Use of antiemetic agents in acute gastroenteritis: a systematic review and meta-analysis
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CRD summary
This review concluded that ondansetron therapy decreased the risk of persistent vomiting, use of intravenous fluid and hospital admissions in children with vomiting due to gastroenteritis. The review was generally well-conducted. The authors' conclusions reflected the data and are likely to be reliable.

Authors' objectives
To evaluate the efficacy and safety of antiemetic agents in children with gastroenteritis.

Searching
MEDLINE/PubMed was searched; dates and terms used were not reported, but were available from the authors. The Cochrane Library, Alternative Medicine Database and International Pharmaceutical Abstracts Database were also searched; search terms were reported, but search dates were not. The Clinical Trials Registry was searched to identify unpublished trials. Reference lists of relevant articles were checked and experts contacted to identify additional studies. Only studies in English were included.

Study selection
Prospective controlled trials that evaluated the use of antiemetic agents in children with gastroenteritis were eligible for inclusion. Inclusion criteria relating to outcomes or study designs were not clearly specified.

The included studies evaluated the antiemetic agents ondansetron, domperidone, trimethobenzamide hydrochloride, pyrilamine-pentobarbital, metoclopramide, dexamethasone and promethazine hydrochloride. Ondansetron was given orally (1.6 mg to 8 mg) or intravenously (0.15 mg/kg to 0.3 mg/kg). Metoclopramide was given intravenously and per rectum (doses not provided); dexamethasone was given intravenously (dose not provided). Other antiemetic agents were given per rectum (doses not provided). Most of the studies evaluating ondansetron provided only one dose; the number of doses given for the other antiemetic agents was not reported. The antiemetic agents were compared with other antiemetic agents or to placebo. The age of the patients in the included studies ranged from one month to 22 years. The severity of the gastroenteritis varied and in some studies included dehydration with failed oral rehydration and/or vomiting. Children in the ondansetron studies were recruited from emergency departments or as inpatients. The other studies were conducted in paediatric clinics or while the children were inpatients. Outcomes reported included hospital admission, intravenous fluid administration, cessation of vomiting in the emergency department, return to outpatient care and adverse events.

It appeared that three reviewers assessed studies for inclusion. Whether this was undertaken independently and how disagreements were resolved were not reported.

Assessment of study quality
Validity assessment was undertaken using two scales and a summary score was calculated. The two scales used were the Downs and Black checklist (maximum score 31) and the Delphi List (maximum score 9).

Validity assessment was undertaken by two independent reviewers. Disagreements were resolved by discussion.

Data extraction
The number of patients experiencing the outcomes were extracted for each treatment group and used to calculate relative risks with 95% confidence intervals (CIs). Authors of studies using ondansetron were contacted when there was missing data.

Data extraction was performed by two independent reviewers. It was not reported how disagreements were resolved.
Methods of synthesis
Pooled relative risks and confidence intervals were calculated using a random-effects meta-analysis when there were three or more studies evaluating the same drug and outcome, and when both statistical heterogeneity and publication biases were absent. The method of study weighting was not stated. Narrative synthesis was used when there were less than three studies available or when it was deemed inappropriate to combine studies in a meta-analysis. Pooled rate differences were also calculated and converted to a number needed to treat.

Heterogeneity was assessed using the Q statistic and publication bias by the Begg and Egger tests. Sensitivity analyses were performed based on the statistical model and the exclusion of lower quality studies; details of the statistical model were not provided.

Results of the review
Eleven studies (n=1,023) were included in the review. Six studies evaluated ondansetron (n=745) (one study also evaluated dexamethasone and another also evaluated metoclopramide); these were randomised double-blind placebo-controlled trials; length of follow-up ranged from 24 hours to two weeks. Five studies evaluated other antiemetic agents (n=278); it was not reported what the study designs were; length of follow-up ranged from two hours to 24 hours.

The quality of the studies varied. The studies which evaluated ondansetron were of higher quality (Downs and Black scores 20 to 26, Delphi scores 7 to 9). Quality scores for the studies that evaluated the other agents were Downs and Black scores 8 to 18 and Delphi scores 2 to 7.

Ondansetron
Ondansetron was associated with a statistically significant decrease in the risk of hospital admission (Relative risk 0.52, 95% confidence interval: 0.27, 0.95. Number needed to treat was 14, 95% confidence interval: 9, 44. Five trials), intravenous fluid administration (Relative risk 0.41, 95% confidence interval: 0.28, 0.62. Number needed to treat was five with 95% CI: 4, 8. Four trials), cessation of vomiting in the emergency department (Relative risk 0.45, 95% confidence interval: 0.33, 0.62. Number needed to treat was five, 95% confidence interval: 4, 7. Four trials) when compared with placebo. There was no significant difference between ondansetron and placebo for return to outpatient care. It was reported that no significant heterogeneity or publication bias was detected. Sensitivity analyses did not significantly affect the results.

The only adverse event reported was diarrhoea. Five studies reported on this outcome. Ondansetron may have been associated with an increase in diarrhoeal episodes up to 48 hours post drug administration, but no differences were found after this time.

Other antiemetic agents
The authors provided a narrative synthesis for the other antiemetic agents domperidone, metoclopramide, trimethobenzamide hydrochloride, pyrilamine-pentobarbital, promethazine hydrochloride and dexamethasone. The authors stated that these studies had low numbers, were of poor quality and produced inconsistent results.

Authors' conclusions
Ondansetron therapy decreased the risk of persistent vomiting, use of intravenous fluid and hospital admissions in children with vomiting due to gastroenteritis.

CRD commentary
The review question was clear, although very broad. Inclusion criteria were not explicitly stated for outcomes or study designs, which may have increased the risk of bias and error at the selection stage of the review. A number of relevant databases were searched and an effort was made to search for unpublished studies. The authors reported that publication bias was not present, although study numbers were very low. The decision to limit the review to studies reported in English may have led to the exclusion of relevant studies and the introduction of language bias. Steps were taken to minimise reviewer bias and errors in the study selection, data extraction and validity assessment parts of the review process. Meta-analysis and narrative synthesis appeared to have been undertaken appropriately. The review was generally well-conducted. The authors' conclusions reflected the data and are likely to be reliable.
**Implications of the review for practice and research**

**Practice:** The authors recommended the use of ondansetron in the emergency department for dehydrated children at risk of oral replacement therapy failure. They stated that antiemetic agents other than ondansetron should not be used for outpatients with gastroenteritis. They also stated that future treatment guidelines should incorporate the use of ondansetron for certain children with gastroenteritis.

**Research:** The authors recommended that studies should be undertaken to evaluate the effect on hospital admission of repeated doses of ondansetron given for home use. They also stated that studies should be undertaken in primary care offices to evaluate whether ondansetron in children with gastroenteritis improved outcomes such as persistence of emesis, need for intravenous fluid, return to care, emergency department use and parental satisfaction. They also recommended that cost-effectiveness and cost-utility analyses be undertaken.

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