PICO SEARCH ASSIGNMENT WORKSHEET **Name: Sirat Zafar**

Brief description of patient problem/setting (summarize the case very briefly)
A 7-year-old Middle Eastern female presents to the pediatric emergency department with one day of persistent non-bloody, non-bilious vomiting, watery diarrhea, and diffuse abdominal pain. She experienced approximately 8-9 episodes of emesis since the previous evening and was unable to tolerate oral fluids. Physical examination revealed mild diffuse abdominal tenderness without guarding, rebound tenderness, or other peritoneal signs. Evaluation was most consistent with acute gastroenteritis with mild-to-moderate dehydration.

Search Question: In pediatric patients presenting to the emergency department with acute gastroenteritis-associated vomiting, does ondansetron administration compared with supportive care alone improve oral rehydration success and reduce the need for intravenous fluid administration?

Question Type: What kind of question is this? (boxes now checkable in Word)

☐ Prevalence	☐ Screening	☐ Diagnosis
☐ Prognosis	☐ **Treatment**	☐ Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)?

Please explain your choices

If a meta-analysis or systematic review is not available, randomized controlled trials (RCTs) would be the next most appropriate type of study because they can directly compare ondansetron administration with supportive care alone and evaluate outcomes such as successful oral rehydration, need for intravenous fluids, hospitalization, and return visits. RCTs provide a high level of evidence by minimizing bias and allowing for direct assessment of treatment effectiveness. Prospective cohort studies may also be useful because they evaluate real-world outcomes in pediatric patients receiving ondansetron in emergency department settings. These studies can provide additional information regarding treatment success, adverse effects, and healthcare utilization when randomized trials are limited or unavailable.

PICO search terms:

P	**I**	**C**	**O**
Children	Odansetron	Supportive care alone	Reduced vomiting
Pediatric patients	Oral Odansetron	No Odansetron	Reduced IV fluid administration
Acute gastroenteritis	Antiemetic therapy	Oral rehydration therapy alone	Decreased hospitalization
ED patients	Early ondansetron administration	No antiemetic therapy	Successful oral rehydration

Search tools and strategy used:

Please indicate what databases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters.

Explain how you narrowed your choices to the few selected articles. For example, if your search returned 25 articles among the several databases used, what was the process used to determine which four articles to use?

Database	Search Term Used	# of Results	Filters/Limiters Applied	Notes/Observations
PubMed	(child OR children OR pediatric) AND ("acute gastroenteritis" OR gastroenteritis) AND (vomiting) AND (ondansetron) AND ("oral rehydration" OR "IV fluids" OR hospitalization)	6 results	Last 5-10 years, Free full text, English, Human studies	PubMed returned 6 articles after applying filters. After reviewing titles and abstracts, two randomized controlled trials were selected because they directly evaluated ondansetron use in pediatric patients with acute gastroenteritis and measured outcomes related to vomiting, oral rehydration success, and need for IV fluids.
Cochrane Library	("acute gastroenteritis") AND (ondansetron) AND (children OR pediatric)	35 results	Last 10 years, English, Research articles	The Cochrane search returned 35 results. After reviewing titles and abstracts, most articles were excluded because they focused on other treatments for gastroenteritis or did not specifically evaluate ondansetron use in pediatric patients. One high-quality article was selected because it examined outcomes directly relevant to my PICO question, including oral rehydration success, IV fluid administration, and hospitalization.
Wiley Online Library	(children OR pediatric) AND ("acute gastroenteritis") AND (ondansetron) AND (vomiting OR "oral rehydration" OR "IV fluids" OR hospitalization)	74 results	2016-2026, Journals	Wiley Online Library returned 74 results. After reviewing titles and abstracts, one systematic review and meta-analysis was selected because it represented the highest level of evidence available and directly evaluated the effectiveness of ondansetron in children with acute gastroenteritis.

From the three databases, 115 articles were initially identified. After applying filters and screening titles and abstracts for relevance, four articles were selected. Preference was given to higher levels of evidence, including randomized controlled trials, a secondary analysis of randomized controlled trials, and a systematic review with meta-analysis. Articles were chosen because they specifically evaluated ondansetron use in pediatric patients with acute gastroenteritis-associated vomiting and examined clinically relevant outcomes such as successful oral rehydration, need for intravenous fluids, hospitalization, and symptom improvement.

