Pharmacoeconomic analysis of ampicillin-sulbactam versus cefoxitin in the treatment of intra abdominal infections


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
Second generation cephalosporins used in the treatment of intra-abdominal infections.

Type of intervention
Treatment; prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients at least 18 years of age suspected of having intra-abdominal infection requiring urgent operation, who had visible serosal inflammation and positive peritoneal exudate culture at time of operation and which would require a minimum of four days antibiotic therapy. Patients were excluded from analysis if they had a hypersensitivity to penicillins or cephalosporins, concomitant antibiotic administration up to 4 days before study enrolment, other major infections, immune deficiencies, neutropenia, renal failure, pregnancy, breast feeding or terminal illness.

Setting
Hospital. The economic analysis was conducted in Chicago, Illinois, USA.

Dates to which data relate
The effectiveness data were taken from a clinical trial published in the literature in 1993. Resource data were collected between July 1994 and 1997. 1997 prices were used.

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

Link between effectiveness and cost data
Costing was undertaken retrospectively, not using the same patient sample as in the effectiveness analysis.

Study sample
385 patients were randomised to receive either 3g A/S or 2g cefoxitin every 6 hours. All patients had suspected bacterial intra-abdominal infections. Of the 385 patients, 188 (48%) were excluded. 127 of these did not have a culture documentation of infection and the remaining 61 were excluded due to other exclusion criteria. There were 96 patients in the A/S group and 101 in the cefoxitin group.
Study design
This was a multi-centre double blind randomised controlled trial. Patients were followed up until hospital discharge. One patient was lost to follow up in both the A/S group (1%) and in the cefoxitin group (1%).

Analysis of effectiveness
The analysis of effectiveness was based on intention to treat. The primary health outcomes were rates of clinical cure and failure and also the incidence of adverse effects. At analysis both groups were comparable in demographic characteristics and in prognostic features for infection.

Effectiveness results
Clinical cure (failure) rates, characterised by the absence of infection and adverse drug reaction were 86% (13%) and 78% (21%) in the A/S and cefoxitin groups respectively, (not significant, P=0.13) Similarly there were 33 adverse effects in the A/S group and 32 in the cefoxitin groups. There were no differences in the severity of adverse effects between the two groups.

Clinical conclusions
It was concluded that no significant differences in safety or efficacy were found between A/S and cefoxitin in the treatment of patients with serious intra abdominal infections.

Modelling
A decision analysis model was used to estimate the outcomes and costs of treatment using probability values taken from the clinical study.

Measure of benefits used in the economic analysis
The benefit measure was infections avoided.

Direct costs
Direct costs for drug acquisition, hospitalisation and additional treatment for patients who failed to respond to antibiotic therapy were estimated. Drug costs were taken from 1997 institution specific acquisition costs. The costs of hospitalisation and resources/costs of additional treatment were taken from submitted charges and Medicare cost:charge ratios between July 1994 and June 1996 derived from the University Hospital Consortium Clinical Information Network (comprising 57 Institutions). Costs were discounted at a rate of 3% per annum and 1997 prices were used. Costs were estimated from the perspective of the hospital and costs of treating adverse events were excluded as these were common to both groups and did not differ in severity. In addition a basic hotel cost estimate of $605 per day for 4 days was deducted from estimates of cost if median duration of hospitalisation was greater than four days, as this time would have been spent in hospital in any eventuality.

Currency
US dollars ($).

Sensitivity analysis
One way and multi-way sensitivity analyses were conducted on all variables in the model and a threshold analysis was also estimated. A probabilistic sensitivity analysis using a Monte Carlo simulation of 10,000 iterations using Latin hypercube sampling was also conducted.

Estimated benefits used in the economic analysis
There were 8% less infections in patients in the A/S group compared with the cefoxitin group.

**Cost results**
The cost per patient of treatment with A/S compared with that of cefoxitin was $1,732 versus $2,622 including the additional costs of treatment for infections not prevented or cured. If these costs were removed from the analysis then the costs of drug acquisition and treatment for the two drugs would be $298.48 for A/S and $335.72 for cefoxitin. Costs of adverse effects were excluded as they did not differ between groups.

**Synthesis of costs and benefits**
A synthesis was not undertaken by the authors since A/S was a dominant intervention compared with cefoxitin. In the base case scenario the cost of A/S was $890 less than that of cefoxitin because of the lower failure rate. In one way sensitivity analysis the only variable to have a significant impact on the model was failure rate of cefoxitin. If this rate fell from 21% to 13% then cefoxitin would be less costly, all other things being equal. In the Monte Carlo analysis it was estimated that $425 saving per patient using A/S compared with cefoxitin would be realised (95% CI: $618 - 1516) although this may not be statistically significant. The analysis also estimated that there was a 78% certainly level that costs would be lower using A/S than cefoxitin.

**Authors' conclusions**
The authors concluded that A/S may be a less expensive option for the treatment of intra-abdominal infections than cephalosporin cefoxitin, due to the difference in the rate of failure and the fact that there would therefore be fewer infections requiring additional treatment in the A/S group. However, further analysis is required, conducted prospectively alongside clinical trials, as the model has only a 78% certainty rate that there will be a cost reduction using A/S.

**CRD COMMENTARY - Selection of comparators**
A justification was provided by the authors for the comparator, cephalosporin cefoxitin, an antibiotic used in the treatment of intra abdominal infections.

**Validity of estimate of measure of benefit**
Probabilities used in the decision model were taken from a double blind randomised clinical trial in which no differences were found in demographic or prognostic characteristics between the two groups.

**Validity of estimate of costs**
Cost estimates were collected retrospectively and not from the study sample used in the clinical analysis. It would have been preferable had this information been collected alongside such a trial, as was indeed noted by the authors. Only direct costs from the perspective of the institution have been considered in the analysis and it would have been useful also to have obtained information relevant to others in society such as patients.

**Other issues**
As noted by the authors the conclusions reached by this model may only be applicable to institutions which fit in with assumptions made in the model and may not be generalisable to other settings. In addition the authors included the additional costs of treatment for infections in the two groups but these costs must be treated with caution given that no significant difference in safety or efficacy was found in the clinical study between the two drugs, and furthermore sensitivity analysis demonstrated that probability of failure was a significant variable in the model.

**Implications of the study**
As noted by the authors, there is a need for well designed economic evaluations to be conducted prospectively alongside
clinical trials further to analyse the cost effectiveness of these two drugs.

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