Comparison of early intravenous to oral switch amoxicillin/clavulanate with parenteral ceftriaxone in treatment of hospitalized patients with community acquired pneumonia

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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
The study examined the early switch from intravenous to oral amoxicillin-clavulanate in the treatment of hospitalised patients with community-acquired pneumonia (CAP). Patients received amoxicillin-clavulanate, 1.2 g intravenously every 8 hours, followed by oral amoxicillin-clavulanate, 625 mg three times a day, when symptoms improved.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with CAP requiring intravenous antibiotic therapy on admission to hospital.

Setting
The setting was secondary care. The economic study was carried out in Lahore, Pakistan.

Dates to which data relate
The effectiveness data were collected between May 1998 and February 2000. The dates to which the cost data related and the price year were not explicitly stated.

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

Link between effectiveness and cost data
The costing appears to have been estimated prospectively from the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations, to calculate the sample size, were not reported to have been performed. Patients were considered for the study if they had given written informed consent and had clinical evidence of pneumonia confirmed on X-ray. Excluded from the study were patients suspected of having atypical pneumonia, pulmonary tuberculosis, or a previous allergic reaction to study medications. Also excluded were those who were immunocompromised (white blood cell count <1,000/mm2) or receiving long-term steroid or immunosuppressive medication, those who were pregnant or...
breastfeeding, and those receiving concomitant antibiotic therapy. The number of patients who refused to participate was not explicitly stated. A total of 50 patients were included, of which 25 were assigned to receive amoxicillin-clavulanate and 25 to receive ceftriaxone. The patients were between 20 and 86 years of age. No evidence was provided to show that the study sample was representative of the study population.

**Study design**
This was a single-centred, open, randomised study that was carried out at the Department of Medicine, Services Hospital, Lahore. Alternate patients were assigned to one of two modes of therapy, such that the first, third and every subsequent odd numbered patient received amoxicillin-clavulanate while the second patient and every subsequent even number received ceftriaxone until 50 patients were enrolled. Follow-up was for 3 to 4 weeks after the end of treatment. One patient was lost to follow-up in each of the two treatment groups.

**Analysis of effectiveness**
The analysis of the clinical study appears to have been conducted on an intention to treat basis. The primary health outcomes used were:

- the number of patients clinically cured in each group,
- the number of those who were asymptomatic at follow-up,
- the number of recurrences,
- the number of patients experiencing adverse events, and
- the overall clinical efficacy in each treatment group.

The study groups appear to have been well balanced with respect to baseline characteristics.

**Effectiveness results**
Twenty-three patients in the amoxicillin-clavulanate group were clinically cured at the end of treatment (92%), 22 of whom were asymptomatic at follow-up. No recurrences or adverse events were reported. The overall clinical efficacy was 88%.

Twenty-two patients in the ceftriaxone group were clinically cured at the end of treatment (88%), 20 of whom were asymptomatic at follow-up. One recurrence was reported and one patient experienced a serious adverse effect. The overall clinical efficacy was 80%.

When the clinical results of the study groups were compared, non significant differences were detected.

**Clinical conclusions**
No statistically significant differences in clinical efficacy were found between the study groups, both at the end of treatment and at follow-up.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was produced. In effect, a cost-consequences analysis was performed.

**Direct costs**
The costs included in the economic evaluation were for the antibiotic used, the average daily cost of hospitalisation in a private hospital, and drug administration (i.e. cost of nursing time and pharmacist time). The resource use data for
antibiotics appear to have been collected prospectively from the effectiveness study. The cost of hospitalisation was based on the average daily cost of hospitalisation in a private hospital. Nursing time and pharmacist time appear to have been derived from authors’ assumptions about the times required per intravenous prescription and from data on the average salaries for a pharmacist and nurse. Overall, the resource quantities and the costs were reported separately. Details of the sources of the unit costs and the relation of prices to costs were not reported. The price year was not specified. Discounting was not relevant given the short timeframe of the analysis. The costs reported were the cost-savings associated with amoxicillin-clavulanate treatment, compared with ceftriaxone, in terms of hospital stay, drugs, nursing and pharmacist time, and overall costs. The savings per patient were also given.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not included in the economic evaluation.

**Currency**
Pakistan rupees (PKR). The exchange rate to other currencies was not given.

**Sensitivity analysis**
A sensitivity analysis was not performed.

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

**Cost results**
The total drug cost was PKR 129,480 in the ceftriaxone group and PKR 34,024 in the amoxicillin-clavulanate group.

The saving related to decreased length of stay with amoxicillin-clavulanate, when compared with ceftriaxone, was PKR 73,600. The saving related to decreased drug costs was PKR 95,456, and the saving related to decreased nursing and pharmacist time was PKR 1,081.

Aggregating these savings gave a total of PKR 170,137 saved, which amounts to PKR 7,397 saved per patient in the amoxicillin-clavulanate group.

**Synthesis of costs and benefits**
The costs and benefits were not combined because of the cost-consequences approach adopted.

**Authors’ conclusions**
The early switch from intravenous to oral amoxicillin-clavulanate was a more cost-effective treatment strategy than parenteral ceftriaxone, as it had comparable clinical efficacy and resulted in reduced hospital stay and decreased treatment costs for community-acquired pneumonia (CAP) in patients requiring an intravenous antibiotic on admission.

**CRD COMMENTARY - Selection of comparators**
Although no detailed justification was given for the choice of the comparator, it would appear that ceftriaxone represented current clinical practice in the authors’ setting. You should decide if the comparator represents current practice in your own setting.
Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on an open randomised study in which alternate recruited cases were allocated to one of the two treatment groups. The authors did not explicitly state that every patient who met the inclusion criteria during the study period was included in the study, nor did they report the number who refused to participate. Bias in patient inclusion into either study group cannot be ruled out in this form of randomisation. One case was lost to follow-up in each of the two groups. The duration of follow-up was appropriate for the study. Statistical analyses were performed and were reported clearly. The sample size did not appear to have been determined by power calculations. In spite of these reservations, the estimate of measure of effectiveness is likely to be valid.

Validity of estimate of measure of benefit
No summary measure of health benefit was reported since a cost-consequences approach was undertaken. The comments in the 'validity of estimate of measure of effectiveness' field (above) therefore apply.

Validity of estimate of costs
The perspective of the study was not reported, although the costs included appear to have been those of the health service. The unit costs of hospitalisation do not appear to have been specific to the condition studied. The sources of the unit cost data were not provided and, therefore, it cannot be inferred whether they were published or unpublished sources. In addition, it appears that authors’ assumptions have been used in the cost calculation. The date to which the drug prices referred was not reported. Overall, the resource use data were reported separately from the unit costs. No statistical or sensitivity analyses were employed. These limitations imply that the cost results must be treated with some caution.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other developing countries was not explicitly addressed. The authors provided an extensive justification for not assessing intravenous ceftriaxone in the outpatient department instead.

Implications of the study
The authors suggested that the widespread application of the concept of switch therapy in developing countries like Pakistan would result in substantial cost-benefits. There were no specific recommendations for further research.

Source of funding
None stated.

Bibliographic details
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Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
Amoxicillin-Potassium Clavulanate Combination; Ceftriaxone; Clinical Trials as Topic; Community-Acquired Infections; Comparative Study; Costs and Cost Analysis; Drug Costs; Haemophilus influenzae; Health Care Costs; Hospital Costs; Hospitalization; Pneumonia; Streptococcus pneumoniae; Treatment Outcome

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