Results found:

1. **Oral ondansetron for paediatric gastroenteritis in primary care: a randomised controlled trial**
Citation: Bonvanie IJ, Weghorst AA, Holtman GA, Russchen HA, Fickweiler F, Verkade HJ, Kollen BJ, Berger MY. Oral ondansetron for paediatric gastroenteritis in primary care: a randomised controlled trial. Br J Gen Pract. 2021 Sep 30;71(711):e728-e735. doi: 10.3399/BJGP.2021.0211. PMID: 34426397; PMCID: PMC8407859.

Article Type: Randomized Controlled Trial

Abstract

Background
Acute gastroenteritis (AGE) affects almost all children aged ≤5 years. In secondary care, ondansetron was found to be effective at reducing vomiting.

Aim
To determine the effectiveness of adding oral ondansetron to care as usual (CAU) to treat vomiting in children with AGE attending out-of-hours primary care (OOH-PC).

Design and setting
A pragmatic randomised controlled trial at three OOH-PC centres in the north of the Netherlands (Groningen, Zwolle, and Assen), with a follow-up of 7 days.

Method
Children were included if they were: aged 6 months–6 years; AGE diagnosed by a GP; ≥4 reported episodes of vomiting in the 24 hours before presentation; ≥1 reported episode of vomiting in the 4 hours before presentation; and written informed consent from both parents. Children were randomly allocated to either the control group or the intervention group. The control group received CAU, namely oral rehydration therapy. The intervention group received CAU plus one dose of oral ondansetron (0.1 mg/kg).

Results
In total, 194 children were included for randomisation. One dose of oral ondansetron decreased the proportion of children who continued vomiting within 4 hours from 42.9% to 19.5%, with an odds ratio of 0.37 (95% confidence interval [CI] = 0.20 to 0.72, number needed to treat: four). Ondansetron also decreased the number of vomiting episodes within 4 hours (incidence rate ratio 0.51 [95% CI = 0.29 to 0.88]) and improved overall parental satisfaction with treatment (P = 0.027).

Conclusion
Children with AGE and increased risk of dehydration due to vomiting could be treated with ondansetron in primary care to stop vomiting more quickly and increase parental satisfaction with treatment. These results could be used to improve the quality and efficacy of general practice medicine.

Keywords
acute gastroenteritis; child; oral ondansetron; out of hours; primary care; vomiting.

INTRODUCTION

Acute gastroenteritis (AGE) is common in young children and, although it is typically self-limiting, severe dehydration is an important complication.[1] Approximately 5% of all GP consultations with children in the Netherlands are for AGE.[2] Among those seen in primary care, 8.1% are referred to specialist care and 8000 are admitted to the hospital each year.[2,3] However, it is thought that many of these referrals and admissions can be avoided.[4]

International guidelines recommend care as usual (CAU) with oral rehydration therapy (ORT) to prevent and treat dehydration in children.[5] It has been shown that prescribing ORT with education can reduce hospital admission by up to 45%,[4,6–8] yet it is still underused in primary care; indeed, only 4% of all children overall with AGE received ORT through their GP.[9,10] A suggested reason for this underuse is that 70% of these children present with vomiting as the predominant symptom.[9] National paediatrics guidelines mention persistent vomiting as a predictor of ORT failure in children who are dehydrated;[11] as such, most GPs are less likely to prescribe ORT when the child predominantly presents with vomiting.[12]

Ondansetron has been reported to be safe and effective at stopping vomiting, increasing ORT success, and reducing hospitalisation rates among children presenting with AGE in secondary care;[13] however, the practical value of ondansetron for treating children with AGE in primary care is unknown. The authors aimed to conduct a pragmatic randomised controlled trial (RCT) to investigate the effect of ondansetron: added to CAU; compared with CAU alone; and on vomiting in children aged 6 months–6 years with AGE consulting out-of-hours primary care (OOH-PC) services.

METHOD

Study design

Participants were enrolled from December 2015 until January 2018 at three OOH-PC centres in the north of the Netherlands: one in Groningen, one in Zwolle, and one in Assen. A detailed description of the study design, recruitment strategy, outcomes, and discussion of the informed consent procedure are described elsewhere.[14] This study started with a pilot (Dutch Trial Register reference number: NL4700) undertaken from December 2015 until October 2016 but, as a result of the low inclusion rate, the primary outcome was changed from 'referrals' to 'vomiting'. In agreement with the Medical Ethics Review Committee of the University Medical Center Groningen, children included from the pilot were also included in the new trial and the RCT was approved.

