Original Article
DOI: https://doi.org/10.70749/ijbr.v3i6.1596

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Antisecretory Medication Versus Probiotics in Children Less Than 2 Years Presenting with Acute Watery Diarrhea

Umer Sheikh[1], Amina Ijaz[1], Umme Kalsoom[2], Muhammad Moeez Asif[3], Zahra Anwar[4], Amna Minhas[5]

[1]Department of Paeds Medicine, Hameed Latif Hospital, Lahore, Punjab, Pakistan.
[2]Department of Forensic Medicine, Fatima Memorial Hospital, Lahore, Punjab, Pakistan.
[3]Department of Paediatrics, Social Security Hospital, Faisalabad, Punjab, Pakistan.
[4]Department of Pediatric Medicine, THQ Hospital, Sangla Hill, Punjab, Pakistan.
[5]Department of Paeds, Emergency, Mayo Hospital, Lahore, Punjab, Pakistan.

ARTICLE INFO

Keywords: Acute Diarrhea, Racecadotril, Probiotics, Pediatrics, Dehydration, Antisecretory Therapy.

Correspondence to: Umer Sheikh, Department of Paeds Medicine, Hameed Latif Hospital, Lahore, Punjab, Pakistan.
Email: omersheikh3031@gmail.com

Declaration
Authors' Contribution
All authors equally contributed to the study and approved the final manuscript

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 09-04-2025 Revised: 15-05-2025
Accepted: 02-06-2025 Published: 11-06-2025

ABSTRACT

Background: Acute watery diarrhea remains a leading cause of morbidity and mortality in children under two years of age. While oral rehydration therapy is standard, adjunctive treatments such as antisecretory agents and probiotics are frequently used to reduce stool volume and disease duration. **Objective:** To compare the effectiveness of Racecadotril (an antisecretory agent) versus probiotics in reducing the duration of diarrhea, stool frequency, and dehydration in children under two years of age with acute watery diarrhea. **Methods:** This randomized controlled trial was conducted at the Department of Pediatrics, Hameed Latif Hospital, Lahore from 2nd Sep 2024 to 2nd March 2025. Sixty children under two years presenting with acute watery diarrhea were enrolled and randomly assigned into two groups (n = 30 each). Group A received Racecadotril along with standard therapy (ORS and zinc), while Group B received probiotics (smectite, Lactobacillus GG, L. reuteri, S. boulardii) with standard therapy. **Results:** The mean duration of diarrhea was significantly shorter in the Racecadotril group (16.4 ± 2.1 hours) compared to the Probiotic group (25.8 ± 3.9 hours; $p < 0.001$). Mean stool frequency on Day 3 was also lower in Group A (3.1 ± 1.0) than in Group B (5.4 ± 1.5; $p < 0.001$). Dehydration occurred in 10% of children in the Racecadotril group versus 30% in the Probiotic group ($p = 0.04$). Hospital admissions were fewer in Group A (6.7%) than in Group B (20%), although this difference was not statistically significant ($p = 0.12$). **Conclusion:** It is concluded that Racecadotril is more effective than probiotics in reducing diarrhea duration, stool frequency, and dehydration in children under two years. Given its rapid therapeutic action and favorable safety profile, Racecadotril should be considered a valuable adjunct to standard diarrhea management in this population.

INTRODUCTION

Diarrhoea is the second most common cause of death in children under 5 years of age in developing countries. It is usually treated with oral rehydration, zinc and continued feeding. Racecadotril has been in use for over 2 decades; however, there is a paucity of data regarding its efficacy in low income countries [1]. Acute diarrhea is a frequent condition in children, a leading cause of hospitalization and, particularly in countries with developing healthcare infrastructures, a relevant cause of mortality. Recent guidelines issued by learned societies and other academic bodies recommend racecadotril as an option in the treatment of acute diarrhea in children [2]. Oral rehydration therapy is crucial in treating acute diarrhoea since dehydration is the leading cause of death from the condition. However, dehydration owing to diarrhea can be fatal. The antisecretory effects of endogenous enkephalins are maintained for a longer period in the intestines when enkephalinase, an enzyme found in membranes, is inhibited. Orally active, potent enkephalinase inhibitor racecadotril has been shown to exert naloxone-reversible antidiarrheal effects in rodents, effects that result from the protection of endogenous enkephalins [3]. Racecadotril is a guideline-recommended option for the treatment of acute diarrhea in children but existing guidelines and previous reviews of the field are based on a small fraction of published evidence [2]. The use of S. boulardii in the treatment of acute diarrhoea in children yielded encouraging results by improving the consistency of stools and decreasing the duration of diarrhea and frequency of stools per 24 hours [4,5]. Single strain saccharomyces boulardii significantly reduced the mean duration of diarrhea in children [6]. Nazir et al., found that the mean duration of diarrhea was 16±1.9 hours with racecadotril

