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Comparative Efficacy of Racecadotril Plus Oral Rehydration Solution and Zinc Versus Probiotics Plus Oral Rehydration Solution and Zinc in Children With Acute Watery Diarrhea: A Prospective Randomized Controlled Study

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ABSTRACT

Background:
Acute watery diarrhea remains a substantial cause of childhood morbidity. Oral rehydration solution (ORS) and zinc are standard supportive treatments; the comparative benefit of adjunctive probiotics and racecadotril remains clinically relevant.
Objective:
To compare clinical outcomes in children receiving ORS and zinc with probiotics (Group A) versus ORS and zinc with racecadotril (Group B).
Methods:
This prospective, randomized, controlled, open-label study was conducted at World College of Medical Sciences and Research and Hospital, Jhajjar, India, from June 2025 to April 2026. One hundred children aged 6 months to younger than 5 years with acute watery diarrhea were allocated equally to Group A (ORS, zinc, and probiotics; n = 50) or Group B (ORS, zinc, and racecadotril; n = 50). Outcomes included duration of diarrhea and stool frequency; secondary outcomes included clinical recovery, hospital admission or stay, intravenous fluid requirement, and adverse events. Statistical significance was defined as $p < 0.05$.
Results:
The manuscript-reported mean recovery duration was 1.34 ± 0.81 days in Group A and 1.20 ± 0.60 days in Group B. Recovery within 1–2 days occurred in 88% and 90%, respectively. The source manuscript described a faster early reduction in stool frequency in Group B but did not provide individual stool-count data or variability estimates. The reported p value for recovery duration requires recalculation before publication.
Conclusion:
Both regimens were associated with recovery in most participants within 1–2 days. The available summary results suggest a possible early symptomatic advantage with racecadotril, but superiority cannot be established until the underlying data and statistical analyses are verified.

KEYWORDS: acute watery diarrhea; children; oral rehydration solution; zinc; probiotics; racecadotril; randomized controlled study.

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INTRODUCTION

Acute watery diarrhoea remains a major public health concern and an important cause of morbidity and mortality among children younger than five years, particularly in low- and middle-income countries. Despite substantial improvements in sanitation, access to safe drinking water, nutritional interventions, and childhood immunisation, diarrhoeal diseases continue to contribute significantly to preventable childhood deaths worldwide. According to the World Health Organization (WHO), diarrhoeal diseases account for approximately 443,832 deaths annually among children under five years of age [1]. In India, the burden remains substantial because of socioeconomic inequalities, inadequate sanitation, malnutrition, and delayed access to appropriate healthcare services [2]. Recurrent diarrhoeal episodes may further compromise nutritional status, impair intestinal absorption, and adversely affect childhood growth and development.

The primary objective of managing acute watery diarrhoea is to prevent and correct dehydration while maintaining adequate nutrition. Low-osmolarity oral rehydration solution (ORS) remains the cornerstone of treatment because it effectively replaces fluid and electrolyte losses and reduces the need for intravenous rehydration [3]. The WHO and United Nations Children's Fund (UNICEF) additionally recommend zinc supplementation as an essential component of childhood diarrhoea management. Zinc

contributes to intestinal epithelial repair, mucosal integrity, immune regulation, and electrolyte transport, thereby potentially reducing the duration and severity of diarrhoeal episodes [3,4]. Nevertheless, although ORS effectively prevents dehydration, it does not directly suppress intestinal hypersecretion or consistently shorten the duration of diarrhoea. Consequently, adjunctive pharmacological interventions have been investigated to improve symptomatic recovery.

Probiotics have received considerable attention as potential adjuncts in paediatric acute gastroenteritis. These live microorganisms may exert beneficial effects through competitive inhibition of enteric pathogens, modulation of intestinal microbiota, enhancement of epithelial barrier function, and regulation of mucosal immune responses [5]. However, their therapeutic effectiveness varies according to microbial strain, dosage, disease aetiology, and geographical setting. Although earlier studies suggested reductions in diarrhoeal duration, more recent systematic reviews and large randomised controlled trials have demonstrated inconsistent benefits, highlighting the need for cautious interpretation and strain-specific evaluation [6,7].