Inclusion and exclusion criteria

Children considered to be at increased risk of dehydration[15] were included if they met the following inclusion criteria:

IJ Bonvanie, MD, trainee paediatrician; **AAH Weghorst**, BSc, MD/PhD candidate; **GA Holtman**, PhD, assistant professor; **HA Russchen**, MD, GP; **F Fickweiler**, MD, GP; **BJ Kollen**, PhD, epidemiologist; **MY Berger**, MD, professor of general practice, Department of General Practice and Elderly Care Medicine, University of Groningen, The Netherlands. **HJ Verkade**, MD, professor of paediatrics; Department of Pediatrics, University of Groningen, The Netherlands.

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Important Findings:

- Children who received oral ondansetron experienced less vomiting compared to those receiving usual care alone.
- Ondansetron improved the success of oral rehydration therapy.
- Patients receiving ondansetron were more likely to tolerate oral fluids and remain hydrated.
- Reduced vomiting decreased the likelihood of dehydration progression and the need for additional medical intervention.

- The study supported ondansetron as an effective adjunct to oral rehydration therapy in children with acute gastroenteritis.

I chose this article because it is a randomized controlled trial that directly addresses my PICO question regarding the use of ondansetron in pediatric patients with acute gastroenteritis-associated vomiting. The study compares ondansetron plus standard care with standard care alone and evaluates clinically relevant outcomes such as vomiting frequency, hydration status, and the success of oral rehydration therapy. These outcomes are highly applicable to emergency department practice because improving oral hydration can help reduce the need for intravenous fluids and potentially prevent hospitalization. This article provides strong evidence supporting the use of ondansetron as part of the management of pediatric gastroenteritis.

2. **Single-dose Intravenous Ondansetron in Children with Gastroenteritis: A Randomized Controlled Trial**

Citation: Rang NN, Chanh TQ, My PT, Tien TTM. Single-dose Intravenous Ondansetron in Children with Gastroenteritis: A Randomized Controlled Trial. Indian Pediatr. 2019 Jun 15;56(6):468-471. PMID: 31278225.

Article Type: Randomized Controlled Trial

Objective: To evaluate the efficacy of ondansetron for the treatment of vomiting and thus reducing the need for intravenous (IV) rehydration in children with gastroenteritis.

Design: Double-blind, placebo-controlled, randomized trial.

Setting: Pediatric ward of An Giang General Hospital, South Vietnam, between December 2013 and June 2014.

Participants: 61 inpatient children (age 11-60 mo) suffering from gastroenteritis with vomiting. Exclusion criteria were: underlying chronic conditions, immunodeficiency, malnutrition or history of allergy to ondansetron.

Intervention: Single bolus of IV ondansetron at a dose of 0.2 mg/kg or placebo.

Outcome measures: Proportion of patients who needed IV rehydration, proportion of patients with cessation of vomiting, amount of oral rehydration solution intake, duration of diarrhea and the length of hospital stay.

Results: After drug administration, 22 (73%) of the 30 patients in the ondansetron group had complete cessation of vomiting compared with 7 (23%) of the 31 patients in the placebo group (RR 0.32; 95% CI 0.16 to 0.63, $P<0.001$). 3 (10%) patients in the ondansetron group required IV rehydration as compared with 12 (39%) in the placebo group (RR 0.51; 95% CI 0.33 to 0.79, $P=0.009$). The median amount of oral rehydration solution intake in 24 hours was significantly greater in the ondansetron group (450 mL *vs* 350 mL, $P=0.019$).The duration of diarrhea and the length of hospital stay were not different between the two groups.

Conclusion: In hospitalized children having gastro-enteritis associated with emesis, ondansetron is effective in the cessation of episodes of vomiting and in lowering the rates of IV rehydration, without reducing the duration of diarrhea and hospital stay.

Keywords: *Acute diarrhea, Antiemetics, Therapy, Vomiting.*

Important Findings:

- Children who received intravenous ondansetron experienced significantly less vomiting compared to the control group.
- Ondansetron improved the success of oral rehydration therapy.
- Patients receiving ondansetron were less likely to require intravenous rehydration.
- Improved symptom control contributed to better hydration status and clinical recovery.
- Ondansetron was found to be safe and well tolerated with minimal adverse effects.

I chose this article because it is a randomized controlled trial that directly addresses my PICO question regarding the use of ondansetron in pediatric patients with acute gastroenteritis-associated vomiting.

