Cochrane for Clinicians

*Putting Evidence into Practice*

# Antiemetics for Acute Gastroenteritis–Related Vomiting in Children and Adolescents

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Dr. Cayley presents a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://www.cochrane.org/reviews/en/ab005506.html.

EB CME

This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 1036.

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## Clinical Scenario

A five-year-old girl is brought to your clinic by her parents. She has had nausea and vomiting for the past two days, has been unable to keep fluids down, and appears dehydrated. The parents would like to avoid hospitalization, if possible, and are wondering if any medications are safe and effective for controlling her symptoms.

## Clinical Question

Should antiemetics be prescribed for vomiting related to acute gastroenteritis in children and adolescents?

## Evidence-Based Answer

Ondansetron (Zofran) given orally can reduce rates of vomiting, improve short-term tolerance of oral fluids, and reduce short-term rates of hospital admission and the need for intravenous hydration. Metoclopramide (Reglan) and ondansetron can reduce episodes of vomiting when given intravenously. Dimenhydrinate suppositories given rectally can reduce the time to cessation of vomiting but not overall rates of hospital admission. (Strength of Recommendation: A, based on consistent, good-quality, patient-oriented evidence.)

## Practice Pointers

Acute gastroenteritis accounts for more than 1.5 million outpatient visits and 200,000 hospitalizations each year among children in the United States.[1] Although oral rehydration therapy (ORT) has been recommended as a first-line treatment for acute gastroenteritis,[1] emergency physicians in the United States use antiemetics more often than ORT.[2] A 2009 review found that older antiemetics (e.g., promethazine, prochlorperazine, metoclopramide) have common, potentially dangerous adverse effects when used in children,[3] but a guideline from the National Institute for Health and Clinical Excellence in the United Kingdom concluded that "oral ondansetron could increase the success rate with ORT."[4]

The authors of this Cochrane review sought to determine the safety and effectiveness of antiemetics for the treatment of vomiting from gastroenteritis in children and adolescents younger than 18 years.[5] Six studies that met inclusion criteria assessed the use of ondansetron in the emergency department setting, comparing it with placebo (four trials), with metoclopramide or placebo (one trial), or with dexamethasone or placebo (one trial). A seventh trial assessed the use of dimenhydrinate (rectal suppository) versus placebo in five children's hospitals and six pediatric practices.

Ondansetron given orally reduced rates of hospital admission and intravenous hydration during the emergency department stay, and reduced the need for intravenous hydration when assessed 72 hours after emergency department discharge (number needed to treat = 5 to 6). Oral ondansetron also reduced rates of vomiting and improved tolerance of oral fluids at eight hours. However, there was no evidence that oral ondansetron reduced rates of hospital admission at 72 hours after emergency department discharge, or that it improved emergency department revisit rates or tolerance of oral fluids at 24 hours.

The study comparing intravenous ondansetron with intravenous metoclopramide and placebo found that both medications reduced the number of episodes of vomiting compared with placebo, with intravenous

## Cochrane Abstract

**Background:** Vomiting is a common manifestation of acute gastroenteritis in children and adolescents. When untreated, it can be a hindrance to oral rehydration therapy, which is the cornerstone in the management of acute gastroenteritis. Evidence is needed concerning the safety and effectiveness of antiemetic use for vomiting in acute gastroenteritis in children.

**Objectives:** To assess the safety and effectiveness of antiemetics on gastroenteritis-induced vomiting in children and adolescents.

**Search Strategy:** The authors searched the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group Trials Register, comprising references identified from comprehensive electronic database searches and hand searches of relevant journals and abstract books of conferences. The search was rerun and is up to date as of July 20, 2010.

**Selection Criteria:** Randomized controlled trials comparing antiemetics with placebo or no treatment, in children and adolescents younger than 18 years, for vomiting due to gastroenteritis.

**Data Collection and Analysis:** Two review authors independently assessed trial quality and extracted data.

**Main Results:** The authors included seven trials involving 1,020 participants. Mean time to cessation of vomiting in one study was 0.34 days less with dimenhydrinate suppository compared with placebo ($P = .036$). Pooled data from three studies comparing oral ondansetron with placebo showed: a reduction in the immediate hospital admission rate (risk ratio [RR] = 0.40; number needed to treat [NNT] = 17; 95% confidence interval [CI], 10 to 100) but no difference between the hospitalization rates at 72 hours after discharge from the emergency department; a reduction in intravenous rehydration rates both during the emergency department stay (RR = 0.41; NNT = 5; 95% CI, 4 to 8) and in follow-up to 72 hours after discharge from the emergency department (worst-best scenario for ondansetron; RR = 0.57; NNT = 6; 95% CI, 4 to 13); and an increase in the proportion of patients with cessation of vomiting (RR = 1.34; NNT = 5; 95% CI, 3 to 7). No significant difference was noted in revisit rates or adverse effects, although diarrhea was reported as an adverse effect in four of the five ondansetron studies. In one study the proportion of patients with cessation of vomiting in 24 hours was 58 percent with intravenous ondansetron, 17 percent with placebo, and 33 percent with metoclopramide ($P = .039$).

