Comparative efficacy of cefpirome and ceftazidime alone or in combination with isepamicin in empiric treatment of sepsis in patients admitted to ICU

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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:

- cefpirome alone in doses of 1 - 2 g/12 hours intravenous (i.v.) (group 1),
- ceftazidime alone in doses of 1 - 2 g/12 hours i.v. (group 2),
- cefpirome 1 - 2 g/12 hours i.v. plus isepamicin 8 - 15 mg/kg per day i.v. (group 3), and
- ceftazidime 1 - 2 g/12 hours i.v. plus isepamicin 8 - 15 mg/kg per day i.v. (group 4).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with sepsis who were admitted to the ICU. The selection criteria included:

- temperature greater than 38 degrees C,
- heart rate greater than 90 per minute,
- respiratory rate greater than 20 per minute or hypocapnoea PaCO2 (partial carbon dioxide pressure) less than 32 mmHg,
- systolic blood pressure less than 90 mmHg, and
- leukocytosis (> 11,000/mm3) with a left shift or leucopenia (< 4,000/mm3).

Patients with a history of hypersensitivity to beta-lactam antibiotics or having resistance to the study drug were excluded from the study. Other criteria for exclusion were pregnancy, lactation, chronic renal failure, non-bacterial pneumonia and Koch’s chest.

Setting
The setting was secondary care. The economic analysis was carried out in the Institute of Medical Sciences, Banaras Hindu University, India.
Dates to which data relate
The effectiveness and resource use data were collected between August 2000 and June 2002. The price year was not reported.

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

Link between effectiveness and cost data
The cost data were collected prospectively on the same patient sample as that used in the effectiveness study.

Study sample
A total of 120 patients included in the study were divided randomly into four groups of 30 patients each. The proportion of males was 60% in group 1, 66.7% in group 2, 50% in group 3 and 56.7% in group 4. The mean age was 46.8 (+/- 13.8) years in group 1, 38.9 (+/- 14.1) years in group 2, 44.8 (+/- 14.8) years in group 3 and 43.1 (+/- 11.6) in group 4. Power calculations were not conducted to determine the sample size. The method of sample selection was not reported.

Study design
The study was a randomised controlled trial that was carried out in a single centre. The method of randomisation was not reported. The length of follow-up was not specifically reported, although it appears to have been up to 7 days (i.e. the total duration of treatment). No loss to follow-up was reported. It would appear that no blinding or allocation concealment took place, although this was not explicit in the reporting.

Analysis of effectiveness
The basis of the clinical study was intention to treat. The primary health outcomes used in the effectiveness analysis were:

- the clinical response (successful rate for the therapies),
- bacteriologic response (eradication, presumed eradication, persistence or indeterminate for the originally isolated pathogen, and colonisation or superinfection), and
- adverse event (frequency of adverse reaction and mortality).

The groups were shown to be comparable at baseline.

Effectiveness results
All patients with confirmed septicaemia were cured in groups 2 to 4, and 50% were cured in group 1.

For patients with suspected septicaemia, 16.7% were cured in group 1, 44.4% in group 2, 52.2% in group 3 and 48.0% in group 4.

In terms of the overall clinical response, 30% were cured in group 1, 50% in group 2, 63.3% in group 3 and 56.7% in group 4.

The comparison among groups was significant for group 1 versus group 3, (p<0.05), and for group 1 versus group 4, (p<0.05). For the others, the difference was not statistically significant, (p>0.05).

A total of 33.3% of pathogens were eradicated for group 1. For all other groups, 100% of pathogens were eradicated. Group 2 was significantly better than group 1, (p<0.05). The comparison between groups 3 and 4 was not significant.
No colonisation was found in any study group. Superinfection that was totally caused by Acinetobacter species was found in groups 1 and 4.

The frequency of adverse reactions was 16.7% in group 1, 13.3% in group 2, 19.9% in group 3 and 13.3% in group 4.

The death rate was 3.3% in group 1, 10% in group 2, 0% in group 3 and 6.7% in group 4.

**Clinical conclusions**

In terms of bacteriological and clinical efficacy, the combination therapy was better than monotherapy. Among the combination therapies, group 3 was better.

**Measure of benefits used in the economic analysis**

No summary measure of benefit was used in the economic analysis and the outcomes were left disaggregated. The economic analysis was therefore based on a cost-consequences approach.

**Direct costs**

Only drug costs were included in the economic analysis. The perspective adopted was not reported. The drug price was reported, but the source of the cost data was not. The resource quantities and the costs were reported separately. Discounting was irrelevant as the costs for each group were incurred during a short time horizon. The price year was not reported.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

No indirect costs were calculated.

**Currency**

Indian rupees (R).

**Sensitivity analysis**

No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**

A cost-consequences approach was adopted. See the 'Effectiveness Results' section.

**Cost results**

The total costs per patient during the ICU stay were R6,304.20 for group 1, R3,080.00 for group 2, R11,551.00 for group 3 and R8,716.80 for group 4.

**Synthesis of costs and benefits**

The costs and benefits were not combined as a cost-consequences approach was taken. However, the results implied that the general dominance among the groups depended upon the consideration of bacteriological and clinical efficacy,
together with low cost.

**Authors' conclusions**
Combination therapy was the best choice. Among the combination therapies, when considering bacteriological and clinical efficacy together with the safety profile, group 3 antibiotics (cefpirome plus isepamicin) was found to be slightly more active though costlier than group 4 antibiotics (ceftazidime plus isepamicin). However, group 4 could be advocated for use if the identical bacteriological efficacy along with low cost were taken into consideration. Among the monotherapies, group 2 (ceftazidime) was the better choice.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. The therapies examined in the study were the commonly used interventions for the treatment of nosocomial infections in the ICU. You should decide whether they are widely used technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The randomised controlled trial used in the effectiveness analysis appears to have been appropriate for the study question. However, the authors did not report full details of the study design (e.g. the randomisation process). In addition, power calculations were not carried out to determine the appropriate size of the sample, which may limit the internal validity of the study. The study groups were shown to be comparable at baseline, and the study sample appears to have been representative of the study population. However, given the lack of reporting on the trial methodology it was difficult to determine the level of internal validity.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The authors did not state the perspective adopted in the study. Only the drug costs were included in the economic evaluation, and the authors did not explain why other categories of costs were excluded. The costs were treated deterministically and no sensitivity analyses were performed. The source of the price data was not provided, although the unit costs and the quantities of resources used were reported separately. In addition, the price year was not given. A lack of reporting of the costing details makes the quality of the results obtained untenable.

**Other issues**
The authors compared their effectiveness findings with those from other studies, and also explained some of their findings. However, the external validity of the analysis would appear to be low as no sensitivity analyses were performed. The issue of the generalisability of the results to other settings was not specifically addressed.

**Implications of the study**
The authors stated that, overall, combination therapy was better than monotherapy for the empiric treatment of nosocomial sepsicaemia in the ICU. Among the combination therapies, cefpirome plus isepamicin (group 3) was better than ceftazidime plus isepamicin (group 4) irrespective of cost. However, group 4 could also be advocated, as it was found to have bacteriological efficacy similar to that of group 3 and was more cost-effective. Among the monotherapies, treatment with ceftazidime was the better choice.

**Source of funding**
None stated.
Bibliographic details

Other publications of related interest


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Subject indexing assigned by CRD

MeSH
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