A comparison of the costs and efficacy of ondansetron and dolasetron in the prophylaxis of postoperative vomiting in pediatric patients undergoing ambulatory surgery


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 dolasetron versus ondansetron in the prevention of postoperative vomiting (POV) in paediatric ambulatory surgery patients. Four doses of dolasetron (45, 175, 350, or 700 microg/kg intravenous, IV) and ondansetron 100 microg/kg IV were studied. These drugs were administered within 15 to 20 minutes after surgery and were diluted to a fixed volume of 30 mL.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised paediatric patients undergoing ambulatory surgery. Patients were eligible to participate in the study if they were aged between 2 and 12 years, and were scheduled to receive general, endotracheal anaesthesia for superficial ambulatory surgery. They also had to have been classified as ASA physical status I or II. Patients were excluded if they were ASA physical status III or more, had a history of gastroesophageal reflux or vomiting from organic causes, or were obese (>95th percentile of weight for age). Other exclusion criteria were emergency surgery, antiemetic therapy within 24 hours before surgery, or the use of neuraxial anaesthesia or drugs known to have antiemetic effects (e.g. steroids, propofol). Children undergoing procedures that involved the administration of steroids (e.g. tonsillectomy and adenoidectomy) were also excluded.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The dates to which the effectiveness evidence, resource use data and prices related were not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single double-blinded, randomised controlled trial.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study. It appears to have been conducted prospectively alongside the effectiveness study.
Study sample
A power calculation was undertaken based on a test for trend across proportions, with a significance level of 0.05 and a power of 80%. The results suggested that a sample size of 204 patients was required, with 136 of these receiving dolasetron (four sub-groups of 34 patients) and 68 ondansetron. The children were selected to participate in the study if they satisfied the inclusion criteria and their parents or guardians consented.

In total, 225 children were identified as potential participants in the study. Of these, 21 did not take part in the study because they declined to participate (9), required additional surgery (1), did not satisfy the inclusion criteria (8), or were lost to follow-up (3). Therefore, 204 patients participated in the study, of which 135 were randomised to receive dolasetron and 69 to receive ondansetron. For dolasetron, there were 35 patients in the 45 microg/kg dosage group, 32 in the 175 microg/kg group, 31 in the 350 microg/kg group, and 37 in the 700 microg/kg group. The majority of the patients in each group were male. More specifically, there were 24 (45 microg/kg), 24 (175 microg/kg), 20 (350 microg/kg) and 28 (700 microg/kg) boys in the dolasetron groups, and 54 boys in the ondansetron group.

For dolasetron, the age of the patients according to dosage group was 6.1 (± 2.8) years in the 45 microg/kg group, 5.3 (± 2.5) years in the 175 microg/kg group, 6.5 (± 2.6) years in the 350 microg/kg group, and 6.1 (± 2.5) years in the 700 microg/kg group. In the ondansetron group, the age was 6.0 (± 2.7) years.

The weight of the patients varied from 20.8 (± 6.4) kg for patients in the 350 microg/kg dolasetron group to 23.8 (± 8.7) kg in the 700 microg/kg dolasetron group.

The most common procedure was herniorrhaphy. Less than 25% of the patients in each group had a history of motion sickness, with 6% or less recording prior incidences of POV. Further, anaesthesia time, surgical time, and time from end of surgery to arrival at postanaesthesia care unit and subsequent discharge were not statistically significantly different for the treatment groups.

There were no statistically significant differences in the demographic variables between the treatment groups.

Study design
The study was a randomised controlled trial that took place in a hospital. The participants were randomly allocated to one of the five treatment groups on the basis of a computer-generated random number table. The duration of follow-up was 5 days, with postoperative telephone interviews conducted at 24 hours and questionnaires at 5 days. Three patients were lost to follow-up. Due to the double-blinded design of the trial, health care professionals who were unconnected with the patient’s anaesthetic care diluted the study drugs to a fixed volume of 30 mL.

Analysis of effectiveness
It was not explicitly stated whether the basis of the clinical study was intention to treat or treatment completers only. Effectiveness was measured as freedom from postoperative emetic symptoms (complete response). Other measures of effectiveness included:

the number of patients who required rescue antiemetics,

the number of patients with at least two episodes of POV,

parental satisfaction scores, and

the numbers completely satisfied with POV control.

Effectiveness results
For dolasetron (dosage in parentheses), the early complete response rates within 6 hours after surgery were 54% (45), 72% (175), 87% (350) and 78% (700). For ondansetron, the early complete response rate was 80%.

For dolasetron (dosage in parentheses), the 24-hour complete response rates were 47% (45), 68% (175), 73% (350) and
73% (700), (95% confidence interval, CI: 56 - 87). For ondansetron, the 24-hour complete response rate was 78% (95% CI: 67 - 86).

Both complete response rates were statistically significantly greater for two doses of dolasetron (350 and 700 microg/kg) and ondansetron than for the lowest dose of dolasetron (45 microg/kg), (p<0.05).

The proportion of patients who experienced at least two POV episodes was statistically significantly lower in the dolasetron 350 and 700 microg/kg groups (3% and 0%, respectively) and in the ondansetron group (9%) than in the dolasetron 45 microg/kg group (25%), (p<0.05). In addition, this proportion was statistically significantly greater in the dolasetron 175 microg/kg group (22%) than in the two higher-dose dolasetron groups (350 and 700 microg/kg), (p<0.05).