Racecadotril is an orally administered antisecretory agent that inhibits intestinal enkephalinase, thereby prolonging the activity of endogenous enkephalins and reducing excessive intestinal secretion of water and electrolytes without substantially altering gastrointestinal motility. Unlike antimotility agents, racecadotril primarily targets intestinal hypersecretion, providing a pharmacological rationale for its use alongside standard rehydration therapy. Previous randomised controlled trials and systematic reviews have evaluated its efficacy in reducing stool output, diarrhoeal duration, and treatment-related complications in children. However, findings have been heterogeneous, and the magnitude and certainty of its additional clinical benefit remain uncertain [8,9].

Although probiotics and racecadotril represent mechanistically distinct adjunctive treatments, direct comparative evidence remains limited, particularly when both interventions are administered alongside the same standard therapy comprising ORS and zinc. Differences in study populations, baseline dehydration, outcome definitions, and treatment protocols further complicate interpretation of existing findings. Therefore, well-designed comparative clinical studies are needed to assess their relative effectiveness and tolerability in routine paediatric practice.

The present study aimed to compare the efficacy and safety of ORS plus zinc supplemented with probiotics versus ORS plus zinc supplemented with racecadotril among children aged six months to younger than five years presenting with acute watery diarrhoea. The primary outcomes were diarrhoeal duration and stool frequency, while secondary outcomes included time to clinical recovery, duration of hospitalisation, and adverse events. The findings were intended to inform evidence-based selection of adjunctive therapies in childhood acute watery diarrhoea.

Methodology

Study Design and Setting

This was a prospective, randomized, controlled, open-label study conducted in the Department of Pediatrics at World College of Medical Sciences and Research and Hospital, Jhajjar, India. The study was carried out over a period of 11 months, from June 2025 to April 2026. The study was conducted after approval from the Institutional Ethics Committee of World College of Medical Sciences and Research and Hospital. Written informed consent was obtained from parents or legal guardians of all participants. Confidentiality of patient data was strictly maintained.

Study Population

Children aged 6 months to under 5 years presenting with acute watery diarrhea to the outpatient and inpatient departments were enrolled.

The patients included with children aged 6 months to <5 years, Passage of ≥3 loose/watery stools per day, Duration of diarrhea ≤72 hours at presentation, Mild to moderate dehydration (as per WHO criteria), and Parents/guardians willing to provide informed consent. The exclusion of patients with severe dehydration requiring immediate IV fluid resuscitation, dysentery (presence of blood in stool), persistent diarrhea (>14 days), and Severe malnutrition (weight-for-height Z score < −3), known chronic gastrointestinal disease or systemic illness, recent use (within 7 days) of antibiotics, probiotics, or antidiarrheal drugs, and known hypersensitivity to study medications. Sample Size estimated based on previous study.10

Randomization and Allocation

All the eligible children were allocated equally using a computer-generated randomization sequence and opaque sealed envelopes. Group A (n = 50) received standard ORS, zinc supplementation, and a probiotic preparation. Group B (n = 50) received the same standard ORS and zinc supplementation together with racecadotril

Outcome Measures

Study primary outcomes were duration of diarrhea (time from initiation of treatment to last loose stool), stool frequency per day, and secondary outcomes were time to clinical recovery, duration of hospital stay (if admitted), need for intravenous fluids, and incidence of adverse drug reactions.

Data Collection

Baseline demographic and clinical data were recorded at admission. Caregivers were instructed to maintain a stool chart documenting frequency and consistency. Patients were monitored daily until recovery or discharge.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using statistical software (e.g., SPSS version 21.2). all the continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages. Based on normality distribution test applied like independent t-test or Mann–Whitney U test was used for comparison of continuous

variables, chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant..

