Inappropriate use of intravenous pantoprazole: extent of the problem and successful solutions
Kaplan G G, Bates D, McDonald D, Panaccione R, Romagnuolo J

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 study examined the use of an intravenous proton pump inhibitor (IV PPI), pantoprazole, in patients with upper gastrointestinal bleeding (UGIB) or patients receiving nil by mouth (NPO). In connection to this, the study examined the use of a multidisciplinary intervention to reduce inappropriate use of IV PPI. This intervention had four components:

- a newsletter detailing appropriate indications of IV PPI was sent to physicians;
- a dose template that highlighted the appropriate indication for IV PPI was implemented in the study hospital, including an auto-stop requiring re-ordering after 72 hours;
- auto-substitution of IV PPI for oral PPI in patients without UGIB who were receiving other enteral food or medications (not truly NPO); and
- a gastroenterology consult was recommended for physicians ordering continuous IV pantoprazole infusions.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised inpatients receiving IV pantoprazole. The study population was stratified according to those patients with UGIB and those without.

Setting
The setting was secondary care. The economic study was carried out in Alberta, Canada.

Dates to which data relate
The effectiveness, cost and price data referred to 2001/02 for the study assessing the inappropriate use of IV PPI. The corresponding dates for the effectiveness, cost and price data for the multidisciplinary intervention were not reported.

Source of effectiveness data
The effectiveness data were derived from single studies.
Link between effectiveness and cost data
The cost data were based on the same patient populations as those used in the effectiveness studies. The cost analysis was retrospective for the study assessing the extent of inappropriate IV PPI use, and appears to have been prospective for the multidisciplinary intervention.

Study sample
The following information relates to the study used to identify the extent of inappropriate IV PPI use (first study). The authors did not report power calculations. They selected 2 summer months and 2 winter months, and identified all inpatients treated with IV PPI during that period. The authors did not describe whether the study sample was appropriate for the clinical study question. A total of 240 patient records were identified retrospectively and no exclusions were reported. Of these 240 patients, 145 had UGIB (60.4%) and 95 did not.

The following information relates to the study that assessed the effectiveness of the multidisciplinary intervention (second study). The authors did not report any power calculations. They selected two 60-day periods, one before the multidisciplinary intervention and one at least 3 months after the control period. All patients receiving IV PPI during those periods were identified. A total of 113 patient records were identified prior to the intervention, of which 68 had UGIB and 45 did not. A total of 105 patient records were identified post intervention, of which 67 had UGIB and 38 did not. An additional 30 patients had been prescribed IV pantoprazole in the post-intervention period but had an oral PPI substituted by the pharmacist because they were NPO.

Study design
The first study was a single-centred retrospective cohort study, while the second was a prospective before-and-after study in one hospital. The duration of follow-up in each study was not reported. Blinding of the assessment was not reported. No loss to follow up was reported in the second prospective study.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The primary health outcome included in the study was inappropriate use of IV PPI (indication and dosing); the first study also attempted to identify predictors of inappropriate use with logistic regression. The authors reported that the patient groups in the second study were comparable at baseline.

Effectiveness results
The retrospective study identified the use of IV PPI for inappropriate indications in 72 (50%) of patients with UGIB.

The correct dosing regimen was used in only 25% of patients with UGIB.

In total, IV PPI was used appropriately in terms of dosing and indication in only 21% (95% confidence interval, CI: 14 to 27) of patients with UGIB.

Only 33% of patients without UGIB were truly NPO, and only 51% received the correct dosing frequency.

In total, IV PPI was used appropriately in terms of dosing and indication in only 14% (95% CI: 7 to 22) of patients without UGIB.

A longer time to delay to endoscopy (odds ratio per extra hour 1.06, 95% CI: 1.01 to 1.1; p=0.006) and younger patient age (odds ratio per increased decade 0.72, 95% CI: 0.5 to 0.99; p=0.02) were found to be independently associated with higher inappropriate use of IV PPI in a multivariate analysis.

