Comparative pharmacoeconomic study of vancomycin and teicoplanin in intensive care patients

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 use of two glycopeptides, vancomycin and teicoplanin, for the treatment of hospital infections caused by Gram-positive organisms.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients of both genders, aged older than 17 years, who were hospitalised in the ICU and were given a glycopeptide antibiotic (teicoplanin or vancomycin) for the treatment of an infection. Patients were excluded if the treatment lasted less than 5 days, if the antibiotics were given in a prophylactic manner, or if both antibiotics were given during the same hospital stay.

Setting
The setting was a hospital. The study was carried out at the Hospital Carlos Haya, Malaga, Spain.

Dates to which data relate
The period during which the effectiveness and resource utilisation data were collected was not reported. The price year was not stated.

Source of effectiveness data
The effectiveness evidence were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on a different patient sample from that used in the effectiveness analysis.

Study sample
Power calculations were not performed to determine the sample size. A sample of 100 consecutive patients selected from those hospitalised at the study hospital was considered. There were 50 patients in the teicoplanin group, of which 31 were men. The mean age was 54.1 years (range: 17 - 81). There were 50 patients in the vancomycin group, of which 40 were men. The mean age was 50.3 years (range: 17 - 78).
Study design
This was a retrospective observational study carried out in a single centre, the Hospital Carlos Haya, Malaga, in Spain. The length of follow-up was unclear. No loss to follow-up was reported. The patients' charts were retrospectively reviewed through computerised records. A further manual verification was then carried out as quality control.

Analysis of effectiveness
All patients included in the study were accounted for in the analysis. Several health outcomes were assessed in the study:

the duration of hospitalisation;

the number of days after admission at which treatment was started;

the duration of the treatment;

the initial dosage;

the number of patients who required serum level monitoring;

concomitant drug usage;

creatinine levels before, during and after treatment;

the number of patients with nephrotoxicity; and

the mortality rate.

The study groups were comparable in terms of their demographics and clinical characteristics, with the exception of creatinine levels. There was a non-statistically significantly greater number of female patients in the teicoplanin group.

Effectiveness results
The mean duration of hospitalisation was 20.5 (+/- 11.6) days (range: 8 - 69) in the teicoplanin group and 23.0 (+/- 21.8) days (range: 5 - 98) in the vancomycin group.

Treatment was started 8.9 (+/- 6.5) days (range: 1 to 34) after admission in the teicoplanin group and 7.0 (+/- 6.7) days (range: 1 - 35) after admission in the vancomycin group.

The mean duration of the treatment was 9.7 (+/- 4.2) days (range: 5 - 27) in the teicoplanin group and 10.4 (+/- 5.8) days (range: 5 - 29) in the vancomycin group.

The initial dose was 741.3 (+/- 185.0) mg/day (range: 133.3 - 1,200) in the teicoplanin group and 1,930.0 (+/- 285.9) mg/day (range: 500 - 2,000) in the vancomycin group.

The number of patients who required serum level monitoring was 0 in the teicoplanin group and 5 (10%) in the vancomycin group.

The number of concomitant drugs used was 8.3 (+/- 2.7) (range: 2 - 17) in the teicoplanin group and 7.4 (+/- 3.1) (range: 0 - 12) in the vancomycin group.

The creatinine levels before treatment were 1.20 (+/- 1.15) mg/dL in the teicoplanin group and 0.71 (+/- 0.32) mg/dL in the vancomycin group. During treatment, the levels were 0.93 (+/- 0.70) mg/dL in the teicoplanin group and 0.69 (+/- 0.28) mg/dL in the vancomycin group. After treatment, the levels were 0.59 (+/- 0.98) mg/dL in the teicoplanin group and 0.35 (+/- 0.40 mg/dL) in the vancomycin group.

The number of patients with nephrotoxicity was 4 (8%) in the teicoplanin group and 2 (4%) in the vancomycin group.
The mortality rate was 32% in the teicoplanin group and 16% in the vancomycin group.

Only the difference in creatinine levels before, during and after treatment was statistically different between the study groups, (p<0.05).

**Clinical conclusions**
The effectiveness analysis showed that, generally, teicoplanin and vancomycin were equally effective in the treatment of patients in the ICU.

**Measure of benefits used in the economic analysis**
The health outcomes were not found to be statistically significantly different in either group. On this basis, the authors considered this to be a cost-minimisation analysis.

**Direct costs**
Discounting was irrelevant due to the short time horizon of the study. The unit costs and the quantities of resource were reported separately. The cost/resource boundary adopted in the study was that of the hospital. The costs included were those directly related to the pharmacological treatment. These included the drug acquisition costs, preparation and administration material, nursing staff, monitoring, and the treatment of adverse events. The costs and the quantities were derived using actual data obtained from the hospital database. In particular, some resources, such as the time required and the materials used by the nursing staff, were calculated prospectively on a series of patients from the intensive care department. The period during which the quantities of resources were collected was not reported. The price year was not reported.

