Mississippi mud no more: cost-effectiveness of pharmacokinetic dosage adjustment of vancomycin to prevent nephrotoxicity


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 pharmacokinetic monitoring of vancomycin serum levels and subsequent dose adjustment, to prevent the risk of nephrotoxicity in patients receiving vancomycin as treatment for severe systemic infections, was examined.

Type of intervention
Secondary prevention (monitoring).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients at risk for nephrotoxicity. Patients younger than 18 years of age, admitted while receiving intravenous vancomycin, receiving intravenous vancomycin for prophylaxis, or administered only oral vancomycin, were excluded. Three sub-groups of patients were also considered. These considered patients receiving concomitant nephrotoxins (aminoglycosides, amphotericin, and acyclovir), patients in the intensive care unit (ICU), and patients on the oncology service.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1988 and 1996. No dates for resource use were explicitly reported. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study and a review of completed studies.

Link between effectiveness and cost data
The costing was not conducted on the same sample of patients as that used in the effectiveness study.

Study sample
A single sample of 200 patients was considered in the analysis. The mean age was 55 years and there were 109 men. Three sub-groups were considered. These comprised 57 patients receiving concomitant nephrotoxins, 68 patients in the ICU, and 78 patients on the oncology service. Three oncology patients were also in the ICU and were receiving concomitant nephrotoxins. Power calculations were not carried out.
Study design
This was a retrospective review of patients' charts, which was carried out at a pharmacokinetic consultation service. The patients were randomly selected from all eligible individuals identified over a 3-year period. The patients served as their own controls as the initial vancomycin treatment was prescribed without monitoring. Pharmacokinetic monitoring was applied only after the initial vancomycin trough concentrations had been gathered.

Analysis of effectiveness
The outcome measure used in the analysis was the percentage of vancomycin trough concentrations (below or above 10 mg/L) in the monitored and the non-monitored groups.

Effectiveness results
In the whole sample, the percentage of vancomycin trough concentrations above 10 mg/L was 14.9% without monitoring and 6.5% with monitoring and dosage adjustment. The percentages of vancomycin trough concentrations <= 10 mg/L were 85.1% (without monitoring) and 93.5% (with monitoring and dosage adjustment), respectively.

In the ICU group, the percentage of vancomycin trough concentrations above 10 mg/L was 23.6% without monitoring and 8.7% with monitoring and dosage adjustment. The percentages of vancomycin trough concentrations <= 10 mg/L were 76.3% (without monitoring) and 91.3% (with monitoring and dosage adjustment), respectively.

In the oncology group, the percentage of vancomycin trough concentrations above 10 mg/L was 11% without monitoring and 3% with monitoring and dosage adjustment. The percentages of vancomycin trough concentrations <= 10 mg/L were 89% (without monitoring) and 97% (with monitoring and dosage adjustment), respectively.

Among patients receiving concomitant nephrotoxins, the percentage of vancomycin trough concentrations above 10 mg/L was 18.4% without monitoring and 5.5% with monitoring and dosage adjustment. The percentages of vancomycin trough concentrations <= 10 mg/L were 81.6% (without monitoring) and 94.5% (with monitoring and dosage adjustment), respectively.

Clinical conclusions
The effectiveness analysis showed that more patients in the non-monitoring group than in the monitoring group had vancomycin trough concentrations greater than 10 mg/L.

Modelling
A decision tree model was constructed to assess the clinical and economic impact of monitoring versus no monitoring in patients receiving vancomycin treatment. The structure of the tree was reported. Patients could develop nephrotoxicity depending on the trough concentrations (below or above 10 mg/L).

Outcomes assessed in the review
The outcome assessed was the probability of nephrotoxicity associated with vancomycin trough concentrations.

Study designs and other criteria for inclusion in the review
A review of the literature was undertaken to identify all controlled studies of nephrotoxicity caused by vancomycin alone or in combination with other nephritic agents. Further details of the primary studies were not provided.

Sources searched to identify primary studies
MEDLINE was searched from January 1985 to December 2001 for relevant studies.
Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Seven primary studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
In the whole sample, the probability of nephrotoxicity was 0.095 (range: 0 - 0.15) for trough concentrations <= 10 mg/L and 0.16475 (range: 0.0952 - 0.27) for trough concentrations above 10 mg/L.

In the oncology group, the probability of nephrotoxicity was 0.1425 (range: 0.135 - 0.15) for trough concentrations <= 10 mg/L and 0.3065 (range: 0.28 - 0.333) for trough concentrations above 10 mg/L.

In the ICU group, the probability of nephrotoxicity was 0.95 (range: 0 - 0.15) for trough concentrations <= 10 mg/L and 0.16975 (range: 0.0952 - 0.27) for trough concentrations above 10 mg/L. Note, the point estimate for the former (trough concentration <= 10 mg/L) is not within the specified range.

In the group of patients receiving concomitant nephrotoxins, the probability of nephrotoxicity was 0.04 for trough concentrations <= 10 mg/L and 0.34 (range: 0.26 - 0.42) for trough concentrations above 10 mg/L.

Measure of benefits used in the economic analysis
The summary benefit measure was the final probability of nephrotoxicity prevented with and without monitoring (and dosage adjustment). This was obtained from the decision model.

