A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures

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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
The use of ondansetron or droperidol given prior to surgery to prevent post-operative nausea and vomiting (PONV).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Female outpatients, who were scheduled to undergo laparoscopic tubal ligation, cone biopsy and diagnostic laparoscopy procedures at the Southwestern Medical Centre at Dallas, Texas.

Setting
Hospital.

Dates to which data relate
The time period during which the effectiveness and resource use data were collected and during which the unit costs and prices were assigned was not specified in the report. The study was accepted for publication in March 1996.

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

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

Study sample
The study sample comprised 161 female outpatients, who were scheduled to undergo laparoscopic tubal ligation, cone biopsy and diagnostic laparoscopy procedures. A sample size of 37 for each cohort was determined by power analysis prior to the commencement of the study. The power analysis was based on the following assumptions: (a) the incidence of PONV in the placebo group would be 65%; (b) a difference of 35% in the incidence of PONV would be considered of clinical importance, such that effective antiemetic prophylaxis would reduce PONV rates to <=30%; and (c) alpha = 0.05 and beta = 0.2. The number of subjects actually enrolled in the cohorts was 40 for each of the placebo, high-dose droperidol and ondansetron groups and 41 for the low-dose droperidol group. The percentage of subjects invited to participate who refused, and the percentage of subjects excluded for any reason from the initial sample, was not stated.
Study design
The study was a prospective, randomised, double-blind, placebo-controlled trial, conducted in a single centre. Patients were randomised on the basis of a computer-generated random number to receive one of four prophylactic treatments as defined for the model. Of the 161 patients originally enrolled in the study, 110 (68.3%) were followed-up at 24 hours and seven days post-surgery to determine the incidence of PONV during that time and the need for “rescue” antiemetic therapy (drugs given to treat uncontrolled vomiting).

Analysis of effectiveness
The report does not specify whether the analysis of the clinical data was based on the intention to treat approach or on treatment completers only. The primary health outcomes were freedom from PONV and the need for rescue antiemetics. Other outcomes were: time to extubation, eye opening, orientation, first oral intake, ambulation, ready for discharge and time in recovery unit. Parameters measured at home after discharge were: time to return to normal activity and resumption of solid food, quality of sleep at 24 hours and 7 days, and the presence of a caretaker at 24 hours and 7 days. A clear definition of an emesis episode was given. The severity of nausea was measured on a 100mm visual analogue scale. Demographic characteristics were shown to be comparable across all four cohorts of patients.

Effectiveness results
The duration of stay in the PACU was significantly longer in the placebo group compared with the three antiemetic treatment groups, but did not differ between the droperidol and ondansetron groups. The times to ambulation, achievement of discharge criteria and time of actual discharge were not significantly different between either of the four study groups. During the first two post-operative hours, the number of patients who were “free” from nausea and emesis was significantly larger in the three antiemetic treatment groups compared with the placebo group. The incidence of emesis and the need for rescue antiemetics was significantly lower in the three antiemetic treatment groups compared with the placebo group, but did not differ between the droperidol and ondansetron groups. Follow-up data after discharge from the ambulatory surgery unit suggested that the incidence of vomiting was significantly less in the groups receiving antiemetics compared with placebo. However, the incidence of nausea was only significantly different between the ondansetron and placebo groups. Among the three antiemetic treatment groups, there were no significant differences in the need for rescue antiemetics after discharge, or in the number of patients who received more than one dose of rescue antiemetic medication during the first 24 hours post-discharge. All significant p-values were reported as <0.05.

Clinical conclusions
Small-dose droperidol IV provides antiemetic prophylaxis comparable to that of high-dose droperidol IV or ondansetron 4 mg IV in women undergoing outpatient gynaecological procedures without increasing side-effects or delaying discharge.

