Dosing adjustment of 10 antimicrobials for patients with renal impairment

Preston S L, Briceland L L, Lomaestro B M, Lesar T S, Bailie G R, Drusano G L

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
Dosage adjustment programme of 10 antimicrobials (intravenous acyclovir, ampicillin/sulbactam, aztreonam, ceftazidime, ceftizoxime, cefuroxime, imipenem/cilastatin, piperacillin, intravenous ciprofloxacin, and intravenous fluconazole) for patients with renal impairment.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients receiving the targeted drugs (intravenous acyclovir, ampicillin/sulbactam, aztreonam, ceftazidime, ceftizoxime, cefuroxime, imipenem/cilastatin, piperacillin, intravenous ciprofloxacin, and intravenous fluconazole). Patients had to be aged over 18 years. Patients with cystic fibrosis, or who were undergoing dialysis or plasmapheresis were excluded.

Setting
Hospital. Although not explicitly stated, is appears that the study was carried out in New York, USA.

Dates to which data relate
Clinical and resources use data were collected between 1993 and 1994. The price date was not stated.

Source of effectiveness data
The effectiveness data were based on a single study and on opinion.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
Patients receiving a targeted drug and meeting the rest of the entry criteria. The sample mean age (+/- SD) was 68.9 +/- 14.72 years (range: 20-97), with mean serum creatinine (Scr) concentrations being 2.5 +/- 2.19 mg/dL (range: 0.5-14.9), median Scr was 1.6 mg/dL, and the mean creatinine clearance (Clcr) was 33.3 +/- 18.88 mL/min (range: 5-10, median 40). The patients were screened for renal impairment using Scr concentrations and recommendations for dosage adjustment were based on the patient's Clcr and corresponding manufacturer's dosing guidelines. Power calculations were not reported. Overall, 137 patients were monitored.
Study design
Case series. The study was conducted at a 667-bed tertiary care teaching hospital. The period of follow-up was 6 months. The loss of follow-up was not stated.

Analysis of effectiveness
The clinical efficacy of therapy was not assessed. The outcomes assessed were a dosage change recommendation of the targeted antimicrobial agents and the acceptance of the pharmacists’ recommendations by prescribers, and were based on pharmacodynamic principles.

Effectiveness results
160 dosage changes were recommended in 137 patients. The prescriber accepted 147 (91.9%) recommendations. Of these, the mean day of therapy on which the dosing change was implemented was day 2. The drugs with the highest percentage (above 12%) of dosing change recommendations were acyclovir, mpenem/cilastatin, and ceftazidime.

Methods used to derive estimates of effectiveness
The estimation of clinical efficacy of the therapies after the intervention programme (dosage adjustment programme used a dosing nomogram) was based on assumptions based on an apparently informal review of the relevant literature, clinical judgement and pharmacodynamic considerations. The programme operated on the assumption of an ideal body weight of patients in the Clcr calculations, and screening was conducted in accordance with the following guidelines:

if the patients had any Scr and were aged 50 years or older, Clcr was calculated (nomograms were used to calculate Clcr for elderly patients with normal appearing renal function, i.e. Scr 0.6-1.1. mg/dL);

if the patients had an Scr of 0.6-1.1 mg/DL and were younger than 50 years of age, renal function was assumed to be normal and no dosage adjustment was applied;

if the patients had an Scr more than 1.1mg/dL and were younger than 50 years of age, Clcr was calculated;

if the patients had a calculated Clcr of less than 50 mL/min, they were referred to a list of predetermined dosage recommendations for doses based on patient-specific Clcr.

Estimates of effectiveness and key assumptions
It was assumed that the adjusted dose would be as effective as 'a normal dose' for a patient with a normal renal function. Further, it was assumed that few of the dosage adjustment recommendations accepted by prescribers would have occurred in the absence of such a programme.

Measure of benefits used in the economic analysis
The benefit measure was the number of dosage adjustments.

Direct costs
Cost discounting was not required due to the 6-month window of analysis. Quantities were reported separately from total costs. The drug acquisition cost of the adjusted regimen and the drug acquisition cost of the original regimen were used to estimate drug costs. The cost of pharmacist time involved in conducting the programme was reported and was based on an approximation. Also included were the costs associated with adjustment to non-target drugs resulting from the programme monitoring. The estimate of the quantities and costs was based on actual data. A crucial assumption was that the implemented changes to dosages (accepted by the prescribers) would not have occurred had the intervention not taken place. Supply (drug administration devices and tubing), monitoring (pharmacist time in assessment of doses), and labour costs (pharmacy preparation and nursing administration) were not included, nor were the costs of adverse effects.
considered in the costing.

**Statistical analysis of costs**
Not conducted.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was not carried out.

**Estimated benefits used in the economic analysis**
147 dosage adjustment recommendations were accepted by prescribers.

**Cost results**
The cost avoidance due to the recommendations for dosage adjustment was $11,702.08. Non-target drugs cost savings were $6,613.75. Total cost savings were $18,316.29. Programme administration was estimated to involve 15 hours per week, costing about $330 per week for pharmacist time. The programme cost was approximately $8,000.

**Synthesis of costs and benefits**
Synthesis of costs and benefits was not carried out, as the programme was the dominant strategy.

**Authors’ conclusions**
Clcr dosage adjustment programme was successful in providing the appropriate dose of targeted antibiotics in patients with renal impairment. This resulted in dosage optimisation to ensure quality, direct and potentially indirect cost avoidance, and suspected decrease in morbidity resulting from excessive dose.

**CRD COMMENTARY - Selection of comparators**
The comparator chosen was that of the 'no-programme' situation. Since the clinical study on which the economic analysis was based lacked a control group, an underlying assumption of the economic study was, as stated by the authors, that "few of the ...dosage adjustments recommendations accepted by prescribers would have occurred" without the programme.

**Validity of estimate of measure of benefit**
The study did not assess directly the effectiveness of the intervention, and thus relied on current clinical evidence about the effects of the programme on the patient's health, the authors pointing out the need to conduct a controlled trial to estimate adverse effects.

**Validity of estimate of costs**
Detailed information about the methods of cost estimation was provided. However, the results depend crucially on the assumption of static dosages under the control group (as mentioned above), and the implications of this assumption
were not investigated.

Other issues
The results obtained in this study were not adequately compared with previous studies. The assumptions (e.g. approximate pharmacist time used by the programme, drug cost savings by the programme) were not subjected to sensitivity analysis, therefore the robustness of the results and their potential generalisability to other countries cannot be assessed.

Implications of the study
This study should be regarded as a tentative exploration of the economic importance of issues associated with a drug-monitoring programme for 10 targeted antimicrobial drugs. Further studies are warranted, using the format of randomised clinical trials if ethical.

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