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Comparative Effectiveness of Ondansetron Versus Domperidone for Vomiting in Pediatric Acute Gastroenteritis: A Systematic Review

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Systematic Review

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Abstract

Introduction

Vomiting in pediatric acute gastroenteritis can interfere with oral rehydration therapy and increase the need for intravenous fluids, emergency department observation, or hospitalization. Ondansetron is widely studied, but its direct comparative effectiveness against other antiemetics remains clinically important.

Objective

This systematic review evaluated the comparative effectiveness of ondansetron versus other antiemetics in children with acute gastroenteritis-associated vomiting.

Methods

A systematic search was conducted in PubMed, Cochrane Library, and ScienceDirect. Eligible studies included pediatric patients with acute gastroenteritis and vomiting who received ondansetron compared with another antiemetic. Outcomes included vomiting cessation, oral rehydration failure, intravenous rehydration, hospitalization, repeat antiemetic dosing, and adverse events.

Results

Four studies involving 1,014 children were included. All compared ondansetron with domperidone, while one also included placebo. Ondansetron generally showed better outcomes than domperidone. At 24 hours, vomiting cessation was higher with ondansetron in Ahmad et al. (89.4% vs 80.6%) and Hanif et al. (95.1% vs 85.5%). Rerksuppaphol and Rerksuppaphol showed a non-significant trend favoring ondansetron (62.2% vs 44.4%). Marchetti et al. found that ondansetron reduced intravenous rehydration compared with domperidone (11.8% vs 25.2%) and improved second oral rehydration success (89.9% vs 65.5%).

Discussion

Ondansetron appears to provide more reliable vomiting control and better support for oral rehydration than domperidone. Safety findings were reassuring, with no serious adverse events reported.

Conclusion

Ondansetron is more effective than domperidone for pediatric acute gastroenteritis-associated vomiting, especially when vomiting threatens oral rehydration success.

Introduction

Acute gastroenteritis remains one of the most common causes of vomiting, diarrhea, dehydration, and emergency department attendance in children. Although most cases are self-limiting, persistent vomiting can interrupt oral rehydration therapy, worsen fluid deficit, increase caregiver anxiety, and lead clinicians to escalate treatment to intravenous rehydration or hospital observation. Current pediatric gastroenteritis recommendations continue to emphasize oral rehydration therapy as the foundation of management, particularly in children without severe dehydration, but the role of antiemetic therapy remains more selective and context-dependent.[1]

Vomiting is clinically important because it directly affects the feasibility of oral rehydration. A child who cannot retain oral fluids may be classified as having failed oral rehydration even when the underlying dehydration is still mild or moderate. In this setting, an effective antiemetic may help break the vomiting–dehydration cycle, allowing oral rehydration to succeed and potentially reducing the need for intravenous fluids, prolonged emergency department stay, or hospitalization. This practical rationale explains why antiemetics are commonly used in pediatric emergency and outpatient settings, despite persistent variation in guideline recommendations and prescribing patterns.[2,3]

Ondansetron, a selective 5-hydroxytryptamine-3 receptor antagonist, has become the most studied antiemetic for children with acute gastroenteritis-associated vomiting. Evidence from randomized trials and meta-analyses suggests that ondansetron can reduce ongoing vomiting, improve oral rehydration success, and decrease the need for intravenous rehydration or hospital-based care in selected children.[3,4] However, its use is not entirely uniform across practice settings, partly because of concerns regarding adverse effects, including diarrhea and rare cardiac rhythm concerns, and partly because benefit may vary according to dehydration status, baseline vomiting severity, and whether oral rehydration has already failed.[5]

Domperidone, a dopamine receptor antagonist, is another antiemetic frequently used in children in several countries. However, compared with ondansetron, its efficacy for acute gastroenteritis-associated vomiting is less consistent, and concerns have been raised regarding cardiac safety, particularly when used in higher doses or in vulnerable patients. In several settings, domperidone continues to be prescribed because of familiarity, availability, and local practice patterns, even though comparative evidence has not consistently shown superiority over other approaches.[6,7]

Direct comparisons between ondansetron and domperidone are especially relevant because clinicians often need to choose between available antiemetic options rather than between an antiemetic and placebo alone. Marchetti et al. showed that, among children who failed initial oral rehydration therapy, ondansetron reduced the need for intravenous rehydration and improved oral rehydration success compared with domperidone.[6] Subsequent comparative

trials from Pakistan also reported better 24-hour vomiting cessation with ondansetron than domperidone, although some outcomes, such as early vomiting cessation or need for a second dose, were not always statistically significant.[6,8]

