A comparison of the costs and efficacy of ondansetron versus dolasetron for antiemetic prophylaxis


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
Use of dolasetron (the newer 5-HT3 antagonist) IV for preventing postoperative nausea and vomiting (PONV) after otolaryngologic (ENT) surgery.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
ASA physical status I and II outpatients undergoing ENT procedures. Patients were excluded if they had received any antiemetic medication within 24 hours before their operation, were pregnant, had clinically significant cardiovascular, neurologic, renal, hepatic, gastrointestinal, or endocrinological diseases, had a history of drug abuse, or were more than 100% above their ideal body weight.

Setting
Hospital. The economic analysis was carried out in the USA.

Dates to which data relate
No dates were reported.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

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

Study sample
Power calculations were used to determine the sample size (power analysis indicated that 49 patients were required in each group for an 80% chance of detecting a 33% reduction in mean total costs for managing PONV from $18 to $12 at the p=0.05 level of significance; this group size would have an 80% power of detecting a 30% difference in the success rates for preventing PONV, assuming the success rates for 4 and 8 mg of ondansetron IV to be similar to those reported in the meta-analysis). A total of 200 patients were randomly assigned to receive one of four IV antiemetic study medications:
(1) 12.5 mg of dolasetron (n = 50, mean (SD) age 45 (14) years);
(2) 25 mg of dolasetron (n = 51, mean (SD) age 44 (14) years);
(3) 4 mg of ondansetron (n = 49, mean (SD) age 45 (14) years); and
(4) 8 mg of ondansetron (n = 50, mean (SD) age 46 (15) years).

**Study design**
This was a randomised, double blind, controlled trial, carried out in a single centre. The duration of the follow-up was 24 hours after discharge. The study appears to have had no loss to follow-up. The study drug was prepared by the operating room (OR) pharmacist according to a computer-generated random number schedule, diluted to a total volume of 5 mL and administered within a 30 minute interval before the end of surgery. A blinded observer recorded the clinical and patient outcomes.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness appears to have been intention-to-treat. The clinical outcomes were perioperative outcomes and included; times to eye opening, tracheal extubation, response to verbal commands, orientation, the time to achieving discharge readiness criteria or the time to actual discharge, time to resuming a normal diet, use of analgesic drugs, unanticipated admissions to the hospital, separate incidence of nausea, vomiting, or failure of a complete response with prophylactic antiemetics during the first 24 postoperative hours, the incidence of emetic symptoms in the Phase 1 (post anaesthesia care unit (PACU)) or Phase 2 (step-down) recovery areas or after discharge from the centre, the incidence of repeated emetic symptoms (2 or more episodes), the need for rescue antiemetics, the incidence of nonemetic side effects (e.g., headache), and patient satisfaction. A trained interviewer, who was blinded to the group assignment, contacted all patients by telephone 24 hours after discharge to inquire about post discharge side effects and the need for any therapeutic interventions at home. Patients were also asked to determine their nausea levels during the previous 24 hours by using a verbal rating scale ranging from 0 (none) to 10 (worst possible). In addition, the interviewer read a structured question designed to assess patient satisfaction on a three-point Likert scale. The study groups were comparable in terms of the demographics and baseline characteristics.

**Effectiveness results**
The effectiveness results were as follows:

There were no significant differences in the times to eye opening, tracheal extubation, response to verbal commands, orientation, the time to achieving discharge readiness criteria or the time to actual discharge among the four study groups.

After discharge, there were no significant differences in the time to resuming a normal diet or in the use of analgesic drugs.

Unanticipated admissions to the hospital occurred in three patients; however no patient was admitted for the management of persistent PONV. One patient in the 8 mg of ondansetron group was admitted for management of persistent pain, and two patients in the 25 mg of dolasetron group were admitted, one for airway considerations and the other for the management of postoperative delirium.

There were no significant differences with respect to the separate incidence of nausea, vomiting, or failure of a complete response with prophylactic antiemetics during the first 24 postoperative hours.

The incidence of emetic symptoms did not differ among the four groups in the Phase 1 (PACU) or Phase 2 (step-down) recovery areas or after discharge from the centre.

The incidence of repeated emetic symptoms (2 or more episodes) and the need for rescue antiemetics, similarly did not differ among the groups.
There were also no significant differences with respect to the incidence of nonemetic side effects (e.g., headache).

There were no significant differences in visual analogue scale (VAS) scores on discharge, or in the number of patients who were completely satisfied with their anaesthetic management.

