Piperacillin/tazobactam versus imipenem: a double-blind, randomized formulary feasibility study at a major teaching hospital


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 antibacterial agent imipenem and an injectable antibiotic combination of Piperacillin sodium and beta-lactamase inhibitor tazobactam used in the treatment of infections in hospitalised patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients aged 16 years or older who had been prescribed imipenem for the treatment of infections.

Setting
Hospital. The economic analysis was conducted in Vancouver, British Columbia, Canada.

Dates to which data relate
Data on effectiveness and resources used were collected between March 1995 and June 1996. The price years used were not stated.

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

Link between effectiveness and cost data
Costing was undertaken using the same patient sample as in the effectiveness analysis. It is not clear whether costing data were collected prospectively alongside the effectiveness analysis.

Study sample
360 patients were prescribed imipenem during the 14 month study period. Patients who were hypersensitive to, or who had infections resistant to, imipenem or P/T were ineligible, as were pregnant or lactating women, and patients with meningitis. 210 patients (52%) were excluded from the initial sample: 15% because patient consent was not obtained and 37% for other reasons. 75 patients were randomly allocated to the imipenem group and 75 to the P/T group. Power calculations were used to determine the sample size required to detect a 20% difference in efficacy between the two drugs, using an alpha = 0.05 and beta of 0.2. The required sample size was 90 patients in each of the two groups.
Study design
This was a single-centre, double-blind randomised controlled trial. The duration of follow-up was thirty days after the end of treatment. Block randomisation (in blocks of 10) was carried out using a computerised random number generator program to allocate patients between the two groups. There was no loss to follow up. All investigators and medical staff associated with the study were blinded.

Analysis of effectiveness
The analysis of clinical effectiveness was conducted both on the basis of intention to treat and also for those who had been treated for at least 3 days with the study medication. The primary health outcomes used in the analysis were clinically determined success or improvement rates and adverse reactions. At analysis, both the intervention and comparator population groups were shown to be similar in demographic and prognostic characteristics.

Effectiveness results
68% of patients in the imipenem group and 70% in the P/T group had clinical outcomes which were defined as successful or improved. This difference was not statistically significant, (p=0.54). For those patients who received treatment for at least 72 hours these rates were 66% and 71%. Again these differences were not significant, (P=0.66). Overall 55 adverse drug reactions were observed in the imipenem group and 52 in the P/T group, (not significant). Furthermore, there were no significant differences in the incidence of specific types of adverse drug reactions.

Clinical conclusions
Similar levels of efficacy and patient tolerability were demonstrated between imipenem and P/T therapy at the dosage levels used in the study.

Measure of benefits used in the economic analysis
Since the clinical analysis found no significant difference in effectiveness between the intervention and the comparator, the economic analysis was based on the difference in costs only.

Direct costs
The direct drug costs for imipenem, P/T and ancillary antibiotics including acquisition, administration and delivery were estimated. These costs were taken from a 1996 drug cost study. Costs were not discounted as they were incurred over a period of time shorter than one year. The price year used was not stated. The duration of hospitalisation was also estimated. Costs were determined from the perspective of the study institution.

Indirect Costs
Not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Not applicable.
Cost results
The mean treatment course costs for imipenem was Can$762 (range: Can$55 - Can$3,192) compared with Can$696 (range: Can$79 - Can$2,967) for a P/T course. This difference was not statistically significant, (p=0.59). Mean costs for additional ancillary antibiotic drugs were Can$518 (range: Can$2 - Can$2,388) in the imipenem group compared with Can$629 (range: Can$6 - Can$2,913) in the P/T group (not significant, p=0.51). The mean duration of drug therapy was also similar for the two groups: 7.7 days for imipenem and 7.5 days for P/T, (p=0.84).

Synthesis of costs and benefits
Not applicable.

Authors’ conclusions
P/T is a suitable alternative to imipenem as it has a similar efficacy and tolerance profile and, additionally, the costs of both treatment courses are similar.

CRD COMMENTARY - Selection of comparators
A justification was provided by the authors for the comparator used, imipenem, which is an accepted antibacterial agent for the treatment of serious infections.

Validity of estimate of measure of benefit
The estimate of clinical benefit was based on the results of a single-centre randomised controlled trial. No significant difference was observed between the two interventions, but, as the authors noted, a difference may not have been detected because of inadequate statistical power, due to insufficient patient numbers being recruited.

Validity of estimate of costs
Insufficient details were provided on the source of cost estimates. It is unclear whether cost data were based on resource use observed in the trial and then costed using a published formula, or whether they were taken directly from this published study. In addition, the price year used for costing was not stated. Only direct costs of drug acquisitions and ancillary antibiotic medications were estimated. It might also have been useful to estimate other direct costs of treatment such as the cost of treating any adverse events. In addition costs to others in society such as patients could also have been included.

Other issues
It may also have been helpful to conduct a sensitivity analysis to identify any sensitive parameters. There is some uncertainty as to whether Canadian or US Dollars were used in this analysis.

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