The dose-response relation and cost-effectiveness of granisetron for the prophylaxis of pediatric postoperative emesis

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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
Granisetron (10 or 40 microg./Kg) for the prophylaxis of pediatric postoperative emesis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of male and female pediatric outpatients who received a placebo or 10 or 40 microg. granisetron intravenously during a standardized anesthetic. No further details were given.

Setting
Hospital postanesthesia care unit (PACU). The economic study was carried out in Texas, USA.

Dates to which data relate
The main effectiveness data were taken from a single study conducted in 1996. Resource and cost data were mainly derived from 1992-94. The price year was not stated.

Source of effectiveness data
The estimates for the incidence and frequency of postoperative emesis and times to discharge readiness were derived from a single study.

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

Study sample
A cohort of 97 children (mean age 5.2 (+/- 3.1) years, range: 2-16 years) scheduled to receive general endotracheal anesthesia for outpatient surgical procedures associated with an increased risk for PONV.

The patients were randomly allocated to three groups:
placebo (n=31, 18 male, mean age 5.6 (+/- 3.4));
granisetron 10 microg./Kg (n=33, 19 male, mean age 5.5 (+/-3.2));

and granisetron 40 microg./Kg (n=33, 13 male, mean age 4.5 (+/-2.8)).

The sample size of the placebo group was determined by power analysis based on the assumption that the incidence of emesis for the placebo and granisetron groups would be similar to a previous placebo-controlled study of ondansetron in the same patient population.

### Study design
Randomized, double-blind controlled study. The duration of the follow-up (after surgery) was 24 hours. The loss to follow-up were not given.

### Analysis of effectiveness
The analysis of the clinical study was based on treatment completers only. The primary health outcomes were the incidence and frequency of postoperative emesis and times to discharge readiness.

### Effectiveness results
The incidence of postoperative emesis was 35% in the placebo, group, 27% in the 10 microg./Kg granisetron group and 3% in the 40 microg./Kg granisetron group (P<0.05). The emesis during the first 24 hours postoperative was 42%, 33% and 9% in the placebo, 10 microg./Kg granisetron and 40 microg./Kg granisetron, respectively. The time to discharge readiness was 152 (+/- 85) minutes, 129 (+/- 56) minutes and 108 (+/- 54) minutes in the placebo, 10 microg./Kg granisetron and 40 microg./Kg granisetron, respectively.

### Clinical conclusions
Granisetron 40 microg./Kg intravenously was estimated to reduce the incidence, frequency of postoperative emesis and discharge readiness when compared with granisetron 10 microg./Kg and placebo, both in the ambulatory surgery centre and during the first 24 hours.

### Modelling
A decision tree was used to divide each study group into nine mutually exclusive subgroups, depending on the incidence of PONV, need for rescue therapy and the side effects of antiemetics.

### Measure of benefits used in the economic analysis
No summary benefit measure was used in the analysis and as such the benefits were considered to be the same as the outcome measures.

### Direct costs
The antiemetic drug, emesis clean-up, materials, nursing labor, housekeeping labour, and side effects of antiemetic drugs costs were included in the analysis. The quantities were reported separately from the prices. The quantity/cost boundary adopted was the hospital. Discounting was not applied. The price year was not stated.

### Statistical analysis of costs
The Mantel-Haenszel test, analysis of variance, Scheffe's test, Kruskall-Wallis test, Fisher's exact and chi-square tests with a Yates' continuity correction were used. P values and mean +/-SD were reported.

### Currency
Sensitivity analysis
A sensitivity analysis was performed on the probabilities used in partitioning the data and the effect of excluding nursing labour costs on the overall conclusions of the relative cost-efficacy of antiemetic drugs.

Estimated benefits used in the economic analysis
The incidence of postoperative emesis was 35% in the placebo group, 27% in the 10 microg./Kg granisetron group and 3% in the 40 microg./Kg granisetron group (P<0.05). The emesis during the first 24 hours postoperative was 42%, 33% and 9% in the placebo, 10 microg./Kg granisetron and 40 microg./Kg granisetron, respectively. The time to discharge readiness was 152 (+/- 85) minutes, 129 (+/- 56) minutes and 108 (+/- 54) minutes in the placebo, 10 microg./Kg granisetron and 40 microg./Kg granisetron, respectively.

Cost results
If 40 microg./Kg intravenous granisetron were administered to all high-risk patients, the ambulatory care centre would have an additional cost of $101 for every patient (95% CI: $91 - $113). If nursing labour costs were excluded from the analysis, the routine use of 40 microg./Kg intravenous granisetron would cost the ambulatory care centre an additional $99 (95% CI: $89 - $112) for every patient free from emesis.

Synthesis of costs and benefits
The cost-effectiveness ratio would be $332 (95% CI: $300 - $372) if nursing costs were included and $329 (95% CI: $298 - $369) if these nursing costs were excluded. An incremental analysis was carried out. The cost-effectiveness results were sensitive to the incidence and severity of postoperative emesis.

Authors’ conclusions
The 40 microg./Kg intravenous granisetron provided effective prophylaxis in children against PONV compared with a placebo, but at a high cost. The effective dose of granisetron for PONV prophylaxis is higher than the Food and Drug Administration recommended dose for chemotherapy-induced emesis.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear. The granisetron provided effective prophylaxis against chemotherapy-induced and postoperative PONV (which delay discharge from hospital) but is expensive. You, as a user of this database, should consider whether these are widely used health technologies in your setting.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis and as such, the benefits are considered to be the same as the outcome measures. However, the data have not been used selectively although a full economic evaluation using one benefit measure would be required to assure greater validity.

Validity of estimate of costs
Resource quantities were reported separately from the prices. Adequate details of methods of quantity/cost estimation were given. Important cost items do not appear to have been omitted.

Other issues
The authors’ conclusions are likely to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. However, appropriate comparisons were made with other studies in terms
of the presence or absence of sedative side effects, costs of drugs, cost-effectiveness of other antiemetics (such as ondansetron) and patients' or parents' preferences. Results do not appear to have been presented selectively.

**Implications of the study**
As noted by the authors, a prospective comparative study in which patients are randomized to the ondansetron and granisetron treatment groups is required. Furthermore, research into decisions regarding drugs usage which include input from patients' or parents' preferences is necessary to improve its cost-effectiveness and wider use.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
8916825

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Antiemetics /economics /therapeutic use; Child; Child, Preschool; Cost-Benefit Analysis; Dose-Response Relationship, Drug; Female; Granisetron /economics /therapeutic use; Humans; Male; Nausea /prevention & control; Parents; Postoperative Complications /prevention & control; Vomiting /prevention & control

**AccessionNumber**
21996001069

**Date bibliographic record published**
31/01/1999

**Date abstract record published**
31/01/1999