The broader evidence base also supports ondansetron as the antiemetic with the most consistent benefit in pediatric acute gastroenteritis. A recent meta-analysis found that ondansetron was the only antiemetic with clear evidence for improving vomiting cessation and reducing hospitalization and intravenous rehydration, while evidence for other antiemetics was weaker or more uncertain.[3] More recent comparative and network evidence has similarly suggested that ondansetron tends to rank favorably against domperidone and metoclopramide for controlling vomiting in children with acute gastroenteritis.[9]

Despite this, several gaps remain. First, direct head-to-head evidence comparing ondansetron with other antiemetics is smaller than the broader placebo-controlled ondansetron literature. Second, trials differ in age range, dehydration severity, clinical setting, dosing strategy, timing of outcome assessment, and whether oral rehydration failure was required before antiemetic administration. Third, many clinically important outcomes, such as oral rehydration failure, hospitalization, repeated vomiting, need for additional antiemetic dosing, and adverse events, are reported inconsistently across studies.[10] These variations limit the ability of clinicians to translate the evidence into a clear bedside choice.

Although a recent network meta-analysis has attempted to rank ondansetron, domperidone, metoclopramide, and other antiemetics for pediatric acute gastroenteritis, its conclusions are still shaped by the inherent limitations of indirect comparison. Treatment ranking in a network model does not always translate into a clinically actionable choice, particularly when included trials differ in dehydration severity, timing of drug administration, failure or non-failure of initial oral rehydration therapy, comparator selection, and outcome measurement. Importantly, the practical question faced by clinicians is often not whether ondansetron is superior to placebo, but whether it performs better than antiemetics that are still commonly used in real-world pediatric practice, especially domperidone. The present systematic review therefore addresses a narrower but more decision-relevant gap by synthesizing only direct comparative studies of ondansetron versus other antiemetics in children with acute gastroenteritis-associated vomiting. By focusing on head-to-head evidence and clinically meaningful outcomes such as oral rehydration failure, vomiting cessation, intravenous rehydration, hospitalization, need for repeat dosing, and adverse events, this review provides a more focused interpretation of the comparative effectiveness of ondansetron beyond treatment ranking alone. This direct-comparison approach strengthens the clinical applicability of the evidence and helps clarify whether ondansetron should be preferred over alternative antiemetics in routine pediatric acute gastroenteritis management.

Therefore, this systematic review aims to evaluate the comparative effectiveness of ondansetron versus other antiemetics in children with acute gastroenteritis presenting with vomiting. The review focuses on clinically relevant outcomes, including oral rehydration failure, vomiting cessation, hospitalization, need for intravenous rehydration, and safety. By synthesizing direct comparative evidence, this review seeks to clarify whether ondansetron offers meaningful advantages over alternative antiemetics used in pediatric acute gastroenteritis.

Methods

This systematic review has been registered in the PROSPERO database with registration number CRD420261445189.

Study Design

This systematic review was conducted to evaluate the comparative effectiveness of ondansetron versus other antiemetics in children with acute gastroenteritis-associated vomiting. The review was structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. The review question was developed using the PICO approach: children with acute gastroenteritis presenting with vomiting as the population, ondansetron as the intervention, other antiemetics as the comparator, and oral rehydration failure, vomiting cessation, hospitalization, need for intravenous rehydration, and adverse events as outcomes of interest.

Eligibility Criteria

Studies were considered eligible if they included pediatric patients with acute gastroenteritis-associated vomiting and directly compared ondansetron with another antiemetic agent, including but not limited to domperidone, metoclopramide, dimenhydrinate, or similar agents. Eligible studies included randomized controlled trials and comparative clinical studies that reported at least one relevant clinical outcome, such as vomiting cessation, repeated vomiting, failure of oral rehydration therapy, need for intravenous or nasogastric rehydration, hospital admission, emergency department observation, need for additional antiemetic dosing, or adverse events.

Studies were excluded if they involved adult populations, non-gastroenteritis causes of vomiting, non-comparative study designs, placebo-only comparisons without another antiemetic comparator, inappropriate participant characteristics, or intervention regimens that did not match the review question. Reviews, editorials, letters, conference abstracts without sufficient extractable data, and studies without accessible full-text data were also excluded.

Information Sources and Search Strategy

A literature search was performed using PubMed, the Cochrane Library, and ScienceDirect. The search strategy was designed to identify studies comparing ondansetron with other antiemetics for vomiting in pediatric acute gastroenteritis. The database search identified 65 records, consisting of 14 records from PubMed, 14 records from the Cochrane Library, and 37 records from ScienceDirect.