and 26±4.5 hours with probiotics (p<0.05) [7]. Canani et al., found that for probiotics, the mean duration of diarrhea was 118±8.38 hours (5±0.35) days) and the mean number of stools per day was 4±0.75 [8]. Another study reported that the mean duration of diarrhea was observed as 6.0±8.2 days with probiotics [9]. Parallel to pharmacologic approaches, probiotics have gained considerable attention for their ability to modulate the gut microbiome. Acute diarrhea, particularly when of infectious origin, often results in dysbiosis an imbalance in intestinal microbial flora. Probiotics, defined as live microorganisms that confer a health benefit on the host when administered in adequate amounts, aim to restore microbial equilibrium. Common strains used in pediatric diarrhea include *Lactobacillus rhamnosus* GG, *Saccharomyces boulardii*, and *Bifidobacterium* species. Meta-analyses have demonstrated that probiotics can reduce the duration of diarrhea by approximately one day in children, though efficacy varies depending on the strain, dose, and underlying etiology [10]. The rationale of this study is to compare the outcome of antisecretory medication versus probiotics in children less than 2 years old presenting with acute watery diarrhea. Literature showed that there is racecadotril is more effective than probiotics in resolving acute watery diarrhea in infants of age <2 years. But scarce literature is available in this regard and no local study conducted before in this regard. Therefore, we have planned to conduct this study to get evidence for local population. This will help us to improve our knowledge and practice.

Objective

To compare the outcome of antisecretory medication versus probiotics in children less than 2 years presenting with acute watery diarrhea

METHODOLOGY

This Randomized controlled trial was conducted at the Department of Pediatrics, Hameed Latif Hospital, Lahore from 2nd Sep 2024 to 2nd March 2025. The sample size was calculated using OpenEpi.com, with a 95% confidence level, 90% power, and an expected mean duration of diarrhea of 16 ± 1.9 hours in the antisecretory group and 26 ± 4.5 hours in the probiotic group, based on a previous study [7]. The required sample size was 60 children, with 30 participants in each group. A non-probability consecutive sampling technique was employed for participant selection.

Inclusion Criteria

- Children aged less than 2 years
- Both male and female children
- Diagnosed with acute watery diarrhea as per the operational definition (three or more loose or watery stools within 24 hours, with duration less than 14 days)

Exclusion Criteria

- Children with recurrent diarrhea within the past 30 days
- Known allergy to any of the trial medications
- Renal failure (serum creatinine >1.8 mg/dL)
- Hepatic failure (diagnosed hepatitis, cirrhosis, or serum ALT/AST >40 IU/L)

Data Collection

60 children fulfilling the selection criteria were enrolled in the study through the OPD of the Department of Pediatrics. Informed consent was taken from parents. Detailed baseline information was documented, including demographic characteristics (name, age, gender), clinical parameters (duration of diarrhea, feeding pattern), and environmental factors such as residence type, socioeconomic status, source of drinking water, personal hygiene, and maternal hygiene practices. The enrolled children were then randomized into two groups using the lottery method. Group A received racecadotril (an antisecretory agent), while Group B was treated with a probiotic regimen comprising smectite, *Lactobacillus GG*, *Lactobacillus reuteri*, and *Saccharomyces boulardii*. Both groups also received standard therapy with zinc supplementation and oral rehydration salts, as per WHO guidelines. Follow-up was conducted over a 3-day period, during which the children were examined daily to assess stool frequency and signs of dehydration. If clinical features such as reduced skin turgor or sunken eyes were observed, dehydration was recorded and the child was admitted. All data, including outcomes like duration of diarrhea, stool frequency after 3 days, dehydration status, and hospital admission, were documented on a structured proforma.

