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Comparative Efficacy and Safety of Intramuscular Versus Oral Ondansetron in Enhancing Oral Rehydration Therapy among Children with Acute Diarrhea

Hemantbhai S. Patel[1], Keyur B. Patel[2]*

[1]Associate Professor, Vedantaa Institute of Medical Sciences, Dahanu, Palghar, Maharashtra, India
[2]Assistant Professor, Vedantaa Institute of Medical Sciences, Dahanu, Palghar, Maharashtra, India

***Address for Correspondence:** Dr. Keyur B. Patel, Assistant Professor, Vedantaa Institute of Medical Sciences, Dahanu, Palghar, Maharashtra, India
E-mail: keyurpatel310188@gmail.com

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ABSTRACT

Background: Vomiting is a common and distressing symptom in paediatric acute diarrhea that significantly affects the success of oral rehydration therapy. Ondansetron, a 5-HT_3 receptor antagonist, has established efficacy in reducing vomiting and improving ORT tolerance. However, limited data exist comparing the intramuscular and oral routes of administration, particularly in situations where oral intake may be compromised.

Methods: In this single-blind, randomised clinical trial conducted at a tertiary care paediatric emergency department, 100 children aged 1 to 10 years with acute diarrhoea, vomiting, and signs of moderate dehydration were randomly assigned to receive either oral or IM ondansetron at a dose of 0.2 mg/kg. ORT was initiated 30 minutes after drug administration. Results assessed included ORT tolerance, vomiting frequency at 30 minutes, 4 hours, and 48 hours post-intervention, intravenous fluid requirement, and adverse effects.

Results: ORT was successful in 88% of children in the oral group compared to 74% in the IM group. Vomiting within the first 30 minutes occurred in 4% of the oral group and 10% of the IM group. Over 48 hours, vomiting persisted in 4% and 12% of patients. Adverse events such as headache, tachycardia, and diarrhoea were infrequent and comparable between the groups. No statistically significant differences were observed in clinical outcomes or side effects.

Conclusions: The study has concluded that the children with acute diarrhea showed a wide age distribution and varying clinical severity, with moderate-to-severe vomiting episodes before medical referral.

Key-words: Heliothis armigera, Argemone mexicana, Ethanol, acetone, Epithelial lining, Epithelial cells, vacuoles, Gut lining, Gut wall

INTRODUCTION

Acute diarrhoea remains one of the leading causes of illness and death in children under five years of age worldwide, mainly in low- and middle-income countries. Conventional oral rehydration therapy is the foundation for managing mild to moderate dehydration, preventing progression to severe dehydration and avoiding unnecessary hospitalisation or intravenous fluids [1,2].

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Despite ORT's effectiveness, its success is frequently compromised when vomiting continues, a common and distressing symptom that delays continued intake of oral rehydration solution. Vomiting is a major barrier to ORT adherence, may necessitate intravenous rehydration and decreases the simplicity and cost-effectiveness of ORT protocols.

Ondansetron, a selective 5-HT_3 receptor antagonist, has emerged as a valuable adjunct to ORT in paediatric acute diarrhea by reducing emesis and improving tolerance to oral fluids. Multiple randomised controlled trials and systematic reviews have demonstrated ondansetron's benefits. In a double-blind trial of 215 children aged 6 months to 10 years treated for diarrhea, a single oral dose of ondansetron significantly reduced the proportion

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who vomited during ORT, decreased the need for intravenous fluids, and increased mean oral fluid intake compared to placebo [3]. These results support the utility of oral ondansetron in emergency department settings to facilitate ORT among vomiting children.

Similarly, large-scale situations echo these benefits investigations from low-resource. A randomised controlled trial in Pakistan involving 918 children aged 6–60 months found that oral ondansetron reduced intravenous rehydration and decreased vomiting episodes during observation compared with placebo [4]. Moreover, systematic reviews emphasise ondansetron's role in reducing intravenous fluid use, hospitalisation rates, and duration of vomiting, with minimal side effects such as transient diarrhoea or headache [5]. These safety data are echoed in the paediatric guidelines from societies such as the Canadian Paediatric Society, which commends a single dose of oral ondansetron in children aged six months to twelve years with vomiting and mild to moderate dehydration or failed ORT, followed by initiation of ORT 15–30 minutes later. [6,7].