Clinical conclusions
This study demonstrated that 12.5mg of dolasetron IV is comparable to 4 and 8 mg of ondansetron IV when given at the end of surgery for preventing PONV after ENT surgery. The study failed to demonstrate increased efficacy with 8 mg of ondansetron compared with a 4-mg dose.

Measure of benefits used in the economic analysis
The measure of benefit used was the percentage of patients with complete response. A complete response to antiemetic prophylaxis was defined as a patient completely free from emesis and the need for antiemetic drugs to control nausea.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs and cost items were reported separately. Cost analysis covered the costs of prophylaxis, emesis cleanup, rescue antiemetics, and nursing labour. The perspective adopted in the cost analysis was that of a freestanding surgicentre in a managed care environment. Costs of drugs were based on acquisition costs rather than patient charges. Cost data were based on the study institution's data. The price year was not reported.

Statistical analysis of costs
A one-way analysis of variance was used to compare the continuous variables (presumably including costs) among the treatment groups.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A one-way simple sensitivity analysis was performed to determine the effect of excluding nursing labour costs on the overall conclusions of the relative costs associated with each antiemetic regimen.

Estimated benefits used in the economic analysis
The proportion of patients with complete response was 74% in the 12.5 mg of dolasetron group, 73% in the 25 mg of dolasetron group, 76% in the 4 mg of ondansetron group, and 72% in the 8 mg of ondansetron group.

Cost results
The cost results were as follows:

The mean (SD) total cost was $17.75 (14.36) in the 12.5 mg of dolasetron group,

$27.41 (9.67) in the 25 mg of dolasetron group,
$26.96 (6.5) in the 4 mg of ondansetron group, and $54.13 (11.87) in the 8 mg of ondansetron group.

The mean total costs for managing PONV were significantly greater with prophylactic 8 mg of ondansetron IV compared with the other three groups; however, there were no cost differences between the 25 mg of dolasetron and 4 mg of ondansetron groups.

**Synthesis of costs and benefits**

The mean cost to achieve a complete response in one patient was calculated as the measure of cost-effectiveness ratio, leading to the following values:

$23.89 (95% CI: 17.18 - 28.79) in the 12.5 mg of dolasetron group,

$37.81 (95% CI: 30.29 - 45.32) in the 25 mg of dolasetron group,

$33.91 (95% CI: 28.92 - 39.35) in the 4 mg of ondansetron group,

and $75.18 (CI: 61.13 - 89.24) in the 8 mg of ondansetron group.

The 95% CI in the 8 mg of ondansetron group did not overlap the 95% CI of the other three groups. Similarly the 95% CI of the 12.5 mg of dolasetron group did not overlap the 95% CI of the other three groups.

The inclusion in, or exclusion from, the total costs of nursing labour costs, did not alter these findings.

**Authors’ conclusions**

The authors concluded that 12.5 mg of dolasetron IV is more cost effective than 4 mg of ondansetron IV for preventing PONV after otolaryngologic surgery and is associated with similar patient satisfaction.

**CRD COMMENTARY - Selection of comparators**

The strategy of using ondansetron, as an older, safe, and effective prototype serotonin 5-HT3 antagonist, appears to have been regarded as the comparator. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness results are likely to be internally valid due to the randomised nature of the study design and the power analysis performed. The study groups were comparable in terms of their demographics and baseline characteristics. It was reported that the study did not include a placebo control because it was felt that it would not be ethical to deny high-risk patients included in the study the benefits of prophylactic antiemetic therapy. The study sample appears to have been representative of the study population (high-risk patients undergoing ENT surgery).

**Validity of estimate of measure of benefit**

Estimation of benefits was obtained directly from the effectiveness analysis. This choice of estimate was justified.

**Validity of estimate of costs**

Some quantities were reported separately from the costs and adequate details of methods of cost estimation were given. The price year was not given, but the perspective adopted in the cost analysis was reported. The effects of alternative procedures on indirect costs were not addressed. Statistical analyses were performed on some resource consumption data, and on cost data. Cost results may not be generalisable to other countries.
Other issues

The authors’ conclusions appear to be justified given the uncertainties in the data. The issue of generalisability to other settings was not addressed, although some comparisons were made with other studies. The degree to which the study sample was representative of the study population was not discussed. It was noted that it was not the aim of this study to compare the cost-effectiveness of a strategy of antiemetic prophylaxis with treatment with an antiemetic drug when patients develop PONV symptoms.

Implications of the study

The authors feel that routine antiemetic prophylaxis is justified in outpatients undergoing high-risk surgical procedures.

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