Evaluation of outcomes in converting from intravenous ondansetron to oral granisetron: an observational study

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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
Prescribing guidelines for drug therapy based on oral granisetron, a 5-HT3 antagonist, to prevent acute chemotherapy-induced nausea and vomiting (CINV) in cancer patients.

Type of intervention
Guidelines.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients suffering from cancer and undergoing chemotherapy.

Setting
The setting was community. The economic study was carried out at the University of North Carolina, NC, USA.

Dates to which data relate
Effectiveness and resource data were collected between 1 July 1995 and October 1996. 1995 prices were used.

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

Link between effectiveness and cost data
Costing was undertaken prospectively from the same patient sample as that used in the effectiveness study.

Study sample
Patients were identified through daily reviews of the pharmacy database. All adult and paediatric (older than 5 years) oncology patients were eligible. Patients receiving a haematopoietic stem-cell transplant were excluded because of an ongoing clinical trial of intravenous granisetron in this population. Patients were also excluded if they were excessively sedated or could not understand English. Eligible patients were interviewed each time they were administered a dose of 5-HT3 antagonist prior to chemotherapy (patients receiving multi-day chemotherapy were interviewed as many times as the number of doses they received). Three periods of time were considered:

a four-week period immediately prior to guideline revision (Period 1, July 1995);
a five-week period immediately after the revision (Period 2, August 1995);

and a five-week period one year after guideline revision (Period 3, October 1996).

Data on Periods 1 and 2 were combined and then compared to Period 3. Data were collected for about 85% of eligible patients. A total of 608 patient interviews were conducted: 187 patients provided 433 interviews during Periods 1 and 2, and 70 patients provided 175 interviews in Period 3. Power calculations were retrospectively performed based on the existing sample size: there was less than 80% power to detect a difference in the means of data in Periods 1 and 2; however, power of greater than 80% was present to detect a difference in emesis episode between patients receiving the two drug regimes.

**Study design**

The study was a population-based case-control study and all patients (interviews) included in the study were accounted for in the analysis. The study was carried out at the University of Carolina Hospitals and Clinics. Interviews were conducted by one of five interviewers, all of whom were trained by the senior author of the paper. Patients were followed till the suspension of the drug regimen.

**Analysis of effectiveness**

The primary health outcomes used in the study were derived from the interviews: a standardised series of 9 questions were asked in reference to the day of chemotherapy administration. The following outcomes were assessed through the patients’ rating on a verbal analogue scale (0 none, 10 as severe as possible): nausea severity, effect of the nausea on daily function, quality of life, and satisfaction with antiemetic control. Total control of nausea and vomiting was defined as no emesis episode and a nausea rating of 0, major control as one or two emesis episodes and/or nausea rating of 1-3. All patients experiencing more than two emesis episodes or nausea rated greater than 3, were classified as control failures. For hospitalised patients, the medication record was evaluated for the administration of rescue antiemetics. Guideline compliance was also assessed by comparing the prescribing regimen with institution guidelines. Several statistical tests were conducted in order to compare the groups in the three periods considered. The two populations (Periods 1 and 2, compared with Period 3) were comparable with respect to demographic characteristics and clinical conditions.

**Effectiveness results**

The effectiveness results were as follows:

The frequency of total control in ondansetron patients was 56% and granisetron patients 60% in the first population (Periods 1 and 2), and 50% in ondansetron patients and 54% in granisetron patients in Period 3.

Frequency of major control in ondansetron patients was 10% and granisetron patients 13% in the first population (Periods 1 and 2), and 11% in ondansetron patients and 17% in granisetron patients in Period 3.

For hospitalised patients, the use of rescue antiemetics in ondansetron patients was 32% and in granisetron patients 30% in the first population (Periods 1 and 2), and 12% in ondansetron patients and 19% in granisetron patients in Period 3.

Immediately following guideline modification (Period 2), the rate of guideline compliance was about 61% (percentage of patients who were prescribed oral granisetron, as recommended). In Period 3, the rate of compliance was 78%.

**Clinical conclusions**

The analysis showed that ondansetron and granisetron were both effective in preventing acute CINV in cancer patients. After the introduction of new prescribing guidelines, the compliance rate for the new drug increased over time.

**Measure of benefits used in the economic analysis**

Clinical outcomes were not aggregated and no summary benefit was used in the economic analysis, thus a cost-
consequence analysis was conducted.

**Direct costs**
Discounting was not carried out as costs were incurred over a period of time less than 2 years. Quantity and costs were not reported separately. The estimation of costs was based on actual data collected in 1995. The quantity/cost boundary was not clear, given that only drug acquisition costs were included in the analysis and that these can be born by patients, hospital or third party payer.

**Statistical analysis of costs**
No statistical analysis of costs was carried out.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**
See effectiveness results above.

**Cost results**
The cost results were as follows:

The acquisition price was $4.20 for ondansetron (1 mg) and $25.86 for granisetron (1 mg). Total costs of each period were calculated.

In Period 1 only ondansetron was used, and the total cost of the 199 treatments carried out was $21,230, resulting in an average cost per treatment of $107.

In Period 2, both the drugs were used in the guidelines and the total cost of 233 treatments was $16,683 ($7,031 for patients treated with ondansetron and $9,652 for those treated with granisetron). The average cost per treatment was $72.

In Period 3, both drugs were still used and the total cost of the 174 performed treatments was $11,328 ($4,320 for ondansetron and $7,008 for granisetron), yielding an average cost of $65 per treatment.

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

**Authors' conclusions**
Over time, the revision of institutional antiemetic guidelines for prevention of acute CINV was successful both in ensuring the same effectiveness as before and in resulting in cost savings for patients and institutions.
CRD COMMENTARY - Selection of comparators
The selected comparator was clearly, and appropriately, represented by the prescribing guidelines adopted before the introduction of the new protocol.

Validity of estimate of measure of effectiveness
Even though the observational study was population-based, the internal validity of the analysis could have been limited not only by the lack of randomisation, but also by some biases due to the uneven allocation of participants to the two groups (i.e. more patients were administered ondansetron in Period 2).

Validity of estimate of measure of benefit
Not applicable.

Validity of estimate of costs
The cost estimates are likely to be specific to the institutions considered in the study. Only drug acquisition price was used in the analysis and this could vary according to the payer status (patient, third party payer, or hospitals). Perhaps societal costs should have been included since patients’ functional status may be heavily affected by the success rate of the drug therapy (total control or major control), and this could have an impact on the level of care these patients need (from family or some institutions).

Other issues
The issue of generalisability to other settings was not addressed and the robustness of the results was not tested using sensitivity analyses. However, the authors compared their findings with those from other studies and similar conclusions were drawn, especially on the effectiveness side of the analysis. The analysis presents some limitations, particularly related to the study design, as recognised by the authors.

Implications of the study
The main implication of the study was that the introduction of the new prescribing protocol was successful, given that guideline revision and outcome documentation by the oncology pharmacists resulted in increased compliance with institution guidelines and a 40% cost saving.

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