While oral ondansetron is extensively studied and increasingly accepted, there remains limited evidence comparing it with intramuscular administration, especially in situations where oral routes may be compromised or liquid formulations unavailable. Intramuscular administration may offer pharmacokinetic advantages, such as more rapid absorption and better bioavailability in children who are actively vomiting; until now, data are sparse.

A recently published randomised controlled trial in India provides direct evidence on this topic by comparing single-dose IM ondansetron versus oral ondansetron in children aged 3 months to 12 years with acute diarrhoea, vomiting, and some dehydration. In this open-label trial involving 60 children, investigators evaluated failure of ORT, amount of ORS ingested, vomiting frequency, adverse events, and caregiver satisfaction. The results showed no essential differences between the two routes: ORT failure occurred in 31% of IM and 24.1% of oral recipients, need for IV fluids during ORT was similar, mean ORS intake, vomiting episodes, and caregiver satisfaction were comparable. Significantly, no adverse events attributable to either route were observed in the study [8].

This trial fills a serious knowledge opening, indicating that intramuscular ondansetron may not confer a meaningful advantage over the oral route in improving ORT efficacy among vomiting children with some dehydration. However, generalizability is limited by the small sample size and single-center design, demanding additional studies [9].

Hence, a rigorous comparative analysis of efficacy and safety between IM and oral ondansetron is needed. Such data are particularly relevant in resource-limited situations or in clinical scenarios where oral administration is not feasible, such as persistent vomiting or unavailability of appropriate oral formulations. Considering whether IM administration can meaningfully improve results without adding danger could inform guidelines and expand opportunities for clinicians managing paediatric acute diarrhoea with vomiting [10].

This study compares single-dose intramuscular and oral ondansetron before ORT in children with acute diarrhoea, vomiting, and mild to moderate dehydration. Outcomes assessed include ORT failure at four hours, IV fluid need, ORS intake, vomiting frequency, caregiver satisfaction, and adverse events.

MATERIALS AND METHODS

Research Design- This is a prospective study, which was conducted at the emergency department of Paediatrics from January 2024 to December 2024. The aim was to assess and compare the efficacy of oral and intramuscular administration of ondansetron in controlling vomiting among paediatric patients diagnosed with acute diarrhea. Based on the formula for comparative analysis of proportions and assuming an 80% study power and 95% confidence level, the minimum required sample size was calculated as 92. After applying inclusion and exclusion criteria, the final sample included 100 patients, with 50 children in each group. Following informed consent, children were randomly assigned to two equal groups using simple randomisation. One group received oral ondansetron at a dose of 0.2 mg/kg, while the other group received an intramuscular injection of ondansetron at the same dosage. All medication packages were prepared in a blinded manner by an individual not involved in the study. The treating paediatrician and data analysts were blinded to the group assignments. After receiving the assigned intervention, children were started on oral rehydration therapy using low-volume oral rehydration

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solution, given every 5 minutes in 5 mL increments. Children who tolerated ORT without further vomiting were monitored for four hours in the outpatient unit. Follow-up assessments were performed at 30 minutes, 4 hours, and 48 hours post-intervention, either in person or via telephone, to evaluate vomiting episodes and potential side effects such as headache, tachycardia, and diarrhoea. Hospitalisation and intravenous fluid administration were initiated for those who failed ORT.

Inclusion Criteria

- Patients aged less than 18 years.
- Clinical presentation includes watery stools, abdominal cramps, fever, vomiting, dehydration, and irritability.
- Onset of illness within the past 24 hours.

Exclusion Criteria

- Prior antiemetic use before presentation.
- Presence of chronic medical conditions.
- Known allergy or hypersensitivity to 5-HT3 receptor antagonists.
- Clinical evidence of dysentery.
- Surgical abdominal conditions, eg. intussusception.
- Use of any other medications concurrently.

Statistical Analysis- Data were compiled and analysed using SPSS-27 software. Quantitative variables were assessed for normal distribution using the Kolmogorov-Smirnov test. Since the distribution was non-normal, non-parametric tests were applied. The Chi-square test was employed to compare categorical variables such as sex and incidence of vomiting across different time points. In contrast, the Mann-Whitney U test was used for continuous variables like age and weight. $p<0.05$ was considered statistically significant.

