High-dose intravenous proton pump inhibition following endoscopic therapy in the acute management of patients with bleeding peptic ulcers in the USA and Canada: a cost-effectiveness analysis

Barkun A N, Herba K, Adam V, Kennedy W, Fallone C A, Bardou M

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 high-dose intravenous proton-pump inhibition (HDPPI) for patients who had undergone successful primary endoscopic haemostatic therapy for the treatment of high-risk, non-variceal ulcer bleeds. The HDPPI strategy consisted of an 80-mg bolus of pantoprazole within 12 hours of endoscopy, followed by an 8 mg/hour infusion for 3 days, then oral pantoprazole (40 mg/day) for the remainder of the hospital stay. The comparator used was no HDPPI. This comprised a 40-mg intravenous bolus of pantoprazole for the first day, followed by 40 mg/day of oral pantoprazole for the rest of the hospital stay.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients, aged 18 years or older, with bleeding ulcers following successful endoscopic therapy for a high-risk lesion.

Setting
The setting was secondary or tertiary care. The economic study was performed separately in the USA and Canada.

Dates to which data relate
The effectiveness data were derived from studies published in 1998 and 2000. Resource use was estimated with 2000 data for the American setting. The resource use data for the Canadian setting related to March 1999 to January 2002. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies.

Modelling
A decision tree model was used to estimate the costs and effectiveness of HDPPI compared with the no HDPPI option. The model structure was based on published trials and two independent physicians confirmed its clinical validity. The model was applied in the USA and in Canada with specific economic data for each country. The assumptions about probabilities of rebleeding and drug utilisation were common to both countries. The simulations were performed for a 30-day time horizon.
Outcomes assessed in the review
The outcomes assessed in the review were the rates of rebleeding for the two strategies evaluated (HDPPI and no HDPPI).

Study designs and other criteria for inclusion in the review
The authors stated that the effectiveness data were collected from randomised trials on the efficacy of HDPPI (80-mg bolus followed by 8 mg/hour for 3 days) after endoscopic therapy in patients with high-risk bleeding ulcer lesions.

Sources searched to identify primary studies
MEDLINE was searched for the last 30 years up to December 2002. The search terms used were "acid suppression", "ulcer bleeding or haemorrhage" and "proton pump". The authors also analysed published narrative reviews on the topic and handsearched relevant articles.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
The methods used to judge the relevance and validity of the studies reviewed were not reported. Two independent reviewers abstracted the primary study results and resolved any discrepancies after discussion with a third reviewer.

Number of primary studies included
Two randomised studies were finally included in the review. Both of these studied intravenous omeprazole.

Methods of combining primary studies
When possible, robust estimates were obtained by pooling numerators and denominators and the 95% confidence intervals (CIs) were calculated using the standard approximation of the binomial distribution.

Investigation of differences between primary studies
Not stated.

Results of the review
The rebleeding rate was 5.88% (95% CI: 2.9 - 11) for the HDPPI group and 22.9% (95% CI: 16.3 - 30) for the no HDPPI group.

Measure of benefits used in the economic analysis
The summary measure of benefit used was the 30-day rebleeding rate. This measure was obtained from the effectiveness results.

Direct costs
The direct costs included in the economic analysis were those associated with the drugs administered and hospitalisation. No discount rate was used due to the short time horizon of the study. The resource quantities and the costs were reported separately. In the American setting, the unit costs and resource consumption were obtained from a national database that used the diagnosis-related group (DRG) system. In the Canadian setting, the unit costs and the resource use were obtained from the data provided by the Canadian Institute for Health Information, combined with the
LOS derived from the National Registry in Upper Gastrointestinal Bleeding and Endoscopy. The price year was 2001.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
The costs were expressed in Canadian dollars (Can$) in the Canadian analysis and in US dollars ($) in the American scenario.

**Sensitivity analysis**
One- and two-way sensitivity analyses were carried out to assess the robustness of the results obtained. All the probability assumptions, lengths of stay and cost variables were considered in the sensitivity analysis. A threshold analysis was also performed to identify values of assumptions and costs for which the conclusion of the economic analysis may change.

**Estimated benefits used in the economic analysis**
The benefits were derived from the review of the literature review. See the "Results of the Review" section.

**Cost results**
In the American setting, the cost per average patient was $8,576 for HDPPI therapy and $9,112 for non-HDPPI therapy. The corresponding values in the Canadian setting were Can$3,099 (HDPPI group) and Can$3,303 (no HDPPI group), respectively.