Direct costs
Discounting was not relevant as the costs were incurred during a short timeframe. The unit costs were not presented separately from the quantities of resources used for all cost items. The health services included in the economic evaluation were monitoring (drug assay kit, calibration, technician time, and other medical supplies), treatment of nephrotoxicity, pharmacist and nursing time. The cost/resource boundary of the health care system was adopted. The costs were mainly derived from hospital charges, which were then reduced by 50% to reflect the true costs. The resource use data were mainly based on authors' assumptions. The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.
Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out to assess the variability in data. Best- and worst-case scenarios were considered for the costs, benefits and cost-effectiveness ratios. The ranges of values used were derived from the literature.

Estimated benefits used in the economic analysis
The final probability of nephrotoxicity prevented was 0.90 (range: 0.842 - 0.994) with monitoring (and dosage adjustment) and 0.894 (range: 0.832 - 0.986) without monitoring when all patients were considered.

In the oncology group, the final probability of nephrotoxicity prevented was 0.853 (range: 0.845 - 0.861) with monitoring (and dosage adjustment) and 0.839 (range: 0.829 - 0.849) without monitoring.

In the ICU group, the final probability of nephrotoxicity prevented was 0.898 (range: 0.840 - 0.992) with monitoring (and dosage adjustment) and 0.887 (range: 0.890 - 0.919) without monitoring. Note, the point estimate for the latter (without monitoring) is not within the specified range.

In the group of patients receiving concomitant nephrotoxins, the final probability of nephrotoxicity prevented was 0.943 (range: 0.939 - 0.948) with monitoring (and dosage adjustment) and 0.904 (range: 0.890 - 0.919) without monitoring.

Cost results
The additional costs of monitoring over no monitoring were $151 (range: 50 - 250) when all patients were considered.

The corresponding values for the sub-groups were $70 (range: -27 - 159) in the oncology group, $92 (range: -83 - 147) in the ICU group, and -$217 (range: -609 - -79) in the group of patients receiving concomitant nephrotoxins.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the alternative strategies.

The additional cost per extra nephrotoxic episode prevented with monitoring over no monitoring was $25,166.67 (range: 15,000 - 27,500) when all patients were considered.

The corresponding values for the sub-groups were $5,000 (range: 1,687.50 - 13,250) in the oncology group, $8,363.64 (range: 4,368.42 - 10,500) in the ICU group, and $5,564.10 (range: -12,468.57 - 2,724.14) in the group of patients receiving concomitant nephrotoxins. Note, the point estimate for the latter group (concomitant nephrotoxins) is not within the specified range.

Authors’ conclusions
In patients receiving concomitant nephrotoxins, monitoring (and dosage adjustment) was a very cost-effective strategy as it dominated no monitoring (which was both less effective and more costly). Monitoring was cost-effective for the sub-group of patients in the intensive care unit (ICU), while the results were less clear for patients in the oncology group.

CRD COMMENTARY - Selection of comparators
The selection of the comparators, that is, monitoring (and dosage adjustment) versus no monitoring, was appropriate as it reflected the two possible approaches for the prevention of vancomycin-related nephrotoxicity. The authors noted that monitoring strategies varied from institution to institution. You should decide whether they are valid comparators...
Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on multiple sources, which were used to populate the decision model. Some data were derived from a retrospective review of patients’ charts with patients serving as their own controls. This was a retrospective within-group comparison study. Baseline values assessed before the implementation of monitoring were assumed to represent values associated with no monitoring. Other data came from published studies after a review of the literature had been undertaken. However, there were few details of the conduct and methods used in the review. The design of the primary studies was not reported. Plausible ranges of values were used in a sensitivity analysis to address the issue of variability in the data.

Validity of estimate of measure of benefit
The benefit measure was specific to the disease considered in the study and would be difficult to compare with the benefits of other health care interventions. The use of a more comparable measure would have been interesting. The impact of the interventions on mortality was not assessed because it was implicitly assumed that there would be no significant difference in mortality between the groups.

Validity of estimate of costs
The authors explicitly stated the perspective adopted in the study. As such, it appears that all the relevant categories of costs have been considered. However, only costs strictly related to monitoring were considered in the analysis. The source of the data was provided and charges were halved to assess the true costs of the services. In general, the unit costs were not presented separately from the quantities of resources used, although a breakdown of the costs was provided. The price year was not reported, which would make reflation exercises in other settings difficult. There were no statistical analyses on the costs, but ranges of values were presented and sensitivity analyses were carried out to present extreme-value scenarios.

Other issues
The authors stated that their findings confirmed those observed in other studies, especially when patients at high risk of developing nephrotoxicity were considered. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analysis, in which best- and worst-case scenarios were considered for both the costs and effectiveness. The authors also acknowledged that approaches to monitoring may vary from institution to institution. The authors noted some limitations of their analysis. However, it was stressed that the data used were the best available. There were a number of inconsistencies between the tables and text in the reporting of point estimates and ranges.

Implications of the study
The authors stated that future studies should consider an analysis of efficacy enhancement through pharmacokinetic dosage adjustment.

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None stated.

Bibliographic details

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Other publications of related interest


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Subject indexing assigned by NLM

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