were followed up for one year to identify recurrence of acute otitis media and hearing loss. To ascertain hearing loss audiometry was conducted by a research assistant in those children aged 4 and over at one month and six months after entry to the trial. The assessment of hearing was performed in a soundproof room, and clinically important hearing loss was defined as 30 db loss at two or more frequencies.

Data were analysed using standard χ^2 statistical tests.

Results

Two hundred and seventy four children were admitted to the trial and 243 completed follow up for three weeks, with 118 in group A (seven days) and 125 in group B (two days). Thirty one (11·3%) children did not complete follow up, 13 from group A and 18 from group B. The reasons for failure to complete the trial were (*a*) presumed side effects in 12, (*b*) unreliable recording in 12, and (*c*) change in diagnosis or treatment by the general practitioner in seven.

Of the 12 children who might have had side effects from amoxycillin, seven had gastrointestinal upsets. The number of reasons for dropping out in the two treatment categories was similar, and the age distributions of children failing to complete follow up in the two groups were also similar. No appreciable differences were found between the two treatment groups in terms of the children's age, sex, or previous medical history.

TABLE I—*Resolution of symptoms at day 1, day 5, and day 10 after entry into trial: group A, seven days' treatment (n = 118 children) and group B, two days' treatment (n = 125 children)*

Symptom	Day 1		Day 5		Day 10	
	A (n=118) (%)	B (n=125) (%)	A (n=118) (%)	B (n=125) (%)	A (n=118) (%)	B (n=125) (%)
Earache	89·8	94·6	9·3	10·4	5·1	5·6
Earache at night	64·4	67·2	3·4	2·4	2·2	2·4
Runny nose	66·9	64·0	33·0	33·6	22·0	20·0
Cough	57·6	70·4	28·8	24·6	16·9	19·2
Night cough	46·6	56·0	7·6	6·4	4·4	4·0

TABLE II—*Symptoms and diary follow up: five main symptoms and occasions on which symptoms were recorded during 20 days after entry to trial*

Symptom	No of occasions that symptom was recorded	
	Group A (seven days' treatment)	Group B (two days' treatment)
Earache	2·63	2·62
Earache at night	1·29	0·99
Nasal discharge	6·36	6·10
Cough	4·60	5·17
Cough at night	0·95	1·22

PRESENTING SYMPTOMS AND OUTCOME

At entry to the trial a total of 1503 symptoms was recorded—a mean of 6·2 symptoms per child, with no appreciable differences in the range of symptoms recorded in the two treatment groups. Table I shows the resolution of the five main symptoms at day 1, day 5, and day 10 and table II the number of occasions on which these symptoms were recorded in the symptom diaries that the mothers completed during the three weeks after entry to the trial. There were no appreciable differences between the two treatment groups, either in time taken for symptoms to resolve or the frequency with which these symptoms were recorded. The findings were similar for other symptoms, including feeling unwell, fever, loss of appetite, and gastrointestinal upsets. The use of analgesics and other over the counter preparations for relief of the associated symptoms of middle ear infection was no different in the two treatment groups.

EARDRUM SIGNS AND OUTCOME

The 867 eardrum signs recorded at entry to the trial by the general practitioners were distributed equally between the two treatment groups. Table III gives the findings on examination of eardrums at entry and at one week. There were no appreciable differences between the two groups at one week after entry to the trial.

TABLE III—*Selected ear drum signs at entry and follow up at one week*

Eardrum signs	Group A (seven days' treatment)			Group B (two days' treatment)		
	At entry (n)	At one week (n)	%	At entry (n)	At one week (n)	%
Uniform redness	75	8	10·7	89	12	13·5
Red rim	54	21	38·9	62	26	41·9
Pink bluish	53	20	37·7	72	28	38·9
Bulging drum	67	7	10·4	85	8	9·4
Lost light reflex	83	27	32·5	86	29	33·7
Discharge	23	2	8·0	13	1	7·7

Bulging of the drum was selected as a pronanent sign, possibly indicating more objectively the presence of infection in the middle ear cleft, and 140 children had this sign with or without other abnormalities. These children were equally distributed between the two treatment groups, and the speed of resolution of their symptoms and the improvement of eardrum appearances at one week were similar for this subgroup in both treatment groups.

PREVIOUS MEDICAL HISTORY OF OTITIS MEDIA AND OUTCOME

A documented history of otitis media was found in 188 children, and these were equally distributed between the two treatment groups. The time taken for symptoms to resolve and the persistence of abnormal eardrum signs were marginally greater in children who had a previous medical history of middle ear infection than in other children in the trial, but this difference was not significant. There were no notable differences in clinical outcome between the two day and seven day courses of treatment in the children with a previous history of otitis media.