The PubMed search strategy was:

(acute gastroenteritis OR gastroenteritis OR diarrhoea OR diarrhea) AND (vomiting OR emesis OR nausea) AND (ondansetron) AND (domperidone) AND (children OR pediatric OR paediatric OR child OR infant)

The Cochrane Library search strategy was:

(acute gastroenteritis OR gastroenteritis OR diarrhoea OR diarrhea) AND vomiting AND ondansetron AND domperidone AND children

The ScienceDirect search strategy was:

"acute gastroenteritis" AND vomiting AND ondansetron AND domperidone AND children

The search terms were adapted to each database while maintaining the core concepts of acute gastroenteritis, vomiting, ondansetron, comparator antiemetics, and pediatric population.

Study Selection

All identified records were screened based on title and abstract. Studies that were clearly unrelated to the review question were excluded at this stage. Duplicate records were then identified and removed. Full-text articles were assessed for eligibility based on the predefined inclusion and exclusion criteria. The study selection process followed the PRISMA flow diagram. From 65 identified records, 59 were excluded during title and abstract screening. Six records were assessed for duplication, and one duplicate was removed. Five full-text articles were assessed for eligibility, of which one was excluded due to inappropriate participant characteristics and inappropriate intervention regimen. Finally, four studies were included in the qualitative synthesis.

Data Extraction

Data were extracted using a standardized extraction table developed for this review. The extracted variables included first author and year of publication, country and setting, study design, population characteristics, sample size, age range or mean age, ondansetron regimen, comparator antiemetic regimen, primary outcome, secondary outcomes, key findings, adverse events, risk of bias, and summary of findings. Particular attention was given to clinically relevant outcomes, including vomiting cessation at 6 and 24 hours, need for second antiemetic dose, failure of oral rehydration therapy, need for intravenous or nasogastric rehydration, emergency department observation, hospitalization, and treatment-related adverse events.

Risk of Bias Assessment

Risk of bias was assessed qualitatively based on key methodological domains, including study design, randomization process, allocation concealment, blinding, comparability of baseline characteristics, completeness of follow-up, clarity of outcome reporting, and appropriateness of statistical analysis.

Outcomes

The primary outcomes of interest were oral rehydration failure and vomiting cessation. Oral rehydration failure was defined according to each study's criteria and included failure to tolerate oral rehydration, need for intravenous or nasogastric rehydration, or inability to continue oral intake because of persistent vomiting. Vomiting cessation was assessed at the reported follow-up points, particularly at 6 hours and 24 hours after treatment.

Secondary outcomes included need for repeat antiemetic dosing, number of vomiting episodes, emergency department observation longer than 6 hours, hospitalization, need for laboratory testing, emergency department revisits, and adverse events. Safety outcomes included reported adverse events such as diarrhea, drowsiness, asthenia, irritability, abdominal pain, or other treatment-related symptoms.

Data Synthesis

A qualitative synthesis was performed because the included studies varied in clinical setting, age range, dehydration status, timing of intervention, comparator regimen, outcome definition, and follow-up duration. The findings were synthesized narratively according to the main outcome domains: vomiting cessation, oral rehydration failure, need for intravenous rehydration, hospitalization or emergency department outcomes, need for additional antiemetic dosing, and adverse events. Where available, numerical outcome data were presented using the original study-reported event counts, percentages, p-values, relative risks, and confidence intervals. No pooled meta-analysis was performed because of the limited number of eligible head-to-head studies and the heterogeneity of outcome definitions and clinical protocols across studies.

Records identified through database searching (n = 65)

PubMed: 14

Cochrane Library: 14

ScienceDirect: 37

Table 1
Characteristics and results of the included studies

First Author (Year)	Country/Setting	Study Design	Population	Sample Size	Age Range/Mean Age	Ondansetron Regimen	Comparator Regimen
Ahmad et al. (2022)	Pakistan; Pediatric Emergency Department, Tehsil Headquarter Hospital, Liaqatpur, South Punjab	Open-label randomized controlled trial	Children aged < 12 years with acute gastroenteritis and ≥ 3 non-bilious, non-bloody vomiting episodes within 24 hours; signs/symptoms of AGE included diarrhea with or without fever, abdominal pain, and bloating/discomfort; severe dehydration and major comorbidities were excluded	300 children; 150 ondansetron, 150 domperidone	Mean age 4.7 ± 2.3 years overall; ondansetron 4.6 ± 2.2 years, domperidone 4.9 ± 2.5 years	Oral ondansetron suspension 0.15 mg/kg body weight; second dose given if vomiting occurred within 15 minutes after first dose	Oral domperidone suspension 0.5 mg/kg body weight; second dose given if vomiting occurred within 15 minutes after first dose
Hanif et al. (2019)	Pakistan; pediatric emergency department of a public tertiary pediatrics hospital	Open-label, two-arm randomized trial	Children aged 3–60 months with acute gastroenteritis-associated vomiting, defined as ≥ 3 non-bilious, non-bloody vomiting episodes within 24 hours with signs of AGE such as diarrhea, abdominal pain, bloating/discomfort, with or without fever; children with severe dehydration, severe malnutrition, major comorbidities, recent antiemetic use, or inability to tolerate oral feed were excluded	282 enrolled; 27 excluded due to severe persistent dehydration/admission and 15 lost to follow-up; 240 completed analysis: 123 ondansetron, 117 domperidone	Mean age 29 ± 16 months overall; ondansetron 28 ± 15 months, domperidone 27 ± 19 months	Oral ondansetron suspension 0.15 mg/kg body weight; second dose given within 15 minutes if immediate vomiting occurred after administration	Oral domperidone suspension 0.5 mg/kg body weight; second dose given within 15 minutes if immediate vomiting occurred after administration

