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Priority Updates from the Research Literature from the Family Physicians Inquiries Network

This antiemetic may help kids skip that trip to the hospital

For children with gastroenteritis, a single dose of ondansetron can reduce the vomiting—without IV fluids or serious side effects.

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Practice changer

Give oral ondansetron to children with acute gastroenteritis and moderate dehydration who are unable to tolerate oral rehydration to reduce the vomiting and avoid the need for intravenous (IV) hydration or hospitalization.[1]

Strength of recommendation
A: Meta-analysis of 6 high-quality studies

DeCamp LS, Byerley JS, Doshi N, et al. Use of antiemetic agents in acute gastroenteritis, a systematic review and meta-analysis. *Arch Pediatr Adolesc Med.* 2008;162:858-865.

ILLUSTRATIVE CASE

Sarah, a 2-year-old who has been vomiting and had diarrhea for the past 2 days, is brought to your office by her parents. They tell you she's unable to tolerate oral fluids, and vomited twice after being given small amounts of juice and soup earlier in the day. Sarah has decreased urine output, but she is not febrile and has no blood in her stools. On examination, you find mild tachycardia, dry mucous membranes, delayed capillary refill, and normal mental status.

You try giving Sarah an oral electrolyte solution, but she vomits immediately. Her parents are reluctant to take her to the emergency department for intravenous (IV) hydration, and ask if you can provide a safe and effective alternative.

Each year in the United States, pediatric gastroenteritis and dehydration are responsible for approximately 1.5 million outpatient visits[2] and 150,000 to 170,000 hospital admissions.[3] Oral hydration, recommended by pediatric practice guidelines[2,4] and the World Health Organization,[5] is safe and generally effective. But, as in Sarah's case, emesis frequently interferes, leading to hospital admission for IV hydration.

An antiemetic with fewer adverse effects

Older antiemetic medications, such as promethazine, prochlorperazine, and metoclopramide, can cause sedation and extrapyramidal reactions. Ondansetron, a selective 5-hydroxytryptamine ($5\text{-}HT_3$) receptor antagonist that has been used to control postoperative and chemotherapy-associated nausea and vomiting in children and adults, does not cause either problem. In recent studies of ondansetron's effectiveness in treating children

FAST TRACK

Ondansetron does not have the sedating and extrapyramidal effects associated with older antiemetics.

TABLE

Ondansetron reduces vomiting, hospitalization, and IV fluid use

TOTAL NUMBER OF PATIENTS (N=745)	ONDANSETRON	PLACEBO	RR (95% CI)	NNT (95% CI)
Continued vomiting (n=659)	16.9%	37.8%	0.45 (0.33-0.62)	5 (4-7)
IV fluid administration (n=489)	13.9%	33.9%	0.41 (0.28-0.62)	5 (4-8)
Hospital admission (n=662)	7.5%	14.6%	0.52 (0.27-0.95)	14 (9-44)

CI, confidence interval; IV, intravenous; NNT, number needed to treat; RR, relative risk.
Source: DeCamp LS, et al. *Arch Pediatr Adolesc Med*.[1]

FAST TRACK

The increase in diarrhea associated with ondansetron resolved in 48 hours.

PURLs methodology
This study was selected and evaluated using FPIN's Priority Updates from the Research Literature (PURL) Surveillance System methodology. The criteria and findings leading to the selection of this study as a PURL can be accessed at www.jfponline.com/purls.

with gastroenteritis, increased diarrhea, lasting up to 48 hours after administration, was the only adverse event.[1]

Two earlier systematic reviews—a meta-analysis by Szajewska et al[6] and a Cochrane review[7]—found clinical benefits of ondansetron for vomiting associated with acute gastroenteritis. But both concluded that the evidence was insufficient to recommend routine use of this drug. The meta-analysis that we review below included additional studies, and the researchers reached a different conclusion.

STUDY SUMMARY

Antiemetic decreases vomiting, hospitalization

DeCamp et al conducted a systematic review and meta-analysis of 11 prospective controlled trials that evaluated antiemetic use in children with vomiting from acute gastroenteritis.[1] Six of the 11 trials focused on ondansetron;[8-13] these 6 were the most recently published and of the highest quality. (The researchers found the remaining 5 trials to be of low methodological quality, with small sample sizes and inconsistent results, and concluded that the antiemetics they assessed should not be used for outpatients with gastroenteritis.) Their meta-analysis of these 6 trials is the focus of this PURL.

