Management of post-strabismus nausea and vomiting in children using ondansetron: a value-based comparison of outcomes

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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 prophylactic ondansetron (PO), 100 microg/kg intravenously (i.v.) for the treatment of postoperative nausea and vomiting (PONV) in children undergoing strabismus repair.

Type of intervention
Primary prevention (prophylaxis).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children (ASA I or II), aged 2 to 15 years, who were undergoing strabismus repair under general anaesthesia. Patients receiving drugs known to have anti-emetic effects in the 24 hours before surgery were excluded.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
Neither the dates for the effectiveness and resource use data, nor the price year, were reported.

Source of effectiveness data
The effectiveness evidence came from a single study.

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

Study sample
Preliminary power calculations showed that 68 children would be required in each study group to detect a statistically significant (beta = 0.2; type-1 error: 5%) reduction of 25% in the incidence of PONV between the groups with a basal PONV incidence of 55%. The method of sample selection was not reported. An overall sample of 150 patients was enrolled in the study. There were 75 children in the PO group, who received PO as reported above (up to 4 mg), and 75 children in the EO group who received saline. The mean age in the PO group was 6.9 years (range: 2 - 15), there were 29 boys, and the children's weight was 22.2 (+/- 8.5) kg. The mean age in the EO group was 6.3 years (range: 2 - 14), there were 33 boys, and the weight of the children was 21.3 (+/- 9.9) kg. Any child experiencing nausea or vomiting...
was treated with ondansetron (100 microg/kg i.v.) as the first postoperative anti-emetic. Second-line anti-emetics were also used in case of ondansetron failure.

**Study design**

This was a prospective, randomised, double-blind controlled trial. The number of centres in which the study was conducted was not reported. Patient allocation to study groups was conducted using a random number generator. The anaesthetist who prepared the study drugs was not involved in patient care. The nursing staff who carried out the patient evaluation was blind to the treatment administered to the children. The patients were followed until discharge from the postanaesthesia care unit (PACU). No loss to follow-up was reported. The outcome assessment was performed at intervals of 0 to 2, 2 to 6, and 6 to 24 hours.

**Analysis of effectiveness**

The basis of the clinical study appears to have been intention to treat. The primary health outcomes used in the effectiveness analysis were incidence of PONV, incidence of nausea, rescue requirements, rescue anti-emetics (ondansetron, metoclopramide and promethazine), fast tracking time (FTT), PACU stay, the number-needed-to-prevent (NNP) and the number-needed-to-treat (NNT) PONV, a parental satisfaction score, and the number-needed-to-improve satisfaction (NNS). The FTT was calculated as the time from the discontinuation of anaesthesia to the time at which a child had patent airway without support, no PONV or pain, and a modified Aldrete recovery score of 10. Parental satisfaction was scored using an 11-point verbal linear numerical scoring system ranging from 0 (“not at all satisfied”) to 10 (“fully satisfied”). The NNS was calculated as the reciprocal of the absolute percentage of unsatisfied parents. The study groups were shown to be comparable at baseline in terms of their demographics and clinical characteristics.

**Effectiveness results**

Over the 24 postoperative hours, the incidence of PONV was 34.7% in the PO group and 72% in the EO group, (p<0.0001); the incidence of nausea was 40.9% in the PO group and 76.9% in the EO group, (p=0.0009); and the proportion of rescue requirements was 34.7% in the PO group and 72% in the EO group, (p<0.0001).

Ondansetron as first-rescue anti-emetic was used in 34.7% of the PO group and 72% of the EO group, (p<0.0001). Metoclopramide as second-rescue anti-emetic was used in 9.3% of the PO group and 29.3% of the EO group, (p=0.0019). Promethazine as third-rescue anti-emetic was used in 2.7% of the PO group and 13.3% of the EO group, (p=0.0351).

The FTT was 21.6 (+/- 4.1) minutes in the PO group and 28.2 (+/- 5.3) minutes in the EO group, (p<0.0001). PACU stay was 126.5 (+/- 13.9) minutes in the PO group and 141.1 (+/- 30.6) minutes in the EO group, (p=0.0002).

The NNP/NNT PONV was 2 in the PO group and 9 in the EO group.

The NNS was 1.6 in the PO group and 4 in the EO group.

The parental satisfaction score was 8.2 (+/- 1.8) in the PO group and 6.8 (+/- 1.7) in the EO group, (p<0.0001).

**Clinical conclusions**

The effectiveness analysis showed that the PO strategy was more effective than the EO treatment for the management of PONV in children undergoing strabismus repair. The parents were more satisfied and all outcome measures performed significantly better with PO.
Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was PONV incidence. This was derived directly from the effectiveness study and was used to calculate the proportion of PONV-free patients. The NNP/NNT was also derived from the effectiveness study, to estimate the proportion of children who benefited from the interventions.

Direct costs
Discounting was irrelevant since the costs were incurred over a short time period. The unit costs were only reported separately from the quantities of resources used for the drug costs. The economic evaluation included only the costs of drug acquisition. These were derived from the authors' assumptions, on the basis of the prices observed at their institution. The cost/resource boundary adopted in the study was not reported. The resource use was estimated using prospectively collected data derived from the same patient sample as that used in the effectiveness study. No price year was reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The total costs in the two study groups were not reported.

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated to combine the costs and benefits of the two strategies. No incremental analysis was calculated. The cost per PONV-free child was $21.3 with PO and $28.9 with EO. Thus, PO led to a 35.5% reduction in the cost per PONV-free patient. The cost to benefit a child was also calculated as the product of the drug acquisition cost per child and the NNT/NNP. It was $17.8 with PO and $76.7 with EO.

Authors' conclusions
Prophylactic ondansetron (PO) was more cost-effective than standard early ondansetron (EO) treatment in the management of postoperative nausea and vomiting (PONV) in children undergoing strabismus repair under general anaesthesia. Parent satisfaction was significantly higher with PO than with EO treatment.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. EO treatment was selected since it represented the standard ("wait and treat") approach for the management of PONV in patients undergoing strabismus repair. You should decide...
whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a prospective randomised trial, which was appropriate for the study question. The internal validity was enhanced by the double-blind assessment, the description of the randomisation process, the baseline comparability of the study groups, and the use of preliminary power calculations to identify the appropriate sample size. Statistical analyses were conducted to test the statistical significance of differences in all the outcome measures. The basis of the clinical study was presumably intention to treat. However, the method of sample selection was not reported and it was unclear whether the study was carried out only at the authors’ institution.

Validity of estimate of measure of benefit
The benefit measures were derived from the effectiveness study and were fairly specific to the disease considered in the analysis.

Validity of estimate of costs
The perspective adopted in the study was not reported and only the drug acquisition costs were included in the economic evaluation. Overall, few details of the cost analysis were reported. The unit costs were reported and were based on data derived from the authors’ institution. However, the total costs estimated in each study group were not reported. The costs and the quantities were treated deterministically and sensitivity analyses were not performed. Thus, the cost estimates were specific to the study setting. No price year was reported, thus making reflation exercises in other settings difficult.

Other issues
The authors made some comparisons of their findings with those from published studies. However, they did not address the issue of the generalisability of the study results to other settings. Overall, the external validity of the analysis appears quite low. The study enrolled children undergoing strabismus repair under general anaesthesia, and this was reflected in the conclusions of the analysis.

Implications of the study
The study suggests that PO improves patient recovery and duration of PACU stay at a lower direct cost than standard EO treatment. However, it appears that the economic implications of the present study should be interpreted with caution due to the limitations of the cost analysis.

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