First Author (Year)	Country/Setting	Study Design	Population	Sample Size	Age Range/Mean Age	Ondansetron Regimen	Comparator Regimen
Rerksuppaphol & Rerksuppaphol (2013)	Thailand; pediatric outpatient department, Srinakharinwirot University Hospital	Open-label randomized controlled trial	Children ≤ 15 years with acute gastroenteritis and ≥ 3 non-bilious, non-bloody vomiting episodes within 24 hours, plus AGE symptoms such as diarrhea, abdominal pain, bloating/discomfort, or low-grade fever; children with severe dehydration, severe malnutrition, need for IV fluid, major comorbidities, recent antiemetic use, or inability to tolerate oral feeding were excluded	76 randomized: 38 ondansetron, 38 domperidone; 73 included in 24-hour primary analysis: 37 ondansetron, 36 domperidone	Median age 3.8 years, range 0.4–14.6 years; ondansetron mean age 3.7 years, domperidone 4.7 years	Orally disintegrating ondansetron tablet: 2 mg if < 15 kg, 4 mg if 15–30 kg, and 8 mg if > 30 kg; repeated as needed at intervals > 8 hours after discharge	Domperidone suspension: 2.5 mg if < 15 kg, 5 mg if 15–30 kg, an 10 mg if > 30 kg; repeated as needed at intervals > 8 hours after discharge
Marchetti et al. (2016)	Italy; 15 pediatric emergency departments	Prospective multicenter double-blind randomized controlled trial	Children aged 1–6 years with vomiting due to presumed acute gastroenteritis, with or without diarrhea, who had > 3 non-bilious, non-bloody vomiting episodes within 24 hours and failed an initial oral rehydration attempt; children with severe dehydration, chronic disease, recent antiemetic/antidiarrheal use, QT-prolonging drugs, or inability to complete follow-up were excluded	356 randomized after failed initial ORT: 119 ondansetron, 119 domperidone, 118 placebo	Median age: ondansetron 3.1 years, domperidone 3.2 years, placebo 3.3 years	Single oral dose of ondansetron syrup 0.15 mg/kg; second dose allowed if vomiting occurred within 15 minutes	Domperidone syrup 0.5 mg/kg as active comparator; placebo syru also included second dose allowed if vomiting occurred within 15 minutes

First Author (Year)	Country/Setting	Study Design	Population	Sample Size	Age Range/Mean Age	Ondansetron Regimen	Comparator Regimen

Results

Study Selection

The database search identified 65 records, consisting of 14 records from PubMed, 14 from the Cochrane Library, and 37 from ScienceDirect (Fig. 1). After title and abstract screening, 59 records were excluded because they were not relevant to the review question. Six potentially relevant records were then assessed for duplication, and one duplicate record was removed. Therefore, five full-text articles were assessed for eligibility. One study was excluded at the full-text stage because of inappropriate participant characteristics and an unsuitable intervention regimen. Finally, four studies were included in the qualitative synthesis: Ahmad et al. (2022), Hanif et al. (2019), Rerksuppaphol and Rerksuppaphol (2013), and Marchetti et al. (2016).

Study Characteristics

The four included studies were published between 2013 and 2022 and were conducted in Pakistan, Thailand, and Italy. Three studies directly compared ondansetron versus domperidone, while one multicenter trial compared ondansetron, domperidone, and placebo. Overall, the included studies enrolled 1,014 children with acute gastroenteritis-associated vomiting. The study populations generally consisted of children presenting with at least three episodes of non-bilious, non-bloody vomiting within 24 hours, with associated clinical features of acute gastroenteritis such as diarrhea, abdominal pain, bloating, discomfort, or fever. Children with severe dehydration, major chronic comorbidities, recent antiemetic use, severe malnutrition, or inability to tolerate oral intake were generally excluded (Table 1).