The study specifically evaluated whether ondansetron could reduce vomiting and decrease the need for intravenous rehydration, which are clinically important outcomes in the emergency department. The findings support the use of ondansetron as an adjunct to oral rehydration therapy by improving tolerance of oral fluids and reducing the need for more invasive interventions. This article provides strong evidence that ondansetron can improve patient outcomes and may help reduce hospital resource utilization in children with acute gastroenteritis.

3. **Variables Associated With Intravenous Rehydration and Hospitalization in Children With Acute Gastroenteritis**

Citation: Poonai N, Powell EC, Schnadower D, Casper TC, Roskind CG, Olsen CS, Tarr PI, Mahajan P, Rogers AJ, Schuh S, Hurley KF, Gouin S, Vance C, Farion KJ, Sapien RE, O'Connell KJ, Levine AC, Bhatt S, Freedman SB; Pediatric Emergency Care Applied Research Network (PECARN) and Pediatric Emergency Research Canada (PERC). Variables Associated With Intravenous Rehydration and Hospitalization in Children With Acute Gastroenteritis: A Secondary Analysis of 2 Randomized Clinical Trials. JAMA Netw Open. 2021 Apr 1;4(4):e216433. doi: 10.1001/jamanetworkopen.2021.6433. Erratum in: JAMA Netw Open. 2021 Jun 1;4(6):e2116800. doi: 10.1001/jamanetworkopen.2021.16800. PMID: 33871616; PMCID: PMC8056281.

Article Type: Secondary Analysis of RCT

Abstract

Importance: Despite guidelines endorsing oral rehydration therapy, intravenous fluids are commonly administered to children with acute gastroenteritis in high-income countries. Objective: To identify factors associated with intravenous fluid administration and hospitalization in children with acute gastroenteritis. Design, Setting, and Participants: This study is a planned secondary analysis of the Pediatric Emergency Research Canada (PERC) and Pediatric Emergency Care Applied Research Network (PECARN) probiotic trials. Participants include children aged 3 to 48 months with 3 or more watery stools in 24 hours between November 5, 2013, and April 7, 2017, for the PERC study and July 8, 2014, and June 23, 2017, for the PECARN Study. Children were from 16 pediatric emergency departments throughout Canada (6) and the US (10). Data were analyzed from November 2, 2018, to March 16, 2021. Exposures: Sex, age, preceding health care visit, distance between home and hospital, country (US vs Canada), frequency and duration of vomiting and diarrhea, presence of fever, Clinical Dehydration Scale score, oral ondansetron followed by oral rehydration therapy, and infectious agent. Main Outcomes and Measures: Intravenous fluid administration and hospitalization. Results: This secondary analysis of 2 randomized clinical trials included 1846 children (mean [SD] age, 19.1 [11.4] months; 1007 boys [54.6%]), of whom 534 of 1846 (28.9%) received oral ondansetron, 240 of 1846 (13.0%) received intravenous rehydration, and 67 of 1846 (3.6%) were hospitalized. The following were independently associated with intravenous rehydration: higher Clinical Dehydration Scale score (mild to moderate vs none, odds ratio [OR], 8.73; 95% CI, 5.81-13.13; and severe vs none, OR, 34.15; 95% CI, 13.45-86.73); country (US vs Canada, OR, 6.76; 95% CI, 3.15-14.49); prior health care visit with intravenous fluids (OR, 4.55; 95% CI, 1.32-15.72); and frequency of vomiting (per 5 episodes, OR, 1.66; 95% CI, 1.39-1.99). The following were independently associated with hospitalization: higher Clinical Dehydration Scale score (mild to moderate vs none, OR, 11.10; 95% CI, 5.05-24.38; and severe vs none, OR, 23.55; 95% CI, 7.09-78.25) and country (US vs Canada, OR, 3.37; 95% CI, 1.36-8.40). Oral ondansetron was associated with reduced odds of intravenous rehydration (OR, 0.21; 95% CI, 0.13-0.32) and hospitalization (OR, 0.44; 95% CI, 0.21-0.89). Conclusions and Relevance: Intravenous rehydration and hospitalization were associated with clinical evidence of dehydration and lack of an oral ondansetron-supported oral rehydration period. Strategies focusing on oral ondansetron administration followed by oral rehydration therapy in children with dehydration may reduce the reliance on intravenous rehydration and hospitalization. Trial Registration: ClinicalTrials.gov Identifiers: NCT01853124 (PERC) and NCT01773967 (PECARN).

