Comparison of vancomycin versus cefazolin as initial therapy for peritonitis in peritoneal dialysis patients

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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
Patients with renal disease receiving peritoneal dialysis (PD) were given one of two antibiotic regimes, as initial therapy, following a diagnosis of peritonitis and if organisms in the PD fluid were gram positive or showed no growth. The antibiotics used were vancomycin or cefazolin. Peritonitis was diagnosed if the effluent cell count exceeded 100 white blood cells (WBC)/mL, with more than 50% polymorphonuclear cells.

After these conditions were met, the patients received either vancomycin (1 g/L dialysate) or cefazolin (125 mg/L). All of the patients possessed both antibiotics in kits marked A (vancomycin) and B (cefazolin). The decision as to which of the two they should take was made after a telephone call with the dialysis nurse.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Ninety patients who had been trained to perform PD were included in the study population, and all gave their informed consent. Patients were excluded if they were sensitive to penicillin or vancomycin, were already receiving antibiotics, were known to be noncompliant or could not follow instructions. Pregnant women and patients aged younger than 18 years were also excluded. Once patients developed peritonitis, if their cultures grew gram negative or fungal organisms, that episode did not form part of the study.

Thirty of the original 90 patients developed peritonitis. There were 51 episodes of peritonitis altogether. The average age of these patients was 48 years (range: 26 - 74), and there were 17 males and 13 females. Fourteen patients had diabetes mellitus, while the rest had either hypertension or glomerulonephritis. In 42 of the 51 episodes of peritonitis, gram-positive organisms were grown or were culture negative and so could be part of the study.

Setting
The setting was tertiary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were from October 1997 to September 1999. The resource data were from 1997 to 1999. No price year was given.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was carried out on the same sample of patients as that used in the effectiveness study. It was unclear whether or not the costing was conducted prospectively or retrospectively.

Study sample
No power calculations to determine the sample size were reported. All of the patients who met the inclusion criteria during the time period were included in the pool of PD patients who might get peritonitis and then be part of the study. Twenty-two episodes of peritonitis were treated with vancomycin and 20 were treated with cefazolin.

Study design
This was a single-centre, randomised controlled trial in which each episode of illness counted as a new case and would be randomised to one of the two treatments (vancomycin or cefazolin). Each episode was assessed for 4 to 5 weeks.

Analysis of effectiveness
The basis of the analysis was intention to treat. The health outcomes were the WBC count, the number of relapses, evidence of exit site infection, tunnel infection, evidence of Enterococcus and a measure of abdominal pain. The number of patients whose catheters were removed was recorded, along with the reasons for the removal.

Effectiveness results
The WBC count (per mL) of patients treated with vancomycin fell from 1,431 (+/- 432) to 8.2 (+/- 3.2) at the end of treatment, whilst that of patients treated with cefazolin fell from 1,915 (+/- 676) to 7.6 (+/- 2.8). There was no statistically significant difference between the two groups.

There were 3 relapses in 2 patients in the vancomycin group (all S. aureus) and 2 relapses in the cefazolin group (both S. epidermis). There was no statistically significant difference between the two groups. All relapses were successfully treated with vancomycin.

Two patients in the cefazolin group had evidence of exit-site infection. There were no cases of tunnel infection. There were 2 cases of Enterococcus in the cefazolin group that responded to treatment with vancomycin.

The mean abdominal pain score fell from an average of 3.5 to less than 1 for vancomycin, and from 2.7 to less than 1 for cefazolin. There was no statistically significant difference between the two groups.

There were no cases of vancomycin-resistant organisms isolated during the study.

Catheters were removed from 8 patients in the vancomycin group. The reasons given included gram-negative infection (2 patients), fungi (1), recurrent peritonitis with gram-positive organisms (3), failure to thrive (1), and poor compliance (1).

Catheters were removed from 4 patients in the cefazolin group. The reasons given were gram-negative peritonitis (2 patients), fungal peritonitis (1), and recurrent gram-positive infection that would not respond to vancomycin (1). The p-value for the difference in catheter removal rate was 0.63.

Clinical conclusions
The authors concluded that there was no statistically significant difference between the two antibiotics in terms of their clinical effectiveness. No evidence of vancomycin resistance was found. It was reported that the medical staff found that patients found vancomycin easier to administer than cefazolin because it needed fewer doses.
Measure of benefits used in the economic analysis
No summary measure of benefit was used. A cost-consequences analysis was therefore performed.

Direct costs
No discounting was carried out. The cost per episode of peritonitis was broken down into costs and quantities. However, as episodes of illness rather than patients had been randomised, it was not possible to break down the costs per patient for the two kinds of treatment. The cost per episode of peritonitis was broken down into vancomycin or cefazolin, saline, syringes, needles, betadine, and mask. These costs were broken down into quantities, but the drug quantities were given at a different point in the paper. The individual prices were not given, and nor was a common price year. The cost of gentamicin (40 mg intraperitoneal), which was given to all patients while waiting for the culture results, was not included. Presumably, this was because it was common to all patients. The source of the quantity and cost data was actual data.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
No indirect costs were included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost per episode of treating peritonitis for 3 weeks was $30.21 with vancomycin and $39.32 with cefazolin.

Synthesis of costs and benefits
Irrelevant as a cost-consequences analysis was carried out.

Authors’ conclusions
There was no identifiable difference in the effectiveness of the two antibiotics for treating peritonitis. The authors also concluded that vancomycin cost less, that there were no cases of vancomycin-resistant enterococci, and that patients preferred vancomycin.

CRD COMMENTARY - Selection of comparators
The choice of the comparators, vancomycin and cefazolin, was implicitly justified by the widespread use of these two antibiotics to treat PD patients with peritonitis caused by gram-positive organisms, and the fears about vancomycin-resistant enterococci.
Validity of estimate of measure of effectiveness
The effectiveness data were obtained from a randomised controlled trial in which peritonitis episodes, rather than patients, were randomised to receive one of the two antibiotics. There was no sample selection since all of the patients who met the inclusion criteria were included in the study. The authors were aware that the patients preferred vancomycin, but they did not include any measure of patient satisfaction that could have registered this preference.

Validity of estimate of measure of benefit
No summary measure of health benefit was calculated.

Validity of estimate of costs
The costs were broken down into components for a peritonitis episode, and for most of these components the quantities were given so that the price could be deduced. No indirect costs were given. This omission might have prevented the authors' conclusions from being more robust, as vancomycin appeared to have lower indirect costs than cefazolin. The quantities and prices were both taken from a single study. No statistical or sensitivity analyses of the prices or quantities were carried out. No price year was reported.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. However, they did not address the issue of generalisability of their results to other settings.

Implications of the study
The authors conclude that there is no argument against using vancomycin for PD-associated peritonitis, as it is as effective as cefazolin. In addition, it costs less and is more convenient for the patients. The authors could find no evidence of vancomycin-resistant enterococci.

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