The intervention across the studies was oral ondansetron, most commonly administered at 0.15 mg/kg body weight. Comparator treatment was oral domperidone, usually given at 0.5 mg/kg body weight, although Rerksuppaphol and Rerksuppaphol used weight-based fixed dosing for both ondansetron and domperidone. The largest and methodologically strongest study was the multicenter double-blind randomized controlled trial by Marchetti et al., which randomized 356 children across 15 pediatric emergency departments in Italy after failure of initial oral rehydration therapy.

Risk of Bias

All included studies were assessed as having low risk of bias in the extracted dataset. However, some methodological considerations should be noted. Ahmad et al., Hanif et al., and Rerksuppaphol and Rerksuppaphol were open-label randomized trials, which may introduce performance or detection bias, particularly for symptom-based outcomes such as vomiting cessation. Marchetti et al. had the strongest design, using a multicenter, double-blind, randomized controlled approach with active and placebo comparators. Across studies, baseline characteristics were generally comparable between treatment arms, and outcomes were clinically relevant to pediatric acute gastroenteritis management.

Vomiting Cessation

Vomiting cessation was the most consistently reported outcome. Overall, the direction of effect favored ondansetron over domperidone, although statistical significance varied across studies.

Ahmad et al. reported that vomiting cessation at 6 hours occurred in 126/150 children (84.0%) in the ondansetron group and 118/150 children (78.7%) in the domperidone group, without a statistically significant difference. However, at 24 hours, cessation of vomiting was significantly higher with ondansetron, occurring in 127/142 children (89.4%) compared with 108/134 children (80.6%) in the domperidone group.

Similarly, Hanif et al. found that vomiting cessation at 6 hours was numerically higher with ondansetron than domperidone, occurring in 107/123 children (86.9%) versus 95/117 children (81.2%), although this difference was not statistically significant. At 24 hours, ondansetron showed a significant advantage, with vomiting cessation in 117/123 children (95.1%) compared with 100/117 children (85.5%) in the domperidone group.

Rerksuppaphol and Rerksuppaphol also reported a numerically higher 24-hour vomiting cessation rate with ondansetron, but the difference was not statistically significant. Vomiting stopped within 24 hours in 23/37 children (62.2%) in the ondansetron group compared with 16/36 children (44.4%) in the domperidone group. Although this study suggested a favorable trend for ondansetron, the small sample size likely limited statistical power.

In Marchetti et al., vomiting outcomes during emergency department stay strongly favored ondansetron. Children receiving ondansetron had fewer vomiting episodes during the emergency department stay compared with those receiving domperidone, and the proportion of children with vomiting during ED stay was markedly lower in the ondansetron group (16.8%) than in the domperidone group (44.5%).

Oral Rehydration Failure and Need for Intravenous Rehydration

The most direct evidence for oral rehydration failure came from Marchetti et al., where the primary outcome was the need for nasogastric or intravenous rehydration after failure of symptomatic oral treatment. No child received nasogastric rehydration. Intravenous rehydration was required in 14/119 children (11.8%) receiving ondansetron compared with 30/119 children (25.2%) receiving domperidone and 34/118 children (28.8%) receiving placebo. Ondansetron reduced the risk of intravenous rehydration compared with domperidone and placebo.

Hanif et al. also reported better oral rehydration tolerance with ondansetron. Oral rehydration intolerance occurred in 12/123 children (9.7%) in the ondansetron group compared with 23/117 children (19.6%) in the domperidone group. This suggests that ondansetron may improve the success of oral rehydration by reducing ongoing vomiting after antiemetic administration.

Need for Additional Antiemetic Dose

Three studies reported the need for an additional antiemetic dose. Ahmad et al. found that a second dose within 15 minutes was required in 27/150 children (18.0%) in the ondansetron group compared with 38/150 children (25.3%) in the domperidone group. Hanif et al. reported a similar pattern, with a second dose required in 18/123 children (14.6%) receiving ondansetron and 26/117 children (22.2%) receiving domperidone.

In Rerksuppaphol and Rerksuppaphol, children in the domperidone group required more additional antiemetic doses than those in the ondansetron group. The median number of additional doses was 1.5 doses in the domperidone group compared with 1 dose in the ondansetron group. This finding supports the possibility that ondansetron provides more sustained symptom control than domperidone, even when complete vomiting cessation does not differ significantly.

Hospitalization and Emergency Department Outcomes

Hospitalization-related outcomes were most clearly reported in Marchetti et al. Ondansetron reduced the need for prolonged emergency department observation and improved the success of the second oral rehydration attempt. Observation longer than 6 hours was required in 16.8% of children receiving ondansetron compared with 31.1% receiving domperidone and 33.1% receiving placebo. Success of the second oral rehydration attempt was also higher with ondansetron (89.9%) than with domperidone (65.5%) or placebo (64.4%). Hospital admission was numerically lower in the ondansetron group, although the difference was not statistically significant.

