An economic evaluation of vasoactive agents used in the United Kingdom for acute bleeding oesophageal varices in patients with liver cirrhosis

Wechowski J, Connolly M, Woehl A, Tetlow A, McEwan P, Burroughs A, Currie CJ, Bhatt A

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.

CRD summary
The objective was to assess the costs and outcomes associated with terlipressin, octreotide, and placebo in the treatment of bleeding oesophageal varices (BOV) in patients with liver cirrhosis. The authors concluded that terlipressin was the most cost-effective vasoactive treatment for BOV in these patients. The validity of the source for the resource use data was uncertain and the authors' conclusions should therefore be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the costs and outcomes associated with terlipressin, octreotide, and placebo in the treatment of bleeding oesophageal varices (BOV) in patients with liver cirrhosis.

Interventions
The two interventions were terlipressin at 12mg per day, until bleeding was controlled and at half the dose thereafter, for a maximum of five days, and octreotide with an initial bolus of 50μg followed by 50μg per hour for a maximum of five days. These were compared with placebo.

Location/setting
UK/secondary care.

Methods
Analytical approach:
A discrete event simulation model was developed to estimate the cost and outcomes of each strategy. This model allowed the bleeding and treatment status of each patient to be tracked for 14 days; after this salvage surgery became an option. The time horizon was one year and the authors did not report the study perspective.

Effectiveness data:
The effectiveness data were derived from published studies, which were identified through a search of the MEDLINE and EMBASE databases (1972 to 2006) and meta-analysed in Cochrane reviews of terlipressin and octreotide. The transition probabilities were obtained from double-blind, randomised controlled trials and the mortality, re-bleeding rate, and rate of failure to control bleeding were obtained from the meta-analyses. Observational studies provided the estimates of survival and bleeding rates. The main clinical parameters were the risk of failure to control bleeding and the risk of re-bleeding.

Monetary benefit and utility valuations:
The weights for health-related quality of life were based on expert opinion and estimates from published studies.

Measure of benefit:
The summary benefit measures were life-years (LY) and quality-adjusted life-years (QALY) gained and these were discounted at an annual rate of 3.5%.

Cost data:
Hospitalisation, treatment, drug, and general practitioner costs were included. The hospital, drug, and treatment costs were obtained from the National Health Service (NHS) reference cost publication, while drug costs were obtained from the British National Formulary. The resource use data were obtained from the Proceedings of the 4th Baveno International Consensus workshop recommendations. The price year was 2005 and all costs were in UK pounds sterling (£) and were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
Both univariate and probabilistic sensitivity analyses were conducted to assess the stability of the results. The results of the probabilistic sensitivity analysis were presented in cost-effectiveness acceptability curves.

Results
Over one year of treatment per person, terlipressin resulted in a net gain of 0.107 LYs over both octreotide and placebo and 0.079 QALYs over octreotide and 0.078 QALYs over placebo. The total per person cost was £2,623 with terlipressin, £2,758 with octreotide, and £2,890 with placebo. Terlipressin dominated octreotide and placebo as it was more effective and less costly.

The one-way sensitivity analysis showed that terlipressin was the most cost-effective option regardless of the input values used. The probabilistic sensitivity analysis showed that, at a willingness to pay £20 000 per QALY gained, terlipressin was the most cost-effective option in 98.9% of simulations.

Authors’ conclusions
The authors concluded that terlipressin was the most cost-effective vasoactive treatment for BOV in cirrhotic patients.

CRD commentary
Interventions:
The chosen interventions were appropriate as they represented the current practice in the authors’ setting. Details of the interventions, including their dosage and duration, were reported.

Effectiveness/benefits:
The effectiveness estimates were derived from published studies and the systematic review of the literature should have ensured that the most recent and relevant estimates were included. The use meta-analyses and randomised controlled trials, where possible, should also have ensured the validity of these estimates, but the inclusion criteria were not stated. The authors did not describe how the clinical data were adapted to determine the relevant probabilities for the model. The effectiveness estimates were well reported, with details of the ranges used in the sensitivity analysis. The primary measures of benefit (LYs and QALYs) were appropriate, but little detail was given on the method used to derive the utility weights for the QALYs.

Costs:
The authors did not report the study perspective, so it is not clear if the appropriate cost categories were included. The sources of the resource use and unit costs were reported, but it is not clear that the resource use estimates were appropriate as they were based on the proceedings of a workshop. In some instances, the costs and quantities were reported separately increasing the generalisability of the study to other settings. In other instances, the aggregated costs were reported, which may reduce the generalisability of the results. Adjustments, including the price year and discount rate, were reported.

Analysis and results:
The authors conducted an appropriate incremental analysis comparing terlipressin and octreotide with each other and with placebo and the full results were presented. The results of the sensitivity analyses were discussed and in some instances displayed graphically. The authors acknowledged some minor limitations to their analysis.

Concluding remarks:
The validity of the source for the resource use data was uncertain and the authors' conclusions should be considered with caution.
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