**Synthesis of costs and benefits**
In both settings (Canadian and American) HDPPI therapy was dominant, as it was both less costly and more effective than no HDPPI.

In the American setting, the cost-effectiveness ratios were $9,112 per patient in the HDPPI group and $11,819 per patient with the no HDPPI option. The corresponding ratios in the Canadian setting were Can$3,293 (HDPPI group) and Can$4,284 (no HDPPI group), respectively.

In the American setting, the results of the sensitivity analysis showed that HDPPI therapy remained dominant over the non-HDPPI option for all values tested in the analysis. Only with extreme assumptions of costs or lengths of stay did the cost-effectiveness ratios vary by more than 20%.

In the Canadian setting, the results of the sensitivity analysis showed that the rebleeding rates and the length of stay considered for the HDPPI and non-HDPPI options may influence the study conclusions. However, the threshold analyses confirmed, for both settings, the robustness of the study results over all clinically plausible ranges of variables.

**Authors' conclusions**
The study supported the routine use of high-dose proton-pump inhibition (HDPPI) therapy for patients with bleeding ulcers who had undergone endoscopic treatment.
CRD COMMENTARY - Selection of comparators

No HDPPI was chosen as the comparator. This seems to have been an acceptable alternative for the health technology under investigation (i.e. treatment with HDPPI). Pantoprazole was considered in the HDPPI option because it was the only intravenous proton-pump inhibitor that was widely available in both the USA and Canada. You should decide if this is a widely used drug in your own setting.

Validity of estimate of measure of effectiveness

It seems that the estimates of effectiveness have been obtained from a systematic review of published randomised trials. Therefore, the validity of the results should be high. The method and conduct of the review were satisfactorily reported and the authors calculated, when possible, robust estimates by pooling numerators and denominators and 95% CIs. It should be noted that the effectiveness estimate for the HDPPI group was obtained from studies that evaluated omeprazole, whereas the economic study considered pantoprazole. This fact should be considered when interpreting the results obtained. Nevertheless, sensitivity analyses on the effectiveness estimates were conducted, using ranges that appear to have been appropriate.

The reliability of the effectiveness estimation depended largely on the quality of the two randomised trials included in the review (see Other Publications of Related Interest).

Validity of estimate of measure of benefit

The estimation of benefits was obtained directly from the effectiveness analysis. This choice of estimate may have been implicitly justified because the authors wished to analyse the most clinically relevant outcomes of the alternatives. Nevertheless, it would have been interesting had the authors considered other summary measures of health benefits, such as the number of life-years gained.

Validity of estimate of costs

The resource quantities and the costs were reported separately and the price year was stated. These factors enhance the possibility of reflation exercises to other settings. All the categories of costs relevant to the perspective adopted were included in the analyses. Discounting was not carried out, which was appropriate since the period considered at analysis was shorter than 2 years. Sensitivity analyses on the resources quantities and costs were performed, using ranges that appear to have been appropriate.

Other issues

The authors compared some of their findings about the cost and cost-effectiveness with those from other studies. The issue of the generalisability of the results was addressed. The authors commented that there would be problems in generalising the results of any study due to the heterogeneous sources of data.

Implications of the study

The study results suggested that the use of HDPPI for patients who have undergone successful primary endoscopic haemostatic therapy for the treatment of high-risk, non-variceal ulcer bleeds is cost-effective. However, as already highlighted, the effectiveness analyses was based on studies that evaluated omeprazole, while the authors considered pantoprazole in the economic analysis. This issue was implicitly assessed in the sensitivity analyses and it does not appear to have strongly influenced the results obtained.

Source of funding

Supported by the Canadian Association of Gastroenterology and an unrestricted grant from Altana Pharma Canada (formerly Byk Canada Inc.).

Bibliographic details

PubMedID
14987328

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Ulcer Agents /administration & dosage /economics; Canada; Cost-Benefit Analysis; Decision Trees; Endoscopy, Gastrointestinal /economics /methods; Humans; Infusions, Intravenous; Length of Stay; Peptic Ulcer Hemorrhage /drug therapy /economics; Proton Pump Inhibitors; Proton Pumps /administration & dosage; Secondary Prevention; Treatment Outcome; United States

AccessionNumber
22004000395

Date bibliographic record published
30/09/2004

Date abstract record published
30/09/2004