RECURRENCE OF OTITIS MEDIA

In the health centre where children were followed up for one year 185 children completed the trial and 76 (41%) had at least one further episode of acute otitis media that required medical care during the 12 months after entry to the trial. Thirty seven (49%) of these 76 children with a record of recurrence had the first episode of recurrence within three months of the index episode. There was a significantly higher ($\chi^2 = 4{\cdot}054$; $p<0{\cdot}05$) number of children with recurrence under age 4, 34 (45%) of the 76 with recurrence being under 4. This compares with 33 (30%) of the 109 children with no recurrence being under 4. There was a trend for children with recurrent episodes to have had a previous history of otitis media, but the trend was not significant.

Table IV shows that irrespective of age there was no appreciable difference in the number of children who had a recurrence in the two treatment groups. One hundred and ten of the 185 children had bulging of at least one eardrum. There was no association between the duration of treatment for the index episode and subsequent recurrence in this subgroup. Among the 110 children with initial bulging of the eardrum 52 (47%) had a record of recurrences compared with 24 (32%) of the 75 children with less prominent eardrum signs, and this relation between bulging of the drum and recurrence was significant ($\chi^2 = 4{\cdot}298$, $p<0{\cdot}05$).

TABLE IV—*Recurrence of acute otitis media in 12 month period after entry to trial: in group A (seven days' treatment) and group B (two days' treatment)*

Group	Total No	Mean age (years)	No (%) with recurrence	Mean age (years)
A	86	4·8	34 (39·5)	4·2
B	99	5·0	42 (42·4)	4·1
Total	185	4·9	76 (41·1)	4·1

AUDIOMETRY

In the health centre where follow up audiometry was performed 106 children aged 4 and over completed the trial. Of these, 73 had audiometry performed at both one month and six months after entry to the trial. Among these children there were no appreciable differences in hearing loss between the two treatment groups, and only five children (two in group A and three in group B) had a hearing loss of 30 db or more at both one month and six months after entry to the trial.

Discussion

A course of high dose antibiotic treatment of short duration was as effective as the conventional one week course in resolving symptoms and signs in acute otitis media. The type of treatment received had no appreciable affect on recurrence of otitis media during the one year of follow up and made no difference to hearing loss recorded at one month and six months after entry to the trial.

Compliance with antibiotic treatment for seven to 10 days in children is poor, with up to half failing to complete the full course.[10] In a review of compliance with treatment Stewart and Cluff showed that the longer the treatment and the greater the frequency of dosage schedules the less likely a patient is to complete the recommended course of treatment.[10] The results of previous trials with smaller numbers of children (84 and 103 respectively[7,8]) showed no convincing differences between two and three day treatments and conventional dosages of antibiotics for seven and 10 days. There is even less evidence on the optimum dose beyond the suggestion that more treatment failures occur in patients who are treated with low doses for seven days than with higher doses for 10 days.[10]

When children receive 10 to 12 doses over 48 to 72 hours there is still a possibility of doses being missed and inadequate concentrations of antibiotics being achieved. If mothers are advised to give amoxycillin 750 mg 12 hourly for four doses the regimen is simplified even further with the aim of adequate therapeutic concentrations being sustained over the short period of treatment.

Ampicillin and amoxycillin are effective against most bacteria that are implicated in acute otitis media.[3] Amoxycillin was chosen as the antibiotic for the study because it has the advantages of better absorption and a lower incidence of gastrointestinal side effects.[3,10] Of the 31 children who failed to complete the trial, 12 had presumed side effects, but seven only were related to gastrointestinal upsets. There were similar numbers in the two treatment groups. Leigh *et al* found that 17·5% of adult patients who received single high dose treatment with amoxycillin had diarrhoea,[11] but in other studies of high dose treatment in adults gastrointestinal upsets were not a problem.[12,13] The evidence from this trial suggests that a high dose, short course of treatment with amoxycillin does not lead to noticeable gastrointestinal disturbances in children aged 3 and over.

The clinical diagnosis of middle ear infection is often limited to a definition of abnormalities observed on the tympanic membrane. The general practitioner often sees a child during the early stages of the disease, and a precise diagnosis is difficult to make. We have to accept that children were included in this trial who may not have had pus formation in the middle ear cleft. The results, however, emphasise that in reality clinical presentation in general practice encompasses clusters of symptoms and signs, and given that myringotomy is not conducted in general practice decisions about treatment have to be made from a complex of symptoms and signs.

Studies of the treatment of otitis media often omit any reference to symptoms, and the duration of follow up is often short. Though the main aim of this study was to compare different treatment regimens, the results provide valuable information about the clinical course of otitis media in general practice. Earache tended to resolve rapidly, but the signs of associated upper respiratory tract infection were more persistent, with roughly one in five children continuing to have symptoms such as cough and nasal discharge 10 days after entry to the trial. Children under 4 were more likely to have a recurrence, which is consistent with the experience of clinical practice where the preschool child presents more frequently with upper respiratory and middle ear infections.

There is no overall agreement about which eardrum appearances are diagnostic of bacterial infection, but the importance of bulging of the tympanic membrane is cited as one of the most useful indicators of suppurative otitis media.[1,4,5] The presence of a bulging drum was a predictor of a recurrence of otitis media. Thus younger children and those with bulging of the drum should probably be regarded as an important subgroup who require more careful follow up.

