The efficacy and cost-effectiveness of prophylactic 5-hydroxytryptamine3 receptor antagonists: tropisetron, ondansetron and dolasetron

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 tropisetron 2 mg at induction, ondansetron 4 mg at induction, and dolasetron 12.5 mg at the end of surgery to prevent postoperative nausea and vomiting (PONV) after major open abdominal gynaecological or gynaecological oncological surgery. Vomiting occurring more than 10 minutes after arrival in the recovery room was treated with intramuscular prochlorperazine (12.5 mg), while intravenous droperidol (1 mg) was given if prochlorperazine was ineffective one hour after administration.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women undergoing major open abdominal gynaecological or gynaecological oncological surgery. The exclusion criteria were preoperative nausea, the use of anti-emetics, and contraindications to nonsteroidal anti-inflammatory or epidural anaesthesia. Patients in whom an open procedure was not performed were excluded, as were those who underwent unplanned bowel surgery.

Setting
The setting was secondary care. The economic analysis appears to have been conducted in Australia.

Dates to which data relate
The dates to which the effectiveness, resource use and unit cost data related were not reported. The price year was not given.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was performed prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Sample size calculations indicated that 40 patients per group were required to demonstrate a reduction in the incidence of vomiting of 50% in the first 24 hours by tropisetron or dolasetron, compared with ondansetron (90% power and a
significance level of 0.05). The authors did not report the method used to select the sample. Of the 120 eligible patients, two were excluded from the ondansetron group (one did not undergo surgery, while the other was transferred to an intensive care unit postoperatively). A total of 118 patients were assigned randomly to three study group. The tropisetron group comprised 42 patients, the dolasetron group 40 patients, and the ondansetron group 36 patients. The authors did not report any evidence that the study sample was representative of the study population.

**Study design**

The study was a double-blind, randomised clinical trial that appears to have been conducted in a single centre. The patients were randomly allocated to the study groups by means of a computer-derived sequence in blinded envelopes. The study drug administered was known only to the attending anaesthetist, who took no part in the collection of subsequent data. The drug was administrated diluted with normal saline to a 4-mL volume in all patients. The patients were followed up for 24 hours, with assessments performed at arrival in the recovery room to 30 minutes later, and from then until 2, 6, 12, 18 and 24 hours. No loss to follow-up was reported.

**Analysis of effectiveness**

Although not explicitly stated, it appears that the basis for the analysis of the clinical study was intention to treat. The health outcomes used in the analysis were:

- the incidence and severity of vomiting and nausea during the first 24 hours, and up to 2 hours, from 2 to 6 hours, from 6 to 12 hours, from 12 to 18 hours, and from 18 to 24 hours;
- the number of anti-emetic doses administered; and
- the patients' assessment of control of PONV.

Visual analogue scales (ranging from 0 to 100) were used to assess the severity of nausea (100 being the worst possible outcome) and patient satisfaction (100 being the best possible outcome). The study groups were well balanced in terms of the patient demographics and baseline characteristics (e.g. age, weight, history of PONV, history of motion sickness, prior surgery).

**Effectiveness results**

The results among the tropisetron (T), ondansetron (O) and droperidol (D) groups, respectively, were as follows.

- The incidences of vomiting during the first 24 hours were 57% (T), 75% (O) and 72.5% (D), (p=0.18).

- The incidences of vomiting in the recovery room to 30 minutes later were 28.6% (T), 36.1% (O) and 22.5% (D), (p=0.42).

- The incidences of vomiting in the recovery room up to 2 hours were 22% (T), 25% (O) and 17.5% (D), (p=0.72).

- The incidences of vomiting in the recovery room from 2 to 6 hours were 11.9% (T), 11.1% (O) and 17.5% (D), (p=0.67).

- The incidences of vomiting in the recovery room from 6 to 12 hours were 14.3% (T), 13.9% (O) and 15.4% (D), (p=0.98).

- The incidences of vomiting in the recovery room from 12 to 18 hours were 14.3% (T), 22.2% (O) and 27.5% (D), (p=0.34).

- The incidences of vomiting in the recovery room from 18 to 24 hours were 28.6% (T), 47.2% (O) and 35.0% (D), (p=0.23).

- The percentages of patients with complete response were 23.8% (T), 16.7% (O) and 20.0% (D), (p=0.74).
The median numbers of anti-emetic doses administered were 1 (interquartile range, IQR: 0 - 2) (T), 1 (IQR: 0 - 2) (O) and 1 (IQR: 0 - 2.5) (D), (p=0.82).