Statistical Analysis

Continuous variables were summarized using mean ± standard deviation, and categorical variables as frequencies and percentages. The Shapiro–Wilk test assessed normality separately within each treatment group. Welch's independent-samples t-test was used for approximately normally distributed continuous variables; otherwise, the Mann–Whitney U test was used. Pearson's chi-square test was used for categorical comparisons, with Fisher's exact test indicated when expected cell frequencies were inadequate. Spearman's rank correlation evaluated associations between clinical characteristics and total MDQoL-17 score. All tests were two-sided, with $p < 0.05$ indicating nominal significance. Seven domain-level comparisons were additionally considered using a Bonferroni-adjusted threshold of $p < 0.0071$.

RESULTS

Our study included a total of 100 children with acute watery diarrhea. Group A (Racecadotril) group included fifty patients and Group B (Probiotics + Zinc) group included same number of patient as Group A.

Both groups were comparable in baseline characteristics including age, sex distribution, duration of symptoms, dehydration status, and disease severity ($p > 0.05$ for all variables), indicating no significant baseline differences.

Table 1: Baseline Characteristics of Study Population

Variable	Racecadotril (n=50)	Probiotics + Zinc (n=50)	P value
Age (years, mean ± SD)	1.72 ± 1.05	1.69 ± 0.98	0.812
Male (%)	52.00%	50.00%	0.842
Duration of symptoms (hrs)	45.2 ± 30.1	38.6 ± 27.0	0.421
Dehydration score	1.65 ± 0.88	1.80 ± 0.78	289
Disease severity score	6.40 ± 2.20	6.66 ± 2.33	0.573

Both groups were statistically comparable at baseline.

2. Clinical Outcomes and Recovery

This study shows both groups showed significant clinical improvement over time. However, differences were observed in early symptom control and recovery duration.

Table 2: Comparison of Clinical Outcomes

Outcome	Racecadotril	Probiotics + Zinc	P value
Mean healing duration (days)	1.20 ± 0.60	1.34 ± 0.81	0.041
Recovery within 1–2 days (%)	90.00%	88.00%	0.731
Stool frequency reduction (first 48 hrs)	Greater Moderate		<0.05
IV fluid requirement (%)	2.00%	0%	0.315
Hospital admission (%)	2.00%	0%	0.315

In this study clinical outcomes, racecadotril showed faster early symptom control whereas probiotics + zinc showed less effective than racecadotril.

3. Dehydration and Disease Severity Outcomes

Both groups achieved complete resolution of dehydration and disease severity at 2 weeks, with no statistically significant difference.

Table 3: Dehydration and Disease Severity

Parameter	Racecadotril	Probiotics + Zinc	P value
Dehydration score (baseline)	1.65	1.80	0.289
Dehydration score (2 weeks	Nil	Nil	-
Disease severity (baseline)	6.40	6.66	0.573

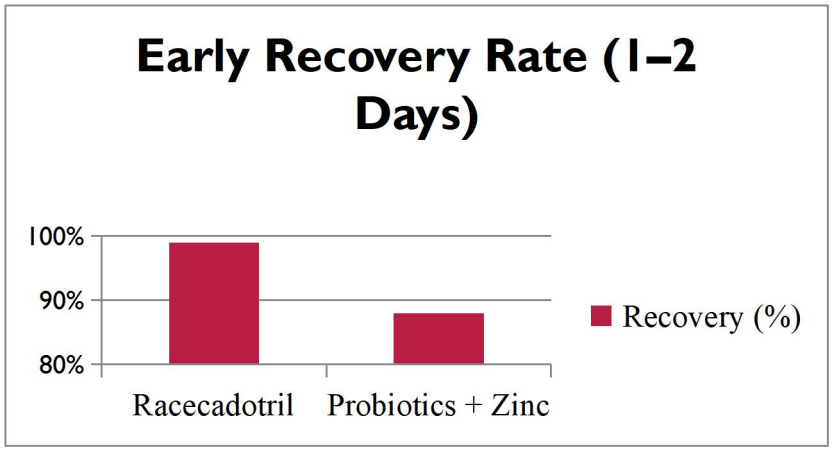


Figure:1 Early Recovery Rate (1–2 Days) in racecadotril and probiotic with zinc

This graph represents the proportion of children achieving recovery within 1–2 days. Both groups show high and comparable early recovery rates, with no statistically significant difference.