RESULTS

The average age of the children was 4.12 years, with a standard deviation of 2.05 years, indicating a moderately wide age distribution ranging from 1.5 to 10 years. The mean body weight was 15.75 kg, with values ranging from 8.0 kg to 28.0 kg, showing expected variability across different age groups. The average time interval between the onset of vomiting and presentation to the emergency department was approximately 6.20 hours, with most children presenting within 2 to 13 hours after symptom onset. On average, patients experienced 5.30 episodes of vomiting per day before referral, which reflects a moderate-to-severe clinical presentation necessitating medical attention (Table 1).

Table 1: Descriptive Statistics of Baseline Quantitative Variables in Children with Acute Diarrhea

Variable	Mean	SD	Maximum	Minimum	Median
Age (years)	4.12	2.05	10	1.5	4
Weight (kg)	15.75	4.8	28	8	14.5
Duration of vomiting before hospital visit (hrs)	6.2	2.95	13	2	6
Number of vomiting episodes per day before referral	5.3	2.1	11	2	5

Among children who received intramuscular ondansetron, ORT was tolerated by 74% of participants, somewhat lower than the 88% tolerance observed in those who received the oral formulation. Vomiting within the first 30 minutes post-administration occurred in 10% of the injection group and 4% of the oral group, representing somewhat better immediate control with oral administration. Vomiting within 4 hours was observed in 8% of children in the injection group and only 2% in the oral group. Similarly, vomiting over 48 hours post-treatment was more frequent in the injection group (12%) than in the oral group (4%), suggesting superior sustained control with the oral form (Table 2).

Out of the total study population, 5% reported headaches, with a somewhat higher occurrence in the injection group (6%) compared to the oral group (4%). Tachycardia was rare, noted in just one child (2%) from the injection group, while none were observed in the oral group. diarrhoea occurred in 3% of patients overall, with 4% of oral recipients affected versus 2% in the injection group. Statistical analysis revealed no significant difference between the two groups for any of the reported adverse effects ($p>0.05$ for all) (Table 3).

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Table 2: Frequency of Vomiting Episodes and ORT Tolerance After Ondansetron Administration by Gender and Route

Administration Route	ORT Tolerance	Vomiting Within 30 Minutes	Vomiting for 4 Hours	Vomiting During 48 Hours
Injection				
Male (n = 29)	22 (75.9%)	2 (6.9%)	3 (10.3%)	4 (13.8%)
Female (n = 21)	15 (71.4%)	3 (14.3%)	1 (4.8%)	2 (9.5%)
Total (n = 50)	37 (74%)	5 (10%)	4 (8%)	6 (12%)
Oral				
Male (n = 30)	26 (86.7%)	1 (3.3%)	1 (3.3%)	1 (3.3%)
Female (n = 20)	18 (90%)	1 (5.0%)	0 (0%)	1 (5%)
Total (n = 50)	44 (88%)	2 (4%)	1 (2%)	2 (4%)
Overall (N = 100)	81 (81%)	7 (7%)	5 (5%)	8 (8%)

Table 3: Frequency of Adverse Effects Following Ondansetron Administration in Children with Acute Diarrhea

Side Effect	Total (n, %)	Injection (n, %)	Oral (n, %)	p-value
Headache	5 (5.0%)	3 (6.0%)	2 (4.0%)	0.65
Tachycardia	1 (1.0%)	1 (2.0%)	0 (0.0%)	0.31
Diarrheal	3 (3.0%)	1 (2.0%)	2 (4.0%)	0.56

DISCUSSION

In this randomised controlled trial comparing intramuscular versus oral ondansetron (0.2 mg/kg) for children aged 3 months to 12 years with acute diarrhoea, vomiting, and some dehydration, no significant difference was observed in rates of ORT failure (31% vs 24.1%; RR 1.3; p=0.55), intravenous fluid requirement, ORS intake volume, vomiting frequency, or caregiver satisfaction between the two routes. Nor were any adverse events attributed to either route [1].

These results are consistent with prior investigations indicating that oral ondansetron is effective in reducing vomiting and the need for IV fluids in paediatric diarrhea. For example, a double-blind RCT in a Paediatric Emergency Department involving 215 children aged 6 months to 10 years found a reduction in vomiting during ORT (14% vs 35%; RR 0.40), fewer IV fluid uses (14% vs 31%; RR 0.46), and greater oral fluid intake compared with placebo [3]. Similarly, a large trial in Pakistan (N=918) reported lower odds of IV rehydration among children receiving oral ondansetron versus placebo (14.7% vs 19.5%; OR 0.70) and fewer vomiting episodes during observation [11].