**Authors' Conclusions:** Oral ondansetron increased the proportion of patients who had ceased vomiting and reduced the number needing intravenous rehydration and immediate hospital admission. Intravenous ondansetron reduced hospital admissions and the number of episodes of vomiting. Intravenous metoclopramide reduced episodes of vomiting, and dimenhydrinate rectal suppository reduced the duration of vomiting.



ondanestron being more effective. Intravenous ondansetron and intravenous metoclopramide were associated with an increased risk of diarrhea.

The study of dimenhydrinate given rectally by suppository found that, when compared with placebo, it reduced the time to cessation of vomiting (0.6 versus 0.94 days), the number of episodes of vomiting, and the proportion of patients with vomiting at 18 and 24 hours. However, dimenhydrinate given rectally showed no improvement over placebo in parental satisfaction or rates of hospitalization.

Overall, the interventions studied in this review appeared to be safe, with adverse effects limited primarily to diarrhea, rash, drowsiness, and sedation. No severe adverse effects attributable to the antiemetics studied were reported.

A few cautions are warranted in applying these data to clinical practice. First, because most comparisons assessed in the review were of an antiemetic versus placebo, this Cochrane review did not directly compare the effectiveness of ondansetron and dimenhydrinate. Second, this review did not examine the relative benefits of ORT versus antiemetic medication. However, because ORT was typically started soon after administering study medications, ORT could be considered the equivalent of a "placebo" treatment in this setting (Ben Carter, PhD, Bangor University, United Kingdom, written communication, January 2012). Another Cochrane review found no clinically important differences between ORT and intravenous rehydration therapy.[6] ORT is more commonly used for acute gastroenteritis in Canada than in the United States, even though the two countries have similar populations and medical systems.[2] Lastly, because the studies included in this review were conducted in emergency departments in the United States, Canada, Turkey, and Venezuela, their results may not be completely generalizable to settings in the developing world. Only the German study of dimenhydrinate assessed the use of an antiemetic in a setting typical of primary care.

Although this review did not assess the relative benefits of antiemetics versus ORT, it provides evidence that the antiemetics ondansetron (given orally or intravenously) and dimenhydrinate (by suppository) improve some short-term clinical outcomes in acute gastroenteritis, and have reasonable safety profiles in children and adolescents.

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# Cochrane Briefs

## Could Selenium Supplementation Prevent Cancer?

### Clinical Question

Does selenium supplementation prevent the development of cancer?

### Evidence-Based Answer

Selenium deficiency is associated with a higher risk of cancer, but selenium supplementation does not decrease that risk. (Strength of Recommendation: A, based on consistent, good-quality, patient-oriented evidence.)

### Practice Pointers

Selenium is a mineral that is a cofactor in enzymes (e.g., glutathione peroxidase) that protect against oxidative stress of cellular metabolism. Selenium is present in plant-based foods such as oatmeal, wheat, and rice, and also is absorbed through consumption of beef, tuna, cod, and chicken. The U.S. recommended dietary allowance of selenium for adults is 55 mcg per day.[1] A prospective study performed in a nutrient-poor region of China from 1985 to 1991 showed that supplementation with a combination of selenium, vitamin E, and beta carotene resulted in lower mortality rates compared with placebo.[2] However, selenium deficiency is rare in the United States.[1] Selenium toxicity can cause nausea, mild nerve damage, or hair and nail loss.[1]

To determine if there is a link between selenium levels and cancer risk, and whether selenium supplementation prevents cancer, the authors of this review searched for relevant prospective observational studies and randomized controlled trials. Forty-nine observational studies that involved more than 1 million participants showed a 31 percent lower risk of cancer and a 45 percent lower risk of cancer-related death in those with higher selenium levels (generally, the top quartile) than in those with lower levels. Notably, the risk of death was 33 percent lower for bladder cancer and 22 percent lower for prostate cancer in those with higher selenium levels. However, six randomized trials that included 43,408 participants did not show a reduced risk of cancer with selenium supplementation. The results of the two trials with the lowest risk of bias suggest that supplementation does not prevent prostate cancer and may increase the risk of nonmelanoma skin cancers.

Since the publication of this Cochrane review, another trial of 423 men considered to be at high risk of developing prostate cancer revealed no difference in cancer rates in those supplemented with selenium (35.6 percent) versus placebo (36.6 percent) over a three-year period.[3] Physicians should counsel patients that selenium levels may serve merely as a marker of overall health, and that supplementation does not decrease cancer risk. The National Institutes of Health statement on chronic disease prevention makes no mention of selenium for the prevention of cancer.[4]

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