Adverse Events

Safety outcomes were generally reassuring. Ahmad et al., Hanif et al., and Rerksuppaphol and Rerksuppaphol reported no major adverse events in either treatment group. Hanif et al. specifically noted that no adverse events or diarrhea exacerbation occurred.

Marchetti et al. reported no serious adverse events. Mild adverse events occurred in 6 children receiving ondansetron, 5 receiving domperidone, and 2 receiving placebo. Reported symptoms included drowsiness, asthenia, irritability, diarrhea, and abdominal pain. Ondansetron was associated with a small increase in diarrhea episodes during the emergency department stay, but this was not considered clinically substantial in the context of its benefit in reducing vomiting and intravenous rehydration.

Overall Synthesis

Across the four included studies, ondansetron generally showed better clinical effectiveness than domperidone for pediatric acute gastroenteritis-associated vomiting. The benefit was most consistent for 24-hour vomiting cessation, oral rehydration success, and reduction in intravenous rehydration requirement. The strongest evidence came from the multicenter double-blind randomized trial by Marchetti et al., which showed that ondansetron substantially reduced intravenous rehydration and vomiting during emergency department stay compared with domperidone. Smaller open-label trials from Pakistan and Thailand also supported a favorable trend toward ondansetron, particularly for 24-hour vomiting cessation and reduced need for additional dosing.

Overall, the findings suggest that ondansetron is more effective than domperidone for improving vomiting control and facilitating oral rehydration in children with acute gastroenteritis, with no clear increase in serious adverse events. Domperidone showed limited comparative benefit and was generally less effective than ondansetron across clinically relevant outcomes.

Discussion

Principal Findings

This systematic review found that ondansetron generally demonstrated better comparative effectiveness than domperidone for controlling vomiting in children with acute gastroenteritis. Across the four included head-to-head studies, the direction of effect consistently favored ondansetron for clinically relevant outcomes, particularly 24-hour vomiting cessation, tolerance of oral rehydration, reduction in intravenous rehydration, and lower need for repeat antiemetic dosing. The strongest evidence came from Marchetti et al., a multicenter double-blind randomized controlled trial, which showed that ondansetron significantly reduced intravenous rehydration compared with domperidone and placebo, while also improving the success of repeated oral rehydration attempts.6 These findings support the clinical value of ondansetron not merely as a symptom-relieving agent, but as a facilitator of successful oral rehydration in children who continue to vomit during acute gastroenteritis.

Interpretation of the Findings

The superiority of ondansetron is clinically plausible. Vomiting in acute gastroenteritis may prevent adequate fluid intake and can quickly shift management from oral rehydration to intravenous therapy or prolonged observation. Ondansetron, through serotonin 5-HT3 receptor antagonism, can suppress emetic signaling from the gastrointestinal tract and central vomiting pathways, thereby improving the child's ability to retain oral fluids.[3,4,11,12] In contrast, domperidone acts mainly as a dopamine receptor antagonist and has shown inconsistent efficacy in pediatric gastroenteritis. The included studies reflected this difference: domperidone was associated with lower vomiting cessation rates, greater need for additional dosing, and poorer oral rehydration success in several comparisons.[6,11]

Comparison With Previous Evidence

The findings of this review are aligned with previous systematic reviews and meta-analyses showing that ondansetron is the antiemetic with the most consistent evidence for pediatric acute gastroenteritis-associated vomiting. Niño-Serna et al. reported that ondansetron improved vomiting cessation and reduced hospitalization and intravenous rehydration, whereas evidence for other antiemetics was weaker or less certain.[3] Earlier reviews also supported the benefit of ondansetron in reducing persistent vomiting and intravenous fluid use, although they emphasized that the evidence base was mainly placebo-controlled rather than based on direct active-comparator trials.[12,13] The present review adds value by narrowing the focus to direct head-to-head comparisons, which are more relevant to real-world prescribing decisions where clinicians must choose between commonly used antiemetics rather than between ondansetron and placebo alone.

Clinical Relevance of Direct Comparison

This review is particularly important because domperidone remains used in some settings despite limited evidence of benefit. The comparative question is therefore practical: whether ondansetron should be preferred over domperidone when an antiemetic is considered necessary. The available evidence suggests that ondansetron provides more reliable clinical benefit, especially among children with ongoing vomiting after initial oral rehydration. In Marchetti et al., ondansetron reduced the need for intravenous rehydration by more than half compared with domperidone, while domperidone performed similarly to placebo for several outcomes.[7] This is clinically meaningful because avoiding intravenous therapy can reduce procedural discomfort, emergency department burden, healthcare cost, and unnecessary hospitalization.[10]

Oral Rehydration and Emergency Department Outcomes

The most important practical implication is that ondansetron may help preserve oral rehydration as the primary treatment strategy. Oral rehydration remains the cornerstone of pediatric acute gastroenteritis management, and international recommendations continue to emphasize its use in children without severe dehydration.[1,5] However, vomiting is one of the main reasons oral rehydration fails in practice. In this review, ondansetron improved oral rehydration tolerance and reduced escalation to intravenous therapy.[5–7] These findings suggest that ondansetron is best understood as an adjunct to oral rehydration rather than as a replacement for standard fluid therapy. Its greatest value may be in children with mild-to-moderate dehydration or repeated vomiting who are otherwise candidates for oral rehydration but are unable to retain fluids.