**Statistical analysis of costs**
The statistical significance of the cost results was tested by statistical analysis, using a two-tailed Student's t-test for unpaired samples.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Spanish pesetas (ptas).

**Sensitivity analysis**
One-way sensitivity analyses were performed to take into account the impact of some variables on the total costs. Two sensitivity analyses were carried out, both of which were designed to favour teicoplanin. First, the teicoplanin acquisition cost was reduced by 25%. Second, it was assumed that those patients who were administered vancomycin required two serum levels to be measured every 6 treatment days, and the cost of each measurement was 3,000 ptas rather than 750 ptas.

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

**Cost results**
The mean drug acquisition costs were 91,906 ptas (standard deviation, SD=56,018; 95% confidence interval, CI: 76,379 - 107,433) in the teicoplanin group and 44,660 ptas (SD=24,322; 95% CI: 37,917 - 51,401) in the vancomycin group.
The mean material costs were 2,160 ptas (SD=1,331; 95% CI: 1,791 - 2,529) in the teicoplanin group and 7,130 ptas (SD=3,830; 95% CI: 6,068 - 8,191) in the vancomycin group, (p<0.05).

The mean personnel costs were 2,973 ptas (SD=1,831; 95% CI: 2,465 - 3,480) in the teicoplanin group and 4,436 ptas (SD=2,308; 95% CI: 3,797 - 5,076) in the vancomycin group, (p<0.05).

The mean monitoring costs were 0 in the teicoplanin group and 116 ptas (SD=448; 95% CI: 0 - 240) in the vancomycin group, (p>0.05).

The total per patient costs were 97,039 ptas (SD=59,175; 95% CI: 80,637 - 113,441) in the teicoplanin group and 56,342 ptas (SD=30,303; 95% CI: 47,942 - 64,741) in the vancomycin group, (p<0.05).

The total cost per day was 9,893 ptas (SD=2,988; 95% CI: 9,065 - 10,722) in the teicoplanin group and 5,508 ptas (SD=716; 95% CI: 5,310 - 5,706) in the vancomycin group, (p<0.05).

The mean cost-savings associated with vancomycin over teicoplanin were 4,386 ptas per day per patient (95% CI: 3,524 - 5248). Vancomycin remained the cheapest strategy even when the scenarios favouring teicoplanin were set.

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
Vancomycin was as effective and safe as teicoplanin in the treatment of patients in the ICU. However, the overall costs were significantly lower, entirely due to the high acquisition costs of teicoplanin.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was not specifically justified, although both drugs represented widely used glycopeptides for the treatment of infections caused by Gram-positive organisms. You should assess whether they are commonly used in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used a retrospective observational design. The authors pointed out that even though the study groups appear to have been comparable (in the characteristics identified) at baseline, selection bias could not be excluded due to the lack of randomisation. In fact, the creatinine levels did differ statistically significantly at baseline. In addition, the study population was carefully selected and power calculations were not performed. Finally, the low number of adverse events was likely to have been determined by the retrospective design, since mild adverse events were not recorded in the patients' charts. No statistical analyses were undertaken to take into account these issues, which might have limited the internal validity of the study.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis since the two drugs were found to be statistically similar. However, it would have been interesting had the authors used a summary benefit measure, especially in the light of the issues already raised (see 'Validity of estimate of measure of effectiveness'). In particular, the non-statistically significant difference in the outcome measure, due to the lack of both randomisation and power calculations.

**Validity of estimate of costs**
The perspective adopted in the study was that of the hospital, but only treatment-related costs were included in the...
Hospitalisation costs, generally accounting for the greatest share of total costs in Spain, were excluded. The period during which the quantities of resources were collected was not specified. Also, the price year was not reported. The cost estimates appear to have been somewhat specific to the study setting. However, statistical analyses were carried out to assess the significance of the results. The unit costs and the quantities of resources were also reported separately.

Other issues
The authors made several comparisons of their findings with those from other studies. However, the issue of the generalisability of the study results to other settings was not explicitly addressed. There were few sensitivity analyses on the cost side but the authors stated that the results could be extrapolated to other hospitals, due to the robustness of the results to variations in some parameters. However, the conclusions of the analysis should not be extended to study populations different from those examined in the study. The authors pointed out some limitations of the analysis, which have been reported already in this commentary.

Implications of the study
The authors suggest that patients requiring treatment for hospital infections caused by Gram-positive organisms should be administered a vancomycin-based therapy. However, further research within randomised controlled trials is required to confirm these findings.

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