Epidemiology, resistance, and outcomes of acinetobacter baumannii bacteremia treated with imipenem-cilastatin or ampicillin-sulbactam

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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
Antimicrobial treatment with imipenem-cilastatin (I-C) was compared with ampicillin-sulbactam (A-S), for the management of Acinetobacter baumannii (A. baumannii) infections in the intensive care unit.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised all in-patients over the period 1987 to 1999 with documented A. baumannii bacteraemia. Patients were excluded if they died before starting treatment with an antibiotic; they received antibiotics for less than 72 hours; or if they received antibiotics other than the study drugs.

Setting
The setting was secondary care. The study was carried out in Detroit, USA.

Dates to which data relate
The clinical outcome and cost data were gathered from 1987 to 1999. The drug price data were based on the figures for 1999.

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 on the same sample of patients as that used for the effectiveness data.

Study sample
No power calculations were reported. The study sample included all patients treated at the trauma centre from 1987 to 1999 for an A. baumannii infection, as confirmed by the microtitre well method. A total of 100 patients were potentially evaluable. Of these 52 were excluded: 16 due to death before starting treatment, 18 for receiving treatment for less than 72 hours, and 18 for receiving antibiotics other than the study drugs. The final analysis included 18 patients in the I-C group and 30 patients in the A-S group. Baseline characteristics were given, which enabled comparison with the general population.
Study design
This study used a single-centre, retrospective cohort design. Patients were followed-up until presumed eradication of the disease, defined as documented clearance of bacteraemia, or living discharge from the hospital for patients without repeat cultures. One patient receiving A-S did not have repeat cultures but died before hospital discharge. A blinded investigator assessed all patient outcomes.

Analysis of effectiveness
The clinical study data were analysed on the basis of treatment completers only. The primary health outcome used in the analysis was treatment success, defined as complete resolution of the signs and symptoms of bacteraemia; normal temperature, heart rate, blood-pressure and white blood cell count; and a reduced need for vasopressor drugs. This included patients stable for discharge or eligible to go home.

Failure was defined as the progression of most clinical signs and symptoms of bacteraemia, such as increasing temperature, heart rate or white blood cell count; decreasing blood-pressure; and a continuing need for vasopressor drugs. This included patients whose cause of death was directly attributable to A. baumannii, and those whose therapy change was based on poor clinical response, no objective evidence of deterioration or no change in status. An indeterminate response indicated that circumstances precluded classification.

The two groups, A-S and I-C, appeared to be comparable in terms of gender, age and source of admission, although no statistical analysis was conducted. The median Acute Physiology and Chronic Health Evaluation (APACHE) II score at positive culture was 16.5 (range: 5 - 33) for A-S and 19 (range: 10 - 34) for I-C. The median number of hospital days to positive culture was 8.5 days (range: 0 - 58) for A-S and 13 days (range: 0 - 127) for I-C. Combination therapy with an aminoglycoside was administered to 44% of I-C-treated patients and 37% of A-S treated patients.

Effectiveness results
Presumed eradication occurred in 100% of patients receiving I-C and 97% of patients receiving A-S.

There were no differences between I-C and A-S in terms of the following clinical outcomes.

Time to normal white blood cell count: 8.5 days (range: 3 - 22) for A-S and 11 days (range: 3 - 62) for I-C.

Clinical response, in terms of the number of patients with treatment success: at day 2, 6 for A-S and 6 for I-C; at day 7, 10 for A-S and 4 for I-C; and at the end of the treatment, 16 for A-S and 9 for I-C.

Antibiotic-related length of stay in the intensive care unit: 17 days (range: 0 - 140) for A-S and 13 days (range: 6 - 62) for I-C.

Total length of hospital stay: 28 days (range: 10 - 151) for A-S and 40 days (range: 14 - 173) for I-C.

No p-values were given

The median antibiotic-related length of stay was 10 days (range: 3 - 22) for A-S and 13 days (range: 6 - 62) for I-C (p=0.05).

With regard to combination therapy, results were reported selectively. For I-C, they included the median total length of stay, for combination versus monotherapy, 57 and 33 days respectively (p=0.03).