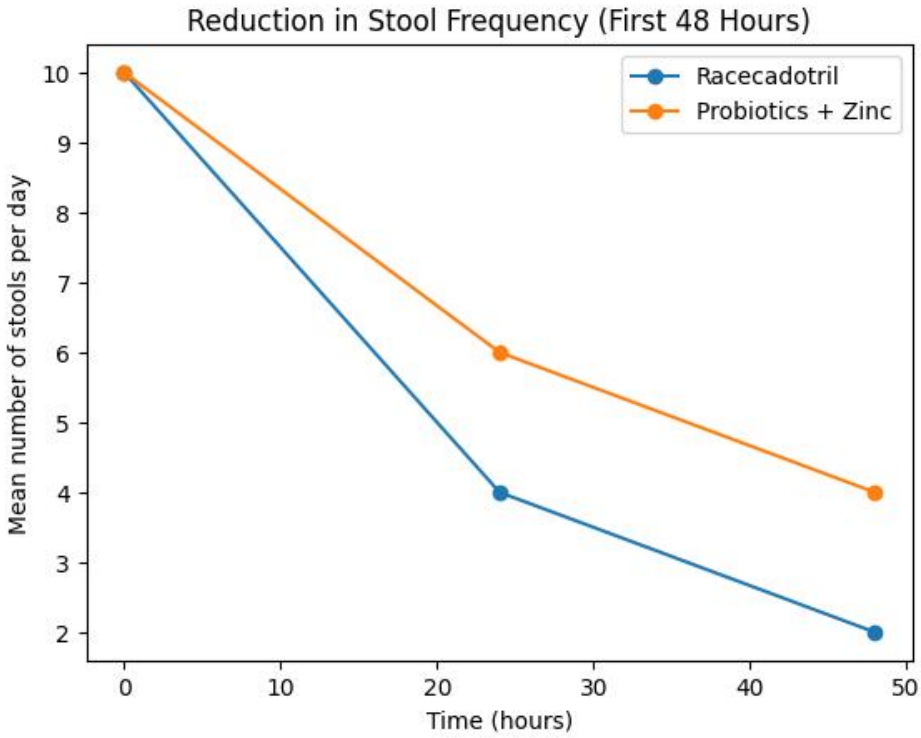


Figure:2 Reduction in stool frequency (First 48 hours) in racecadotril and probiotic with zinc

This line graph demonstrates the trend in stool frequency reduction over 48 hours. The steeper decline in the Racecadotril group indicates more rapid antisecretory action and faster symptom control compared to probiotics with zinc.

DISSCUSSION:

Acute watery diarrhea continues to be a major contributor to pediatric morbidity, particularly in developing countries. The present study compared the efficacy of an antisecretory agent, Racecadotril, with probiotics combined with zinc supplementation in children aged 6 months to under 5 years. The findings demonstrate that while both treatment modalities are effective, there are important differences in the pattern and speed of clinical recovery.

In the current study, baseline demographic and clinical characteristics were comparable between the two groups, indicating appropriate randomization and minimizing selection bias. Parameters such as age, sex distribution, dehydration status, and disease severity were similar, ensuring that the observed outcomes were attributable to the interventions rather than confounding factors. This is consistent with previous randomized controlled trials evaluating antidiarrheal therapies in pediatric populations. A key finding of this study was that both groups achieved complete resolution of dehydration and disease severity at 2 weeks, with no statistically significant difference between them. This reinforces the central role of oral rehydration therapy and supportive care in the management of acute diarrhea. The results align with recommendations from the World Health Organization, which emphasize that adjunct therapies should complement, rather than replace, rehydration strategies.