Safety Considerations

The safety profile observed across the included studies was reassuring. No serious adverse events were reported in the smaller comparative trials, and Marchetti et al. reported only mild adverse events, including drowsiness, asthenia, irritability, diarrhea, and abdominal pain.[10,13,14] A small increase in diarrhea has been repeatedly noted with ondansetron, but this effect is usually mild and self-limiting.[3–5] Cardiac safety remains an important consideration, particularly in children with electrolyte abnormalities, congenital long-QT syndrome, or concomitant QT-prolonging medications. However, available pediatric evidence suggests that a single oral dose in appropriately selected children has a low risk of clinically important QT prolongation.[14] Domperidone, meanwhile, has been restricted in several regulatory settings because of concerns regarding QT prolongation, ventricular arrhythmia, and sudden cardiac death, particularly with higher doses or vulnerable patients.[15] Therefore, the balance of efficacy and safety appears more favorable for ondansetron than domperidone when used selectively and appropriately.

Implications for Practice

The findings support the selective use of ondansetron in children with acute gastroenteritis-associated vomiting, especially when vomiting interferes with oral rehydration. It should not be used indiscriminately in all children with diarrhea or mild symptoms, because many cases improve with oral rehydration alone. In the Marchetti trial, more than half of eligible children were successfully managed with oral rehydration before randomization, highlighting that antiemetics are not universally required.[7] The most reasonable clinical approach is therefore stepwise: initiate oral rehydration, consider ondansetron when vomiting prevents successful fluid intake, reassess hydration status, and reserve intravenous therapy for persistent oral rehydration failure or clinical deterioration. This approach is consistent with guideline-based care and minimizes unnecessary pharmacologic exposure.[1,5]

Strengths and Limitations

The strength of this review lies in its focused synthesis of direct comparative evidence between ondansetron and other antiemetics, particularly domperidone. This approach improves clinical interpretability compared with broader evidence syntheses that rely heavily on indirect comparisons or placebo-controlled trials. However, several limitations should be acknowledged. First, only four eligible studies were included, and three had open-label designs, which may introduce performance and detection bias. Second, the studies differed in age range, clinical setting, dehydration severity, dosing regimen, timing of outcome assessment, and definitions of treatment success. Third, most available direct evidence compared ondansetron with domperidone, meaning that conclusions regarding metoclopramide, dimenhydrinate, or other antiemetics remain limited. Fourth, adverse event detection was not uniformly powered or standardized, so rare safety outcomes could not be confidently assessed.

Future Research

Future studies should prioritize adequately powered, double-blind randomized trials comparing ondansetron with other active antiemetics using standardized outcome definitions. Important outcomes should include vomiting cessation, oral rehydration failure, intravenous rehydration, hospitalization, emergency department length of stay, caregiver satisfaction, cost-effectiveness, and adverse events. Additional research is also needed to identify which children benefit most from ondansetron, including stratification by dehydration severity, vomiting frequency, age group, and presence of predominant diarrhea. Future evidence should also clarify whether single-dose strategies are sufficient or whether selected patients benefit from carefully supervised repeat dosing.

Overall Interpretation

Overall, the evidence suggests that ondansetron is more effective than domperidone for improving vomiting control and supporting oral rehydration in children with acute gastroenteritis. Its benefit is most apparent when vomiting threatens oral rehydration success or leads to escalation of care. Domperidone showed limited comparative effectiveness and has a less favorable regulatory safety context. Therefore, in children with acute gastroenteritis-associated vomiting who require antiemetic therapy, ondansetron appears to be the preferred option over domperidone, provided that it is used selectively, at appropriate doses, and with attention to contraindications.

Conclusion

This systematic review suggests that ondansetron is more effective than domperidone for managing vomiting in children with acute gastroenteritis, particularly in improving 24-hour vomiting cessation, facilitating oral rehydration, and reducing escalation to intravenous rehydration. The strongest evidence came from a multicenter double-blind randomized trial showing that ondansetron reduced intravenous rehydration compared with domperidone, while smaller open-label trials consistently showed a favorable trend toward better vomiting control with ondansetron. Safety findings were generally reassuring, with no serious adverse events reported across the included studies, although mild diarrhea and other minor symptoms may occur. Overall, ondansetron appears to be the preferred antiemetic option when vomiting interferes with oral rehydration in pediatric acute gastroenteritis, while domperidone shows limited comparative benefit. Further high-quality head-to-head trials are still needed to compare ondansetron with other antiemetics beyond domperidone and to standardize outcome definitions across clinical settings.