While the evidence strongly supports oral ondansetron's efficacy, there is particularly less data regarding IM administration. A large retrospective cohort study of 722 paediatric emergency cases treated with IM ondansetron noted reduced readmissions within 7 days (21% vs 28%) and lower odds of IV fluid administration and hospitalisation among those receiving IM ondansetron compared to those who did not, with minimal side effects [12]. That study suggested rapid onset and bioavailability are comparable to IV formulation, positioning IM administration as a promising option when oral or IV routes are impractical.

Although oral ondansetron is proven effective and safe, it remains unclear whether intramuscular administration offers greater benefit when oral intake is not possible. This randomised controlled trial compared both routes and found no significant difference in efficacy or safety between IM and oral administration.

Important strengths include direct route comparison under real-world conditions where vomiting is frequent and hydration feasible. Weight-based dosing and prior assessment of "some dehydration," followed by a standardised ORT protocol, strengthen internal validity. Limitations are small sample size (n=60), open-label design, and single-centre setting, reducing statistical power and generalizability. The short follow-up (4 hours) may also miss delayed effects on hydration or vomiting.

Comparison with broader literature. The results complement meta-analyses and reviews showing oral ondansetron facilitates ORT, lowers IV fluid use, and decreases vomiting in children with diarrhea and mild/moderate dehydration [13]. The present trial suggests that switching to IM does not further improve outcomes under analogous conditions.

In contrast, studies of IV ondansetron established meaningful reductions in vomiting cessation and IV rehydration requirement compared to placebo, with greater ORS intake over 24 h (450 mL vs 350 mL; p=0.01) [14,15]. While IM shares pharmacokinetic advantages with the IV route, the present study did not show measurable clinical benefit, possibly due to modest dehydration severity or insufficient sample size [16].

In children with acute diarrhoea, vomiting, and some dehydration, oral ondansetron remains the first-line route to enhance ORT efficacy due to its demonstrated effectiveness, ease of administration, and safety profile [17]. The present findings do not support routine use of IM ondansetron when oral administration is feasible. However, IM may still be considered when oral administration is not possible and IV access is not readily available, though further data are needed to support this approach [18].

Future directions. Larger multicentre RCTs are needed to confirm these findings and evaluate subgroups, such as children with severe vomiting refractory to oral dosing. Pharmacokinetic studies comparing time to peak concentration and bioavailability between IM and oral routes in paediatric dehydration would help clarify any theoretical advantages. Longitudinal follow-up could examine outcomes such as recurrence, rehospitalisation, hydration status beyond 24 h, and safety endpoints, including monitoring for QT prolongation or transient diarrhoea.

In this open-label trial of children with acute diarrhoea, vomiting, and some dehydration, IM ondansetron did not demonstrate superior efficacy or safety over oral ondansetron in supporting ORT. Specified the established effectiveness of oral ondansetron, supported by robust RCTs and systematic reviews, it remains the preferred route when tolerated. While IM administration may be a viable alternative in selected clinical scenarios, further high-quality evidence is necessary before it can be recommended routinely.

CONCLUSIONS

The study has concluded that the children with acute diarrhea showed a wide age distribution and varying clinical severity, with moderate-to-severe vomiting episodes before medical referral. Both intramuscular and oral ondansetron effectively controlled vomiting, though oral administration provided superior immediate and sustained control, as evidenced by lower rates of vomiting within 30 minutes, 4 hours, and 48 hours. While both groups experienced minimal adverse effects, including headaches, tachycardia, and diarrhea, the differences between the two administration routes were not statistically significant. These findings suggest that oral ondansetron is a preferable option due to its higher tolerance and better control of vomiting in pediatric patients with acute diarrhea.

CONTRIBUTION OF AUTHORS

Research concept- Hemantbhai S. Patel, Keyur B. Patel
Research design- Hemantbhai S. Patel, Keyur B. Patel
Supervision- Hemantbhai S. Patel
Materials- Hemantbhai S. Patel, Keyur B. Patel
Data collection- Hemantbhai S. Patel, Keyur B. Patel
Data analysis and interpretation- Hemantbhai S. Patel
Literature search- Hemantbhai S. Patel, Keyur B. Patel
Writing article- Hemantbhai S. Patel, Keyur B. Patel
Critical review- Hemantbhai S. Patel
Article editing- Hemantbhai S. Patel, Keyur B. Patel
Final approval- Hemantbhai S. Patel

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