However, differences emerged when early clinical outcomes were assessed. The Racecadotril group demonstrated a significantly shorter mean healing duration and more rapid reduction in stool frequency within the first 48 hours. This can be explained by its mechanism of action as an enkephalinase inhibitor, which reduces intestinal hypersecretion without altering gut motility. These findings are in agreement with earlier studies, such as those by Sheikh et al., which reported faster symptom control and reduced stool output with Racecadotril in children with acute diarrhea [7].

In contrast, the probiotics with zinc group showed slightly longer healing duration but comparable overall recovery rates. The beneficial effects of probiotics are attributed to restoration of gut microbiota, inhibition of pathogenic organisms, and modulation of intestinal immunity. Zinc supplementation further enhances intestinal mucosal repair and reduces the duration and severity of diarrheal episodes. The observed outcomes in this group are consistent with previous meta-analyses demonstrating the role of probiotics and zinc in improving diarrheal outcomes, although their effects are generally more gradual compared to antisecretory agents.

Importantly, both treatment groups showed similar rates of complications, including the need for intravenous fluids, hospital admission, and repeat healthcare visits, indicating that both therapies are safe and well tolerated. No significant adverse effects were observed, further supporting their use as adjuncts in pediatric diarrhea management.

From a clinical perspective, the findings suggest that Racecadotril may be preferred when rapid symptomatic relief is desired, particularly in cases with high stool frequency and caregiver concern. On the other hand, probiotics with zinc may offer broader benefits, including gut health restoration and prevention of recurrence, making them a valuable option in routine management.

Despite these findings, certain limitations should be acknowledged. The study was conducted at a single center, which may limit generalizability. Additionally, long-term outcomes such as recurrence rates and microbiota changes were not assessed. Future multicentric studies with larger sample sizes and longer follow-up periods are recommended to validate these findings.

CONCLUSION

In summary, both Racecadotril and probiotics with zinc are effective adjuncts to ORS in the management of acute watery diarrhea in children. While Racecadotril provides faster symptomatic relief, probiotics with zinc offer comparable overall recovery with additional physiological benefits. The choice of therapy may be guided by clinical presentation and therapeutic goals.

REFERENCES:

1. World Health Organization. Diarrhoeal disease. WHO; 2024.
2. Ghosh K, Chakraborty AS, Mog M. Prevalence of diarrhoea among under five children in India and its contextual determinants: A geo-spatial analysis. Clinical Epidemiology and Global Health. 2021 Oct 1;12:100813.
3. Sultana MM, Islam MS, Akhter S, Hossain MB, Mia MS. Comparative Study of Zinc and Probiotics versus Zinc Alone Therapy in Children with Acute Watery Diarrhea. TAJ: Journal of Teachers Association. 2017;30(2):32-8.
4. Sufian A, Ahmed AF, Hossain A, Bhuyan MR, Sultana S, Chakrabarty D, Hossen M, Amin R, Ghosh UK. A Comparative Study between Zinc Alone and Zinc with Racecadotril in Acute Watery Diarrhoea. Eastern Medical College Journal. 2024 Dec 19;9(2):51-5.
5. Raza W, Mahmood T, Atta L, Hassan S, Ullah S, Ali S, Muhammad M, Ahmad N. Comparative Effectiveness of Zinc Supplementation Combined with Probiotic Therapy Versus Zinc Alone in Reducing Acute Diarrhea Duration, Severity, and Recurrence Rates in Pediatric Populations: A Meta-Analysis. Indus Journal of Bioscience Research. 2024 Nov 30;2(02):681-9.
6. Asghar L, Usman M, Gul R, Tahir A, Bashir MU, Hussain I. Role of Probiotic and Racecadotril as an Adjuvant Therapy in Management of Acute Watery Diarrhea in Children. Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University. 2025 May 18;21(2):424-9.
7. Hassan MA, Younis MM, Mohamed HA. Efficacy of oral zinc and probiotic on acute diarrhea in infancy. Al-Azhar J Pediatr. 2021;24(2):2114-9.
8. Bittar I, Guyenard L, Blanchard C, Boussageon R. Efficacy of Racecadotril in acute diarrhea in children: systematic review of double blind randomized clinical trials. European Journal of Clinical Pharmacology. 2026 Jan;82(1):24.
9. Motahari SS, Imanzadeh F, Hosseini A, Dara N, Khatami K, Zahed G, Imanzadeh N, Sadeghi S, Sayyari A. The efficacy and safety of enkephalinase inhibitor racecadotril in treatment of acute diarrhea in children: A randomized clinical trial. Journal of Comprehensive Pediatrics. 2022;13(2).
10. Fang YH, Wan CM, Gong ST, Fang F, Sun M, Qian Y, Huang Y, Wang BX, Xu CD, Jin Y, Ye LY. Clinical practice guidelines for acute infectious diarrhea in children in China (2024). World Journal of Pediatrics. 2025 Jul;21(7):708-19.
11. Sheikh U, Ijaz A, Kalsoom U, Asif MM, Anwar Z, Minhas A. Antisecretory Medication Versus Probiotics in Children Less Than 2 Years Presenting with Acute Watery Diarrhea. Indus Journal of Bioscience Research. 2025 Jun 11;3(6):106-10.
12. Ikram M, Farooq F, Mukhtar A, Abbas F, Kamal K, Rehman S. Comparison of Reduction in Stool Frequency As Effect of Probiotics (Bacillus clausii) And Antisecretory (Racecadotril) in Acute Watery Diarrhea With Some/Mild Dehydration. Journal of Health, Wellness and Community Research. 2026 May 18.