The multidisciplinary intervention was found to significantly reduce inappropriate prescribing of IV PPI by 26% (95% CI: 10 to 42) among patients with UBIG and by 41% (95% CI: 24 to 58) among patients without UBIG, (p<0.0001 for both).
When the 30 patients whose IV PPI was considered inappropriate and was corrected by pharmacists were included in the analysis, the results were not changed (a reduction of 22%).

**Clinical conclusions**
The authors concluded that IV PPI was frequently prescribed inappropriately and incorrectly, and that multidisciplinary interventions can be effective in improving physician prescribing behaviour.

**Measure of benefits used in the economic analysis**
No summary measure of health benefit was used, so a cost-consequences analysis was performed.

**Direct costs**
Both studies included direct pharmaceutical costs. The unit costs were reported separately. The cost data were derived from the effectiveness studies and were not extrapolated. The unit costs were based on actual Calgary regional formulary costs. This is appropriate for a study with this objective and perspective. Discounting was not relevant. The authors did not report the price year, or whether the unit costs between the two studies were the same. The studies reported the total costs and average costs.

**Statistical analysis of costs**
The two periods before and after the multidisciplinary intervention were compared using chi-squared for proportions and Wilcoxon rank-sum tests for average weekly costs. The study is unlikely to have been powered to detect a difference in the costs.

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

**Currency**
Canadian dollars (CAD).

**Sensitivity analysis**
The authors conducted a sensitivity analysis in which the 30 patients whose IV PPI was considered inappropriate and was corrected by pharmacists were included in the analysis. The results were not sensitive to this assumption.

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

**Cost results**
The first study identified that CAD 33,164 was spent on IV PPI, compared with CAD 14,566 if IV PPI had only been used appropriately. There were potential cost-savings of CAD 18,598.

The median weekly cost before the multidisciplinary intervention was CAD 4,188, compared with CAD4,485 for the post-intervention period. The difference between the two periods was not statistically significant.

The costs of adverse events were not included in the analysis. If the reduction in inappropriate use of IV PPI led to adverse clinical outcomes, this could affect the study conclusions.
Synthesis of costs and benefits
Not relevant.

Authors' conclusions
Although the multidisciplinary intervention may be effective at correcting inappropriate prescribing behaviour, it does not appear to be effective in reducing pharmacy costs.

CRD COMMENTARY - Selection of comparators
The IV PPI examined in the study was the only formulation approved for use in the study setting. You must consider whether pantoprazole is relevant in your own setting. The study authors designed the multidisciplinary intervention. You must also consider whether the components of the multidisciplinary intervention would be applicable in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from both a retrospective and a prospective single study. The authors acknowledged that a cluster randomised trial would have been preferable to the pre-test post-test study design employed. It is likely that the study sample was representative of the study population. The patient groups were shown to be comparable at analysis, and the analysis of effectiveness appears to have been handled credibly. However, no power calculations were conducted. Thus, it was not possible to ascertain whether the results obtained were due to the intervention or to chance.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit, so a cost-consequences analysis was performed.

Validity of estimate of costs
The authors did not report the perspective of the study. It appears that the study has been conducted from a hospital perspective. The authors only included the pharmacy costs of IV PPI, thus the costs from clinical outcomes associated with a decrease in inappropriate use of IV PPI were not represented. In addition, the authors acknowledged that the inclusion of nursing costs and equipment costs could affect their conclusions. The unit costs were reported separately. The resource use and price data were specific to the study setting. A statistical analysis of quantities was conducted using an appropriate non-parametric test. No sensitivity analysis was conducted on the costs and quantities to assess the robustness of the estimates used. The price year was not reported, limiting future reflation exercises. Discounting was not applied, which was appropriate given the short time horizon of the cost analysis.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They stated that the intervention may be applicable in other settings. The study enrolled patients with and without UGIB who received IV pantoprazole and this was reflected in the authors' conclusions. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors did not report any further limitations to their study.

Implications of the study
The authors recommended that institutions with overspending problems consider using a multidisciplinary intervention to tackle the problem.

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