Modelling
A decision analytic tree was developed to compare the outcomes of four approaches to the prophylaxis of nausea and vomiting for elective outpatient gynaecologic procedures: ondansetron 4 mg intravenous (IV), small-dose droperidol (0.625 mg) IV, high-dose droperidol (1.25 mg) IV and saline placebo. Cost-effectiveness ratios were determined for each approach by summing weighted costs (cost multiplied by probability of event) and dividing by the number of patients free from both post-operative nausea and vomiting (PONV) and side-effects associated with the particular antiemetic therapy.

Measure of benefits used in the economic analysis
The primary health outcome used in the economic analysis was therapeutic success, defined as freedom from both (PONV) and the need for rescue antiemetic therapy.
Direct costs
The direct costs included in the analysis were the acquisition and administration costs of prophylactic ondansetron or droperidol, the incremental costs associated with the management of emesis (costs for "emesis clean up" and rescue antiemetic therapy), the costs associated with the management of side effects of prophylactic antiemetic therapy, and the costs of stay in the postanesthesia (PACU) unit (phase I recovery) and phase II recovery area. The drug acquisition costs, prorated hourly nursing salary and the costs of hospitalisation were provided by the hospital administration. It appears from the article that nursing time was based on researchers' observations, although this is not clearly specified. Costs were identified from several perspectives: (a) the hospital in a managed care environment, (b) the department of anesthesia, (c) the insurance company, (d) the patient, and (e) society as a whole. When the perspective was limited to (a), (b) or (c), indirect costs were excluded. Costs from the patient's perspective were limited to indirect costs and the costs of managing emesis post-discharge. The primary analysis was based on costs from a societal perspective. Costs were not discounted due to the short intervention time.

Statistical analysis of costs
One-way analysis of variance techniques were used to analyse continuous data. When a significant difference was noted, post-hoc intergroup comparisons were performed using Scheffe's test. When appropriate a Kruskal-Wallis test was also performed. P-values of less than 0.05 were defined statistically significant.

Indirect Costs
Indirect costs included in the analysis were the costs to patients and caretakers from lost wages and travel from patients' homes to the doctor's office or a hospital for the management of emesis after discharge from the ambulatory care facility. Estimates were based on the telephone contacts made 24 hours and 7 days post-surgery. Patients were asked whether any person other than themselves had to take time off from work to assist as a result of the surgery and whether any adverse events had occurred or whether they had required additional medical attention, such as a visit to the doctor's office or the emergency room as a result of PONV. The costs for a caretaker were assumed to be equal to the earnings of a minimum wage worker ($40 per eight-hour day).

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was performed to determine the effect of varying the probabilities used in the model on the overall conclusions of the relative cost-effectiveness of the drugs. One-way simple sensitivity analysis was assumed although not specifically stated. Threshold analysis was used to determine the maximum acquisition cost of ondansetron which would make its use more cost-effective than low-dose droperidol, the minimum incidence of pre-discharge emesis beyond which prophylactic antiemetic therapy ceased to be cost-effective, the mean increase in the PACU stay or phase II recovery that would make ondansetron more cost-effective than low-dose droperidol, and the level of readmission rates for unanticipated emesis needed to make the routine use of ondansetron cost-effective. Threshold analysis was also used to determine the mean number of days of earlier return to work required to make ondansetron more cost-effective than low-dose droperidol from both the societal and patient's perspective.

Estimated benefits used in the economic analysis
The incidence of PONV in the hospital and after discharge and the need for rescue antiemetic therapy were similar for the ondansetron and both droperidol groups but differed significantly from that of the placebo group. The percentage in each group free from PONV and side-effects of antiemetic therapy ("successes") was 65% (95% CI: 48 - 79) for the ondansetron 4 mg IV group, 54% (95% CI: 37 - 69) for the small-dose droperidol IV group, 50% (95% CI: 34 - 66) for the high-dose droperidol IV and 25% (95% CI: 13 - 41) for the saline placebo group.
Cost results
The weighted costs of using prophylactic antiemetic therapy from the perspective of society were $9.80 (95% CI: $4.65 - $29.23) for the placebo group, $6.40 (95% CI: $2.85 - $24.67) for the small-dose droperidol group (assuming no waste), $5.66 (95% CI: $2.31 - $24.32) for the high-dose droperidol group (assuming no waste) and $18.52 (95% CI: $11.75 - $42.33) for the ondansetron group.