The percentages of patients for whom the nausea score was equal to zero (i.e. best possible outcome) were 29.3% (T), 33.3% (O) and 25.0% (D), (p=0.73).

The median overall nausea scores were 20 (IQR: 0 - 31) (T), 20 (IQR: 0 - 45) (O) and 14.5 (IQR: 2 - 47.5) (D), (p=0.99).

The median worst nausea scores up to 2 hours were 0 (IQR: 0 - 29) (T), 0 (IQR: 0 - 30) (O) and 0 (IQR: 0 - 36) (D), (p=0.80).

The median worst nausea scores from 2 to 6 hours were 0 (IQR: 0 - 9) (T), 0 (IQR: 0 - 3) (O) and 0 (IQR: 0 - 20) (D), (p=0.63).

The median worst nausea scores from 6 to 12 hours were 0 (IQR: 0 - 0) (T), 0 (IQR: 0 - 0) (O) and 0 (IQR: 0 - 0) (D), (p=0.75).

The median worst nausea scores from 12 to 18 hours were 0 (IQR: 0 - 3) (T), 0 (IQR: 0 - 50) (O) and 8.5 (IQR: 0 - 65) (D), (p=0.02).

The median worst nausea scores from 18 to 24 hours were 10 (IQR: 0 - 61.5) (T), 24.5 (IQR: 0 - 61.5) (O) and 18 (IQR: 0 - 64) (D), (p=0.46).

The median satisfaction with control of PONV were 100 (IQR: 90 - 100) (T), 97.5 (IQR: 80 - 100) (O) and 99.5 (IQR: 78 - 100) (D), (p=0.46).

Clinical conclusions
No significant differences were observed among the three groups in terms of effectiveness during the first 24 hours after major gynaecological surgery.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis since the effectiveness analysis showed that the three groups were comparable in terms of the clinical outcomes. The authors reported that a cost-minimisation analysis was carried out.

Direct costs
The cost/resource boundary of the study was not stated, although it appears to have been that of the hospital. The direct costs considered in the economic analysis included the costs for emesis clean up, rescue anti-emetic dosing and the acquisition costs of an ampoule of the drug under investigation. The unit costs and the quantities of resources used for each group were provided separately. The drug costs were based on acquisition costs rather than patient charges. The cost data appear to have been derived from the study institution's data, although the authors did not clearly report the sources used to collect the resource use and unit cost data. The price year was not reported. Discounting was not relevant as the costs were incurred during a short timeframe. The estimated costs were the average costs per patient.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included.
Currency
Australian dollars (Aus$).

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The estimated costs per patient were $17.15 in the tropisetron group, $23.40 in the ondansetron group and $21.40 in the dolasetron group.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-minimisation analysis was carried out.

Authors' conclusions
The risk of postoperative nausea and vomiting (PONV) remained high in this setting despite prophylaxis with 5-hydroxytryptamine3 (5-HT3) receptor antagonists. Similar efficacy and no clinically relevant side effects were shown in the study. The choice between the agents studied should be based on the lowest available acquisition cost.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators by stating that tropisetron, ondansetron and dolasetron were currently available in Australia for the treatment of PONV. You should consider whether these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness results are likely to be internally valid because of the randomised nature of the study design and the power analysis performed. The method used to randomly allocate the patients to the study groups was reported and appears to have been appropriate. Moreover, it appears that appropriate masking of the interventions to the patients and investigators has been performed. The study groups were comparable in terms of their demographics and baseline characteristics. The study sample was not shown to be representative of the study population. Appropriate statistical analyses were performed to ensure the accuracy of the comparison.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis because the results obtained for the clinical outcomes were not statistically significantly different among the three procedures. Therefore, the authors carried out a cost-minimisation analysis. The reader is thus referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
Although the perspective adopted was not explicitly reported, the cost categories included would appear to relate to the hospital. The unit costs and the resource quantities were reported separately, and the methods used to evaluate the costs and quantities of resources were described. However, the sources used to obtain quantity and cost data were not reported, and the price year was not stated. Statistical analyses of the costs were not carried out. These facts may limit the validity and the generalisability of the study findings.
Other issues
The authors pointed out that, overall, their findings confirmed those from other studies. However, the generalisability of the results to other setting was not discussed. The study enrolled women undergoing major gynaecological surgery and this was reflected in the authors’ conclusions. The authors do not appear to have reported their results selectively. They did not report any limitations of their study.

Implications of the study
The authors recommended choosing the least expensive 5-HT3 antagonist drug for PONV prophylaxis.

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None stated.

Bibliographic details

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Other publications of related interest


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