Four out of 10 children had at least one further episode of acute otitis media requiring an antibiotic during the one year of follow up, and half of these children had their initial recurrence within three months of the index episode—a result similar to the findings of Onion and Taylor.[12] With any given episode of middle ear infection the chance of recurrence in that child within one year is between 30% and 50%. After an acute attack the resolution of middle ear effusion associated with infection may take six weeks or longer, and the child is particularly vulnerable to reinfection during this time.[3]

The results of this study show that shortening the course of antibiotic treatment has no adverse effect on outcome among children with acute otitis media. Several studies have attempted to investigate whether antibiotics are necessary in the treatment of at least some children with middle ear infection, but these studies do not provide sufficiently clear guidelines for taking decisions in individual children.[14,15] It is likely that a number of children in this study did not require antibiotic treatment. The evidence about the clinical course will be helpful in planning a prospective trial of antibiotic *v* placebo.

In circumstances where a general practitioner decides to use an antibiotic the conventional regimen of three to four times a day for one week has a ring of familiarity, but failure to complete a course of treatment for seven days is well recognised. The main advantage of a short course of treatment is that parents have a simpler regimen to follow, and the time during which the child has to take the antibiotic after the acute pain of earache has disappeared is reduced by several days. Where the general practitioner considers that prescribing an antibiotic is warranted a high dose, short course of amoxycillin is an alternative form of treatment that is acceptable to parents and suitable for children aged 3 and over.

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Audit Report

Do patients cash prescriptions?

In 1982 a small survey indicated that nearly 20% of patients failed to cash their prescription within a month of receiving it.[1] I conducted a survey based on carbon copies of 986 prescriptions issued at 1217 surgery consultations by seven doctors in a group practice in Whitby, which showed that 911 (92·4%) prescriptions had definitely been presented at local chemists. A postal questionnaire of the remaining 75 patients elicited 65 replies; six further replies were obtained by home visiting. Forty eight of the 71 prescriptions were said to have been presented, and the remaining 23 replies included, "I got better before cashing the prescription" (five); "I could not afford the prescription fee" (four); "I did not think it was right for me" (four); "I lost the prescription" (two); and "I was not given a prescription" (two). Nobody replied, "I did not want a prescription," although this was an optional reply.

The prescribing habits of the six principals and trainee (myself) were also analysed. All the doctors were seeing 90-110 patients a week and had similar commitments as clinical assistants in the general practitioner hospital. The number of items prescribed by each doctor varied from 168 in 182 consultations to 408 in 208 consultations. The use of generic drugs ranged from 7% to 68%. Eighteen per cent of the drugs prescribed would now be on the "blacklist." The heaviest prescribers had the lowest rates of non-encashment. Analysis of drug groups prescribed showed fairly even proportions of cardiovascular, antibiotic, and psychotropic drugs; the use of "symptomatic" treatments was much more variable but accounted for only 10% of the total.

Previous surveys using smaller numbers indicated that 10-20% of prescriptions were not presented.[1,2] In this study the figure was between 2·7% and 7·6%; whether or not all the drugs were consumed may be a different matter.—IAN STUART, registrar, Family Medicine Training Programme, Victoria, Australia. (Correspondence to: 4 Marine Crescent, Great Yarmouth, Norfolk.)

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100 YEARS AGO

The Amalgamated Society of Engineers has been making an inquiry by means of a printed list of questions circulated among mechanics, through the agency of the branch secretaries of the Society. Five thousand forms were sent out, asking particulars with regard to water-supply, cleanliness, water-closets, and cases of sickness traceable to sanitary defects. Unfortunately, only 126 replies were, according to a statement in the *Pall Mall Gazette*, from which we quote, received from England, nine from Scotland, and one from Ireland. The returns, so far as they go, appear to show that the arrangements are tolerably good in only a small proportion of the shops, and these are situated chiefly in Leeds, Sheffield, Nottingham, or in Government establishments. The water-supply is often scanty, and of doubtful purity; privies are often few in number, badly constructed, and erected over open middens, which are emptied only once or twice a year; the worst kind of closet, however, is not connected with the open midden, nossome and unhealthy as that is. Sunk cesspools are infinitely worse when the water-supply is obtained from wells in the immediate neighbourhood; upon this most important point, no information has been afforded. It is gratifying, and rather surprising, to learn that, in one large workshop, earth-closets for 600 men have been found to work well; and, if this system could be extended, it would be more wholesome and less wasteful than any other, as ashes can be used as the deodoriser. Where this is not possible, good latrines, with an automatic flushing chamber, are the best arrangement, and can generally be erected at a small cost. The replies, incomplete as they are, may be of use in calling the attention of medical officers of health and sanitary inspectors to the matter; they could even be able to prove whether the replies fairly represent the average condition, a point which must remain in some doubt.

(*British Medical Journal* 1885;ii 403.)