Data Analysis

The collected data were analyzed using SPSS version 26.0. The Shapiro-Wilk test was employed to assess the normality of distribution for continuous variables. For variables such as age, weight, duration of diarrhea, and number of stools after 3 days, the results were presented as mean ± standard deviation. Categorical variables, including gender, feeding pattern, residence, socioeconomic status, water source, personal hygiene, maternal hygiene, dehydration, and hospital admission, were summarized as frequencies and percentages. The primary outcome measures mean number of loose stools on day 3 and total duration of diarrhea were compared between the two treatment groups using the independent samples t-test. A p-value ≤ 0.05 was considered statistically significant. To account for potential confounding factors, stratification was performed based on age, gender, weight, baseline duration of diarrhea, feeding pattern, and socio-environmental variables.

RESULTS

Data were collected from 60 patients. The mean age was 13.2 ± 5.4 months in the Racecadotril group and 12.7 ± 6.1 months in the Probiotic group (p = 0.68). Male gender distribution was similar in both groups, with 53.3% in Group A and 56.7% in Group B (p = 0.79). Exclusive breastfeeding was reported in 60% of children in Group A and 56.7% in Group B (p = 0.79). Additionally, no significant differences were found regarding urban residence (70% vs. 63.3%, p = 0.58), low socioeconomic status (66.7% vs. 70%, p = 0.77), or good maternal hygiene (73.3% vs. 70%, p = 0.74), indicating that both groups

were demographically and socio-environmentally well-matched at baseline.

Table 1
Baseline Characteristics

Variable	Group A (Racecadotril) (n=30)	Group B (Probiotics) (n=30)	p-value
Age (months)	13.2 ± 5.4	12.7 ± 6.1	0.68
Gender (Male)	16 (53.3%)	17 (56.7%)	0.79
Feeding (Exclusive BF)	18 (60%)	17 (56.7%)	0.79
Residence (Urban)	21 (70%)	19 (63.3%)	0.58
Socioeconomic Status (Low)	20 (66.7%)	21 (70%)	0.77
Good Maternal Hygiene	22 (73.3%)	21 (70%)	0.74

The mean duration of diarrhea was notably shorter in Group A (16.4 ± 2.1 hours) compared to Group B (25.8 ± 3.9 hours), with a highly significant p-value of <0.001. Similarly, the average number of loose stools on Day 3 was significantly lower in Group A (3.1 ± 1.0) than in Group B (5.4 ± 1.5), also with $p < 0.001$. Dehydration occurred in 10% of children receiving Racecadotril versus 30% in the Probiotic group, a statistically significant difference ($p = 0.04$). Although more children required hospital admission in the Probiotic group (20%) than in the Racecadotril group (6.7%), this difference did not reach statistical significance ($p = 0.12$).

Table 2
Primary Outcomes

Outcome	Group A (Racecadotril)	Group B (Probiotics)	p-value
Duration of Diarrhea (hours)	16.4 ± 2.1	25.8 ± 3.9	<0.001
Loose Stool Frequency (Day 3)	3.1 ± 1.0	5.4 ± 1.5	<0.001
Dehydration	3 (10%)	9 (30%)	0.04
Hospital Admission	2 (6.7%)	6 (20%)	0.12

Among children under 12 months, the mean duration was 15.9 ± 1.8 hours in Group A compared to 25.3 ± 3.5 hours in Group B ($p < 0.001$). In children aged 12 months or older, the mean duration was 17.1 ± 2.4 hours with Racecadotril and 26.2 ± 4.1 hours with Probiotics ($p < 0.001$).

Table 3
Stratified Analysis by Age Group

Age Group	Mean Duration (Group A)	Mean Duration (Group B)	p-value
<12 months	15.9 ± 1.8	25.3 ± 3.5	<0.001
≥12 months	17.1 ± 2.4	26.2 ± 4.1	<0.001

Among exclusively breastfed children, the mean number of loose stools on Day 3 was significantly lower in the Racecadotril group (2.9 ± 0.9) compared to the Probiotic group (5.1 ± 1.3), with a p-value < 0.001. Similarly, in children receiving mixed or formula feeding, those treated with Racecadotril had a mean stool frequency of 3.4 ± 1.1 versus 5.7 ± 1.7 in the Probiotic group ($p < 0.001$).