There was no significant difference in clinical outcomes for A-S.

Clinical conclusions
All clinical outcomes were better for A-S. However, according to the authors, only antibiotic-related length of stay achieved a p-value of 0.05.
Measure of benefits used in the economic analysis
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

Direct costs
The direct costs from the hospital perspective were included in the analysis; these were the cost of antibiotic therapy and hospitalisation costs (length of stay). The resource use data was taken from the period 1987 to 1999. The quantities and costs were not analysed or reported separately. The unit cost of antibiotic therapy was based on the average wholesale price of each agent in 1999, and the hospitalisation cost was determined from the American Hospital Association Hospital Statistics data, which were published in 1998. The authors did not state whether they inflated the hospitalisation costs to match the antibiotic data for the price year 1999. The costs were not discounted due to the short timeframe of the study, which was less than one year. The study reported median costs.

Statistical analysis of costs
The authors reported that the differences between continuous variables were tested using the Mann-Whitney U test.

Indirect Costs
Indirect costs were not included in this analysis because they were not appropriate for the study perspective.

Currency
US dollars ($). No conversion rate was reported.

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See effectiveness results reported previously.

Cost results
The median antibiotic costs were $500 (range: 50 - 1,220) for an A-S treated patient, and $1,500 (range: 220 - 7,520) for an I-C treated patient (p=0.0002). The median hospitalisation costs were $30,000 (range: 9,600 - 177,000) for an A-S treated patient versus $432,000 (range: 13,200 - 178,000) for an I-C treated patient.

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
The authors concluded that A-S was at least as effective as I-C, based on clinical response at days 2, 7 and at the end of treatment, and is a “cost-effective” alternative for the treatment of A. baumannii infections.

CRD COMMENTARY - Selection of comparators
The authors provided adequate justification for their choice of I-C and A-S as comparators, in the management of A. baumannii infections in the USA. The reader should assess whether these are relevant comparators for UK clinical practice before generalising the results to the UK National Health Service.
Validity of estimate of effectiveness:

The authors suggested that the main limitation of this study was that it was retrospective in nature: it may therefore be difficult to determine the role of Acinetobacter in a patient's illness, because evaluation did not occur at the time of infection. No statistically-significant differences were found at the 5% level for the selected clinical outcomes. However, there was no evidence that the study was adequately powered to detect a statistical difference in outcomes, and the absence of a difference may have been due to insufficient power rather than an actual equivalence. There was also no allowance made for confounding, for example by selection or combination therapy. Indeed, there was some evidence that combination therapy was less effective.

Validity of estimate of benefits:

No summary measure of benefit was used. A comparison of effectiveness will therefore depend on the decision-maker considering the trade-offs between the various measures of effectiveness.

Validity of estimate of costs

The study did not state explicitly the chosen price year, and it was unclear if the price year for antibiotic costs was consistent with that for hospitalisation costs. The study did not include a sensitivity analysis, which would have provided information regarding the robustness of the findings from the baseline analysis. Generalisability would have been reduced by the fact that resource quantities and unit costs were not reported separately. The authors concluded that A-S is a "cost-effective" alternative, but this should be interpreted with caution. Cost-effectiveness depends on how much one is willing and able to pay for any improvement in effectiveness.

In this study, the authors showed some decrease in costs by using A-S for, superficially, the same effectiveness, which would indicate that A-S is cost-effective in comparison to I-C. However, they admit that costing was incomplete and, statistically, equal effectiveness could mean A-S is less effective on average. This difference would need to be valued in comparison to other technologies.

Other issues

The authors appear to have been selective in their reporting of the results, and to state there was "no difference" in the clinical outcome is misleading. They did not discuss the generalisability of their results, although they did compare them to the results of another study. The conclusions were in relation to A. baumannii infections. However, the authors did admit that underlying illnesses were a confounding factor, and they did not conduct a full cost analysis.

Implications of the study

The authors suggest that this analysis was not intended to prove A-S to be superior to I-C for the treatment of A. baumannii, only that it is a valid option. They recommend that large, prospective double-blind studies are necessary to determine the best treatment. This study highlights the care needed in the use of terminology such as "cost-effective" and "no difference".

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