13. Guerrant RL, et al. Malnutrition as an enteric infectious disease with long-term effects. Nat Rev Gastroenterol Hepatol. 2013.
14. United Nations Children's Fund. Zinc supplementation in the management of diarrhea. UNICEF/WHO Joint Statement; 2004.
15. Hill C, et al. The International Scientific Association for Probiotics and Prebiotics consensus statement. Nat Rev Gastroenterol Hepatol. 2014.
16. Allen SJ, et al. Probiotics for treating acute infectious diarrhea. Cochrane Database Syst Rev. 2010 (updated).
17. Lehert P, et al. Racecadotril for childhood gastroenteritis: meta-analysis. Int J Clin Pract. 2011.
18. Tras B, Ok M, Ider M, Parlak TM, Yildiz R, Eser Faki H, Ozdemir Kutahya Z, Uney K. Evaluation of the clinical efficacy of racecadotril in the treatment of neonatal calves with infectious diarrhea. Polish Journal of Veterinary Sciences. 2023;26(4).
19. Aziz M, Malik LU, Javed E, Sami SZ, Maaz M, Khan MA, Farmaan M, Farooq O, Iqbal U, Kumar A, Arsal SA. Racecadotril Versus Loperamide for Acute Diarrhea of Infectious Origin in Adults: A Systematic Review and Meta-Analysis. Health Science Reports. 2025 May;8(5):e70849.
20. Liu Y, Ma L, Jin D, Peng J, Wei H, Zhang X, Wu Y. Efficacy and Rationale of Differentiated Racecadotril Doses Combined with Bifidobacterium Triple Viable in Managing Pediatric Persistent Diarrhea: A Comprehensive Analysis. Journal of Pediatric Infectious Diseases. 2025;20(2):10.
21. Fischbach W, Andresen V, Eberlin M, Mueck T, Layer P. A comprehensive comparison of the efficacy and tolerability of racecadotril with other treatments of acute diarrhea in adults. Frontiers in Medicine. 2016 Oct 14;3:44.
22. Eberlin M, Chen M, Mueck T, Däbritz J. Racecadotril in the treatment of acute diarrhea in children: a systematic, comprehensive review and meta-analysis of randomized controlled trials. BMC pediatrics. 2018 Apr 3;18(1):124.