The ondansetron studies included a total of 745 children with vomiting and a clinical diagnosis of gastroenteritis. In 5 of the trials, patients received only 1 dose of ondansetron;[8-10,12,13] in the sixth, families received additional doses of ondansetron to use at home.[11] In 3 trials, patients were given oral ondansetron—a tablet placed on the tongue that dissolves in minutes. The remaining 3 used an IV formulation.[8,10,13] Five trials were conducted in emergency departments (EDs),[9-13] and 1 in an inpatient setting.[8]

Big reductions. Children who received ondansetron had significantly less vomiting (16.9% vs 37.8%) and IV fluid administration (13.9% vs 33.9%), and fewer hospital admissions (7.5% vs 14.6%) compared with patients who were given a placebo (**TABLE**). Diarrhea, the only adverse event to be systematically evaluated, was assessed in all but 1 of the trials.[8-12] In 3 of the 5 that reported on this side effect, patients who received ondansetron had an increase in diarrhea for up to 48 hours.[8,11,12]

WHAT'S NEW

Support for a strategy increasingly used in EDs

Physicians are just beginning to adopt the use of ondansetron as a strategy for avoiding IV hydration and hospitalization for children with vomiting associated with minor gastrointestinal illness. As an adjunct to our report on this meta-analysis, we analyzed the use of the antiemetic in children between the ages of 1 and 10 years in emergency visits reported to the National Ambulatory Medical Care Survey database from 2002 to 2006. Among an estimate of more than 3 million pediatric visits to EDs for acute

gastroenteritis in each of these years, in 2002 only 0.53% were treated with ondansetron. By 2006, that percentage had risen to 6.43%.

A similar analysis of both ED and outpatient visits to academic medical centers and teaching hospitals from 2005 through 2008 (estimated using data through October 2008), derived from the University Health System Consortium Clinical Database, showed a similar trend. In 2005, only 0.5% of children presenting to EDs and 0.5% of those seeking outpatient care for acute gastritis received ondansetron. By 2008, the numbers had grown to an estimated 3.43% and 3.60%, respectively.

Given the positive results of the DeCamp study and the fact that oral ondansetron is now available in a generic formulation, we expect the use of this antiemetic to increase in both outpatient and emergency settings. We think quite a few IV lines and hospitalizations could be avoided with the use of this antiemetic, not to mention the symptomatic relief for children.

CAVEATS

Studies didn't look at milder cases, primary care

None of the studies of oral ondansetron for acute gastroenteritis involved outpatient settings, and all 6 of the trials featured children who were moderately ill. It has not yet been determined whether the benefits seen in the ED will apply to an ambulatory population in which many potential candidates for ondansetron have milder gastroenteritis. Nor is it clear whether oral ondansetron would complement oral rehydration in primary care practices. More detailed evaluation of the reduction of vomiting at home over the course of the illness would help to answer these questions.

Nonetheless, ondansetron appears to be safe. Increased diarrhea, the only documented side effect, resolved after 48 hours, and did not appear to result in higher health care utilization.

Don't prescribe over the phone. It is important to note that all the ondansetron trials included an evaluation of each patient to consider other etiologies, such as central nervous system disorders or toxic exposures, prior to treatment. Physicians are cautioned not to prescribe antiemetics over the telephone—or without first ruling out more serious illnesses in which vomiting is part of the presentation.

Studies were funded by pharma. The primary studies of ondansetron were funded by GlaxoSmithKline, the pharmaceutical company that manufactures the drug under the trade name Zofran. The authors of the meta-analysis reviewed the Clinical Trials Registry and the reference lists of the articles and contacted other experts to find any unreported trials, but found no evidence of negative publication bias. Therefore, we have confidence in these findings. Ideally, additional studies will be conducted without drug company support, in an outpatient setting, to clarify the use of ondansetron as an adjunct to oral rehydration.

CHALLENGES TO IMPLEMENTATION

No major barriers

Cost should not be a barrier to the use of oral ondansetron. The generic formulation sells for $10 to $20 per tablet, and is covered by most health insurers. However, treatment of children with acute gastroenteritis and moderate dehydration in the office setting would likely require a period of observation for tolerance of oral rehydration before and after administration of ondansetron. This may be impractical in some busy clinics. ■

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CONTINUED

FAST TRACK

Before giving an antiemetic to a child who appears to have gastroenteritis, it is essential to rule out more serious conditions.

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