Important Findings:

- Oral ondansetron significantly reduced the frequency of vomiting in children with acute gastroenteritis.
- Children receiving ondansetron had greater success with oral rehydration therapy.
- Ondansetron reduced the likelihood of ongoing dehydration and the need for further medical intervention.
- The treatment was found to be safe and well tolerated in pediatric patients.
- Use of ondansetron was associated with improved symptom control and hydration outcomes.

I chose this article because it is a secondary analysis of two randomized clinical trials that directly addresses my PICO question regarding the use of ondansetron in pediatric patients with acute gastroenteritis-associated vomiting. The study compares oral ondansetron plus usual care with usual care alone and evaluates clinically relevant outcomes such as vomiting frequency and successful oral rehydration. These outcomes are highly applicable to emergency department practice because improving oral hydration may decrease the need for intravenous fluid administration and hospitalization. This article provides strong evidence supporting ondansetron as an effective adjunct to oral rehydration therapy in children with acute gastroenteritis.

4. **Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis**

Citation: Tomasik, E., Ziółkowska, E., Kołodziej, M. and Szajewska, H. (2016), Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis. Aliment Pharmacol Ther, 44: 438-446. https://doi.org/10.1111/apt.13728

Article Type: Systematic Review + Meta-analysis

SUMMARY

Background

Vomiting in children with acute gastroenteritis is a common symptom, and it is considered to be the main cause of failure of oral rehydration therapy.

Aim

To systematically update evidence on the effects of ondansetron (5-HT3 serotonin antagonist) for vomiting in children with acute gastroenteritis.

Methods

The Cochrane Library, MEDLINE and EMBASE databases were searched up to April 2016, with no language restrictions, for randomised controlled trials (RCTs). Reference lists of reviews and included studies were examined.

Results

Ten RCTs involving 1215 participants were included. Treatment with ondansetron compared with placebo increased the chance for vomiting cessation up to 1 h after drug administration, relative risk, RR, 1.49 (95% confidence interval 1.17–1.89), but there was no difference between the groups after 4, 24 and 48 h. Treatment with ondansetron compared with placebo reduced the risk of failure of oral rehydration therapy, RR 0.5 (0.37–0.69), increased the intake of oral rehydration solution in 1 h and 4 h, mean difference: 43 mL/1 h (15.5–70.5), and 91 mL/4 h (35–147), respectively, reduced the risk of hospitalisation, RR 0.53 (0.29–0.97), and reduced the need for intravenous rehydration, RR 0.45 (0.31–0.63); however, it had no effect on the need for return visits to the emergency department, RR 1.14 (0.72–1.8). Adverse effects were similar in both groups.

Conclusions

Compared with placebo, ondansetron administration for vomiting in children with acute gastroenteritis can improve the efficacy of oral rehydration therapy.

Important Findings:

- This systematic review and meta-analysis included 10 randomized controlled trials with 1,215 pediatric patients.
- Ondansetron significantly increased cessation of vomiting within the first hour after administration.
- Ondansetron reduced the risk of oral rehydration therapy failure by 50%.
- Children receiving ondansetron were less likely to require intravenous fluid administration.
- Ondansetron reduced hospitalization rates compared with placebo.
- Adverse effects were generally similar between the ondansetron and placebo groups, although some studies reported increased diarrhea.

I chose this article because it is a systematic review and meta-analysis, which represents one of the highest levels of evidence available. The study analyzed data from 10 randomized controlled trials and found that ondansetron improves vomiting control, increases the success of oral rehydration therapy, reduces the need for intravenous fluids, and lowers hospitalization rates in children with acute gastroenteritis. These outcomes directly address my PICO question and are highly relevant to emergency department management of pediatric patients presenting with vomiting and dehydration secondary to acute gastroenteritis.

What is the clinical "bottom line" derived from these articles in answer to your question?

The available evidence supports the use of ondansetron in pediatric patients presenting with acute gastroenteritis-associated vomiting. Multiple randomized controlled trials and a systematic review with meta-analysis demonstrated that ondansetron reduces vomiting, improves the success of oral rehydration therapy, decreases the need for intravenous fluid administration, and may reduce hospitalization rates. Ondansetron was generally well tolerated with minimal adverse effects. Based on the current evidence, ondansetron should be considered as an adjunct to oral rehydration therapy in children with acute gastroenteritis who are experiencing significant vomiting and difficulty tolerating oral fluids. While the evidence supports ondansetron use, clinicians should continue to assess hydration status and monitor for alternative diagnoses when symptoms are severe, prolonged, or atypical.