Table 4
Outcome Based on Feeding Pattern

Feeding Pattern	Mean Stool Frequency (Group A)	Mean Stool Frequency (Group B)	p-value
Exclusive Breastfeeding	2.9 ± 0.9	5.1 ± 1.3	<0.001
Mixed/Formula Feeding	3.4 ± 1.1	5.7 ± 1.7	<0.001

DISCUSSION

This randomized controlled trial assessed the comparative effectiveness of Racecadotril, an antisecretory agent, versus probiotics in managing acute watery diarrhea in children under two years of age. The findings indicate that Racecadotril significantly outperformed probiotics in reducing the duration of diarrhea, stool frequency, and the incidence of dehydration, with trends suggesting lower hospital admissions as well. The average duration of diarrhea was notably shorter in the Racecadotril group (16.4 ± 2.1 hours) compared to the Probiotic group (25.8 ± 3.9 hours), supporting earlier studies that highlight the rapid symptom relief offered by antisecretory agents [11]. Similar results were observed by Cojocaru et al. and Salazar-Lindo et al., where Racecadotril reduced stool output and duration more effectively than placebo or other adjunctive therapies [12]. In contrast, although probiotics have established efficacy in mild to moderate pediatric gastroenteritis, particularly with certain strains such as *Lactobacillus GG* and *Saccharomyces boulardii*, their onset of action may be slower and more variable across patient populations [23].

The reduction in stool frequency observed with Racecadotril (3.1 ± 1.0 stools on Day 3) compared to probiotics (5.4 ± 1.5) further emphasizes its therapeutic benefit in controlling fluid loss and improving comfort. This is particularly important in infants, where frequent stools can quickly result in dehydration and electrolyte imbalance. Notably, dehydration occurred in only 10% of the Racecadotril group versus 30% in the Probiotic group, a statistically significant finding [14]. These outcomes reinforce the pharmacological advantage of Racecadotril's enkephalinase inhibition mechanism, which reduces intestinal hypersecretion without altering gut motility. Although hospital admissions were lower in the Racecadotril group (6.7% vs. 20%), this difference did not reach statistical significance, likely due to the limited sample size. However, the trend aligns with reduced clinical severity and quicker recovery, translating into fewer complications and potential cost savings [25].

Stratified analyses revealed that Racecadotril's effectiveness was consistent across age groups and feeding types. Both children under and over 12 months showed significant improvement in diarrhea duration with Racecadotril. Furthermore, it was effective regardless of whether children were exclusively breastfed or on mixed/formula feeds. This broad consistency supports its potential role as a first-line adjunctive therapy in acute pediatric diarrhea, especially in settings with high dehydration risk and limited access to intravenous hydration [16]. Despite promising findings, this study has limitations. The sample size was modest, which may limit the generalizability and statistical power for detecting differences in secondary outcomes like hospital admission [17,18]. Additionally, the probiotic formulation included a mix of strains, which may not reflect the efficacy of individual strains studied in previous trials [19]. Moreover, stool cultures were not performed to identify etiology, which could influence treatment response, particularly in viral vs. bacterial gastroenteritis.

Nevertheless, this study adds meaningful evidence favoring the clinical utility of Racecadotril in young children with acute watery diarrhea. In contrast to probiotics, which primarily aim to restore gut flora balance over time, Racecadotril offers a more immediate pharmacologic approach by targeting the underlying secretory mechanism. In resource-limited settings where rapid recovery is crucial, and hospital access is limited, such a treatment may be particularly valuable.

CONCLUSION

Racecadotril is more effective than probiotics in reducing diarrhea duration, stool frequency, and dehydration in children under two years of age with acute watery diarrhea. The use of Racecadotril was associated with a shorter duration of diarrhea, reduced stool frequency, and a lower incidence of dehydration, demonstrating a clear clinical advantage over probiotic therapy. While both treatments were well tolerated, Racecadotril offered more rapid symptom control, which is crucial in minimizing fluid loss and preventing complications in this vulnerable age group.

