Comparative efficacy of amoxicillin, cefuroxime and clarithromycin in the treatment of community-acquired pneumonia in children

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three alternative antibiotics for the treatment of children with community-acquired pneumonia (CAP) were examined. The antibiotics were amoxicillin 75 mg/kg per day intravenously (IV) in three divided doses, cefuroxime 75 mg/kg per day IV in three divided doses, and clarithromycin 15 mg/kg per day IV in two divided doses. If there was no clinical improvement at 48 hours the antibiotic was changed to combination therapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children aged between 2 and 72 months with non-severe and severe CAP admitted into one hospital. Patients with very severe pneumonia (as defined by the World Health Organization) were excluded from the study, as were patients with asthma, congenital heart disease or chronic disease, or those who were neurologically impaired.

Setting
The setting was tertiary care. The economic study was carried out in Peshawar, Pakistan.

Dates to which data relate
The effectiveness evidence was collected from October 2001 to February 2002. No price year was given.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively and was calculated for a hypothetical type of patient rather than on the actual costs incurred.

Study sample
No power calculations were reported. Patients were included if they met the inclusion criteria (see 'Study Population' section). The patients were randomly allocated to one of the three antibiotic treatments. From the initial sample, 20 patients were excluded because they had very severe pneumonia and 25 for other reasons. There were 43 patients in the
amoxicillin group, 41 in the cefuroxime group, and 42 in the clarithromycin group. Thus, the total number of patients in the study sample was 126, though the authors reported the total as 124. The authors reported that the study sample might not have been representative of the study population.

Study design
This was a randomised controlled trial (RCT) that was carried out in a single centre. No loss to follow-up was reported. The patients appear to have been followed up for a maximum of 4 days (i.e. until discharge from the hospital).

Analysis of effectiveness
The analysis was conducted on an intention to treat basis. The primary health outcomes used were respiratory rate, temperature, number of patients requiring oxygen, and the number of patients reluctant to feed at 48 hours and at discharge. The three patient groups were shown to be comparable at baseline in terms of the respiratory rates, temperature, number of patients reluctant to feed and the number requiring oxygen at the time of admission, (p>\( \geq \)0.3).

Effectiveness results
In the amoxicillin group, the mean respiratory rate (+/- standard deviation, SD) was 51.2 (+/- 10) at 48 hours and 41.4 (+/- 4.7) at discharge. In the cefuroxime group, it was 50.4 (+/- 9.5) at 48 hours and 46.8 (+/- 4.5) at discharge. In the clarithromycin group, it was 45.7 (+/- 8.8) at 48 hours and 38.8 (+/- 4.5) at discharge. The p-value for the differences was 0.7.

The average temperature (in degrees F; +/- SD) of the amoxicillin patients was 99.0 (+/- 0.96) at 48 hours and 98.2 (+/- 0.41) at discharge. In the cefuroxime group, it was 99.1 (+/- 1.0) at 48 hours and 98.5 (+/- 0.5) at discharge. In the clarithromycin group, it was 99.2 (+/- 1.2) at 48 hours and 98.4 (+/- 0.4) at discharge. The p-value for the differences was 0.5.

Three patients in the amoxicillin group, 1 in the cefuroxime group and 2 in the clarithromycin group required oxygen at 48 hours; none of the patients needed it at discharge, (p=0.1).

Eleven patients in the amoxicillin group, 9 in the cefuroxime group and 3 in the clarithromycin group were reluctant to feed at 48 hours; none of the patients was reluctant to feed at discharge for any of the groups, (p=0.2).

The proportion of patients experiencing clinical improvement was 97.6% with amoxicillin, 95.2% with cefuroxime and 97.6% with clarithromycin.

Clinical conclusions
There were no statistically significant differences in the effectiveness outcomes among the three antibiotic treatments.

Measure of benefits used in the economic analysis
No summary measure of benefits was carried out. In effect, the authors carried out a cost-consequences analysis.

Direct costs
The only direct costs included in the economic analysis were the cost of the antibiotics. These were calculated for 4 days of IV treatment in hospital followed by 4 days of oral treatment at home. The cost estimation was based on the hypothetical use of antibiotics for a 10-kg patient. The price used was that of the most expensive branded drug on the market. No price year was given. The costs estimated were the average costs per patient for the 8-day period of IV treatment. No discounting was carried out as the costs were incurred during less than one year.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

**Indirect Costs**
No indirect costs were included.

**Currency**
Pakistan rupees (PKR).

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The cost per 8-day IV treatment was PKR 496 with amoxicillin, PKR 1,018 with cefuroxime and PKR 730 with clarithromycin.

The costs of adverse effects were not dealt with in the costing.

**Synthesis of costs and benefits**
The costs and benefits were not combined as the study was a cost-consequences analysis.

**Authors' conclusions**
All three antibiotic treatments were equally effective for the treatment of children with community-acquired pneumonia (CAP), but amoxicillin was the least costly treatment.

**CRD COMMENTARY - Selection of comparators**
The three treatments compared were chosen because they were commonly used in the authors' setting. The treatment administered in the case of lack of clinical improvement at 48 hours (i.e. combined therapy) was not described. You should decide if the antibiotics are widely used in your own setting.

**Validity of estimate of measure of effectiveness**
The source of the effectiveness data was a single study. The analysis was based on an RCT, which was appropriate for the study question. The patient groups were shown to be comparable at analysis. The analysis of effectiveness was handled credibly in some respects, but the lack of statistical significance for differences in the effectiveness of treatments was interpreted as showing equality, whereas it might have been due to the small study sample size. As the authors reported, the patients admitted to their hospital might not have been representative of patients in the community with CAP. Also, the follow-up period was very short (since the patients were not followed up after hospital discharge).

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above) since the health benefits were reflected in the disaggregated effectiveness outcomes reported.
Validity of estimate of costs
The cost perspective adopted was not explicitly reported and only the cost of the antibiotics was included. It is unclear whether the inclusion of other costs would have affected the authors' conclusions. The costs and the quantities were reported separately for the only cost included (i.e. that of the antibiotics). The quantities were the standard prescription for a 10-kg patient, not the actual quantities of resources consumed. The sources used to obtain the unit costs were not reported. No statistical, sensitivity or any other kind of analysis of the quantities or prices was conducted. The price year was not reported, but the study was carried out over a short time period, 2001 to 2002, so the prices presumably related to that time.

Other issues
The authors made comparisons of their effectiveness results with the findings from other studies. The issue of generalisability to other settings was not addressed. The authors did not present their results selectively.

Implications of the study
The authors recommended using amoxicillin for CAP for the kind of patients in the study because of its cost-advantage. They suggested that further research should be performed, in the form of multi-centre trials, to assess the effect of clarithromycin across patients of differing ages.

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