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

Not applicable.

Competing interests:

The authors declare that they have no competing interests

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Author Contribution

RP conceptualized and designed the study, conducted the literature search, performed data extraction and analysis, interpreted the findings, and drafted the manuscript. SD contributed to the study design, supervised the research process, verified the data extraction and analysis, critically revised the manuscript for important intellectual content, and approved the final version. Both authors contributed to the interpretation of the results, reviewed and approved the final manuscript, and agreed to be accountable for all aspects of the work.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author.

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Figures

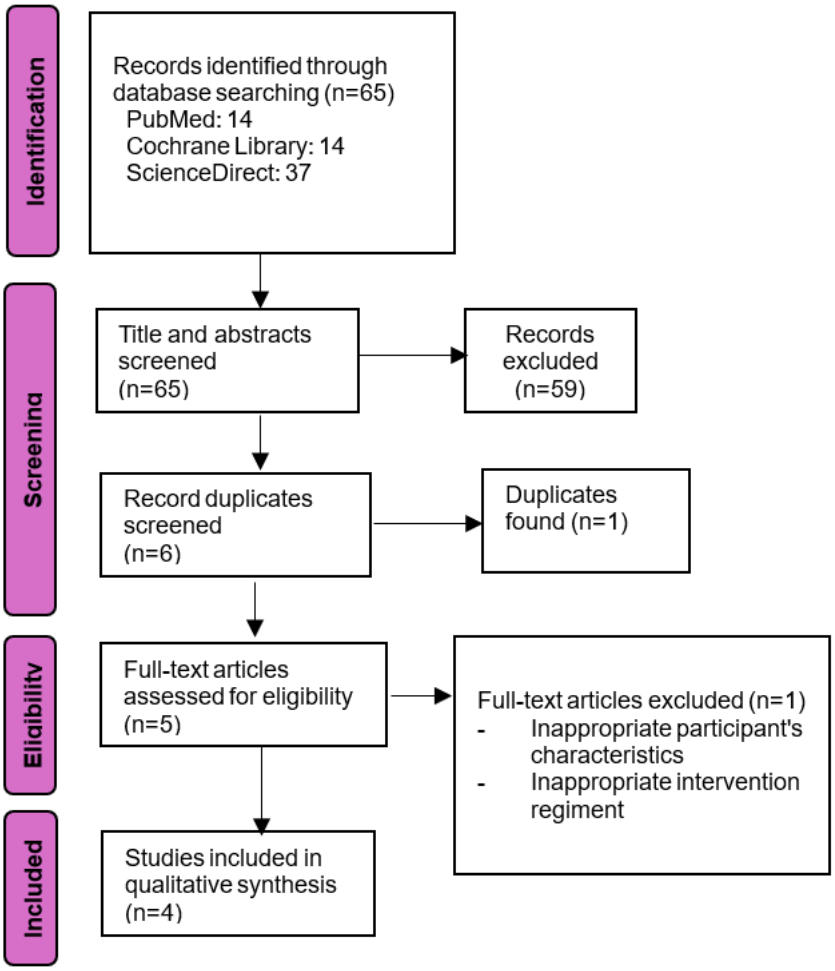

Figure 1

Diagram flow of literature search strategy for this systematic review

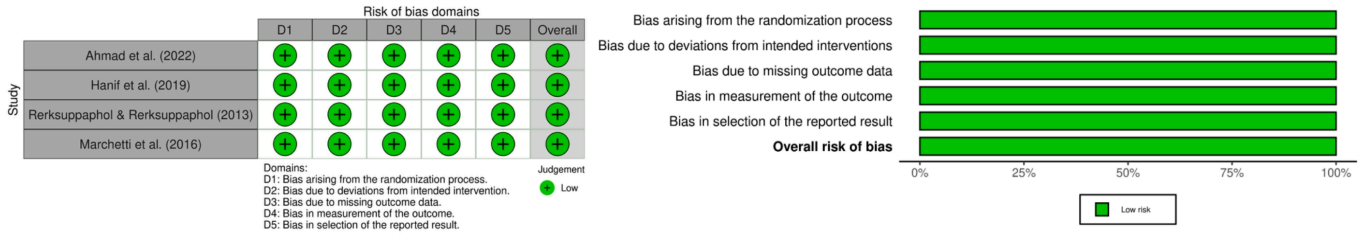

Figure 2

Risk of bias assessment result