Compared with the dolasetron 45 microg/kg group (8.1 +/- 3.3), parental satisfaction scores were statistically significantly greater in the dolasetron 175, 350 and 700 microg/kg groups (9.0 +/- 1.8, 9.2 +/- 2.0, 9.4 +/- 1.9) and the ondansetron group (9.6 +/- 0.9), (p<0.05).

Clinical conclusions
The authors concluded that 350 microg/kg was the smallest dose of dolasetron with an efficacy comparable to ondansetron 100 microg/kg for the prevention of POV.

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

Direct costs
Discounting was not necessary since the costs were incurred during less than one year. The assumptions made about the unit cost data were reported. Data on the quantities were not reported. The estimation of the costs and quantities was derived using modelling. The details of the model used were reported elsewhere (see Other Publications of Related Interest). The resources used in managing POV episodes were recorded. The dates during which resource use was measured were not reported, and neither was the price year. The direct costs for the management of emesis were for "emesis clean up" (used in the hospital before discharge), rescue antiemetics, the management of side effects of prophylactic and rescue antiemetic drugs, plus the acquisition costs of the drugs and materials used to administer them, and labour costs.

Statistical analysis of costs
Statistical tests were not carried out.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
The assumptions made in the cost model were varied in a sensitivity analysis, although the results of this analysis were not explicitly reported.

Estimated benefits used in the economic analysis
Cost results
The total costs for POV management for the dolasetron 45 microg/kg group were $1.50 (+/- 2.82). These costs included prophylaxis ($0.69 +/- 0.24) and additional hospital resources ($0.80 +/- 2.69).

The total costs for POV management for the dolasetron 175 microg/kg group were $3.50 (+/- 2.76). These comprised the costs of prophylaxis ($3.00 +/- 2.10) and additional hospital resources ($0.50 +/- 1.94). There were statistically significant differences between the total costs and costs of prophylaxis for this group and those reported for the dolasetron 45, 350 and 700 microg/kg groups, (p<0.05).

The total costs for POV management for the dolasetron 350 microg/kg group were $6.58 (+/- 3.95). These comprised the costs of prophylaxis ($5.09 +/- 1.07) and additional hospital resources ($1.49 +/- 3.63). There were statistically significant differences between the total costs and costs of prophylaxis for this group and those reported for the dolasetron 45 microg/kg group, (p<0.05).

The total costs for POV management for the dolasetron 700 microg/kg group were $12.95 (+/- 5.87). These comprised the costs of prophylaxis ($11.65 +/- 4.23) and additional hospital resources ($1.30 +/- 3.31). There were statistically significant differences between the total costs and costs of prophylaxis for this group and those reported for the dolasetron 45 and 350 microg/kg groups, (p<0.05).

The total costs for POV management for the ondansetron group were $9.94 (+/- 4.87). These comprised the costs of prophylaxis ($9.05 +/- 2.01) and additional hospital resources ($0.90 +/- 3.84). There were statistically significant differences between the total costs and costs of prophylaxis for this group and those reported for the dolasetron 45 and 350 microg/kg groups, (p<0.05).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Dolasetron 350 microg/kg and ondansetron 100 microg/kg were equally effective in the prevention of postoperative vomiting (POV) in paediatric patients following ambulatory surgery. No increase in efficacy was gained by increasing the dose of dolasetron to 700 microg/kg. Further, there was decreased control of POV and parental satisfaction when patients received dolasetron 45 microg/kg. The institutional costs associated with POV prophylaxis were lower for patients treated with dolasetron 350 microg/kg, compared with those who received ondansetron 100 microg/kg.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. Ondansetron was the prototype of the class of antiserotonin drugs used in POV prophylaxis, and it had received approval from the FDA. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The basis of the analysis was a double-blinded randomised controlled trial, which was appropriate for the study question. The study sample appears to have been representative of the study population. The patient groups were shown to be comparable at analysis. To account for the confounding effects of steroids on POV, patients who underwent a tonsillectomy or an adenoidectomy were excluded.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was, in effect, a cost-consequences study.
Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. The analysis did not include
the costs borne by patients and their families for either groups. The assumptions about the unit cost data were reported.
The resource use data were not reported separately. No statistical analysis of the quantities was performed. It appears
that a sensitivity analysis of the prices has been conducted, although the results were not explicitly reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability
to other settings was not addressed. The authors did not present their results selectively. The presentation of results did
not specify what parameters were being measured. The study enrolled young patients and this was reflected in the
authors’ conclusions. As the results of the study found that the two largest doses of dolasetron and the dose of
ondansetron were more effective than the smallest dose of dolasetron, the authors argued that this supported the internal
validity of their conclusions. The authors acknowledged that a limitation of their study was the absence of a no-
treatment comparator. However, the authors argued that their results were similar to those of other studies, which was
indicative of their validity. A further limitation, recognised by the authors, was the inability to assess nausea in the study
because of the young age of the patients.

Implications of the study
The authors did not make any recommendations for changes in policy or practice.

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Other publications of related interest
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