Synthesis of costs and benefits
The cost-effectiveness ratios were determined as the treatment cost per patient not experiencing PONV and free from side effects of prophylactic antiemetic therapy. From the societal perspective the ratios were $39.19 (95% CI: $23.90 - $75.37) for the placebo group, $8.39 (95% CI: $6.52 - $12.16) for the small-dose droperidol group (assuming no waste), $11.33 (95% CI: $8.88 - $16.66) for the high-dose droperidol group (assuming no waste) and $28.49 (95% CI: $23.44 - $38.58) for the ondansetron group. The cost-effectiveness ratio for ondansetron was significantly greater than the cost-effectiveness ratios for either of the two droperidol groups, although this was sensitive to the acquisition costs of ondansetron. It was determined that if the ratio of the acquisition cost of ondansetron to low-dose droperidol was 2.5:1 or less rather than the current 7:1, ondansetron would be more cost-effective. Other sensitive parameters included the additional time spent by the patient in the PACU (staying for an additional 53 minutes would make ondansetron more cost-effective than droperidol), the incidence of emesis prior to discharge from the ambulatory surgery centre, and the rate of unanticipated admission for management of persistent emesis. The crossover point for the incidence of predischarge emesis, where prophylactic antiemetic therapy was more cost-effective than no prophylaxis, was 13% for droperidol and 30% for ondansetron. From the perspective of the insurance company, the routine use of prophylactic ondansetron would be more cost-effective than droperidol if the difference in admission rates for the management of emesis exceeded 1:3,000 patients. From both a societal and patient’s perspective, ondansetron would be more cost-effective than droperidol if its use was associated with an earlier return to work by a mean of 0.8 days.

Authors’ conclusions
This study demonstrated that droperidol 0.625mg IV is as effective as ondansetron 4mg IV in the prophylaxis of PONV in women undergoing outpatient gynaecologic surgery. In addition, small dose droperidol may be more cost-effective than ondansetron as a prophylactic antiemetic based on the current acquisition costs.

CRD COMMENTARY - Selection of comparators
The choice of comparators was not justified in the article, but seems appropriate given that the drugs and doses in this study are frequently used as prophylaxis for PONV. Placebo seems an appropriate choice because prophylaxis against PONV is not considered standard therapy and many patients do not receive it.

Validity of estimate of measure of benefit
As acknowledged by the authors, it was assumed that the value of avoiding emesis is the same as the value of avoiding the side effects of antiemetic therapy. This may not be true, since there is some evidence to suggest that patients will tolerate some degree of pain, drowsiness and delayed discharge to avoid post-operative nausea and vomiting.

Validity of estimate of costs
The authors stated in the discussion that they chose not to use hospital charges for drugs but rather to estimate the actual costs, assuming here they mean opportunity costs. The validity of their estimate of cost then depends on the perspective of the analysis, since charges are the appropriate costs to include when the perspective adopted is one of the hospital or the insurance company. Opportunity costs are only relevant when the perspective adopted is a societal one. The authors also stated that incremental costs associated with the management of emesis (costs for “emesis clean up” and rescue antiemetic therapy) were noted. Use of the term marginal is likely to have been more accurate in this case, if the estimates were based on additional costs. One of the rescue medications, metoclopramide, was not included in the listing of costs given in Table 1 of the article. The importance of this is unclear.
Other issues
The cost estimates themselves were not subject to sensitivity analysis.

Implications of the study
Among women undergoing outpatient gynaecological procedures, the widespread use of small-dose droperidol IV rather than high-dose droperidol IV or ondansetron IV would be likely to provide comparable antiemetic prophylaxis at a reduced cost.

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