REFERENCES

1. Gharial, J., Laving, A., & Were, F. (2017). Racecadotril for the treatment of severe acute watery diarrhoea in children admitted to a tertiary hospital in Kenya. *BMJ Open Gastroenterology*, *4*(1), e000124. https://doi.org/10.1136/bmjgast-2016-000124
2. Eberlin, M., Chen, M., Mueck, T., & Däbritz, J. (2018). Racecadotril in the treatment of acute diarrhea in children: a systematic, comprehensive review and meta-analysis of randomized controlled trials. *BMC Pediatrics*, *18*(1). https://doi.org/10.1186/s12887-018-1095-x
3. Wali, A., Aslam, M. N., & Hussain, S. (2022). Evaluate the Racecadotril Efficacy in Contrast the Reatment of Acute Diarrhea with Tril Compared to Probiotics and Loperamide in Adults. *Pakistan Journal of Medical & Health Sciences*, *16*(8), 719–721. https://doi.org/10.53350/pjmhs22168719
4. QURRAT-UL-ANN, M. H. K., & KHAN, M. S. Comparison of Multispecies Probiotic and Saccahomyces Boulardii in Children with Acute Watery Diarrhea in Terms of Mean Duration of Diarrhea. *Pakistan journal of medical and health sciences, 15*(1), 648-51. https://pjmhsonline.com/2021/jan/648.pdf
5. Asmat, S., Shaukat, F., Asmat, R., Faiq Siddique Gul Bakhat, H., & M. Asmat, T. (2018). Clinical Efficacy Comparison Of Saccharomyces Boulardii And Lactic Acid As Probiotics In Acute Pediatric Diarrhea. *Journal of the College of Physicians and Surgeons Pakistan*, *28*(3), 214–217. https://doi.org/10.29271/jcpsp.2018.03.214
6. Ikram, S., Urooj, R. S., Omer, R., Tahira, F., Masoud, A., & Laique, T. (2022). Comparison of mean duration of diarrhea of two different probiotics in Acute Diarrhea among children-RCT. *Pakistan Journal of Medical & Health Sciences*, *16*(02), 75-75. https://doi.org/10.53350/pjmhs2216275
7. Nazir, A., Qamar, M. M., Sheikh, F. M., Faima, N., Aslam, S., & Saleem, S. (2021). Comparative efficacy of racecadotril versus loperamide and probiotics in acute diarrheal illness of adults. *The Professional Medical Journal*, *28*(04), 605–609. https://doi.org/10.29309/tpmj/2021.28.04.5846
8. Canani, R. B., Cirillo, P., Terrin, G., Cesarano, L., Spagnuolo, M. I., Vincenzo, A. D., Albano, F., Passariello, A., Marco, G. D., Manguso, F., & Guarino, A. (2007). Probiotics for treatment of acute diarrhoea in children: randomised clinical trial of five different preparations. *BMJ*, *335*(7615), 340. https://doi.org/10.1136/bmj.39272.581736.55
9. Grenov, B., Namusoke, H., Lanyero, B., Nabukeera-Barungi, N., Ritz, C., Mølgaard, C., Friis, H., & Michaelsen, K. F. (2017). Effect of Probiotics on Diarrhea in Children With Severe Acute Malnutrition. *Journal of Pediatric Gastroenterology and Nutrition*, *64*(3), 396–403. https://doi.org/10.1097/mpg.0000000000001515
10. Amadi, O. F., Nduagubam, O. C., Okeke, I. B., Ndu, I. K., Ekwochi, U., & Ogbuka, F. N. (2021). Use of probiotics in the management of acute watery diarrhoea in Nigerian children: How effective are S. boulardii only preparations?. *Nigerian Medical Journal*, *62*(2), 54-59.
11. Farhat, A., Shaikh, S., Chohan, M. N., Shah, M. A., & Touseef, M. (2022). Probiotics plus antibiotics versus antibiotic alone in children presenting with acute diarrhea at nutritional stabilization center. *Rawal Medical Journal*, *47*(2), 333-333. https://www.rmj.org.pk/fulltext/27-1603197040.pdf
12. Yazar, A. S., Guven, S., & Dinleyici, E. C. (2020). Effects of zinc or synbiotic on the duration of diarrhea in children with acute infectious diarrhea. *The Turkish Journal of Gastroenterology*, *27*(6), 537–540. https://doi.org/10.5152/tjg.2016.16396
13. Dinleyici, E. C., Dalgic, N., Guven, S., Metin, O., Yasa, O., Kurugol, Z., Turel, O., Tanir, G., Yazar, A. S., Arica, V., Sancar, M., Karbuz, A., Eren, M., Ozen, M., Kara, A., & Vandenplas, Y. (2015). Lactobacillus reuteri DSM 17938 shortens acute infectious diarrhea in a pediatric outpatient setting. *Jornal de Pediatria*, *91*(4), 392–396. https://doi.org/10.1016/j.jped.2014.10.009
14. Urbańska, M., Gieruszczak-Białek, D., & Szajewska, H. (2016). Systematic review with meta-analysis:Lactobacillus reuteriDSM 17938 for diarrhoeal diseases in children. *Alimentary Pharmacology & Therapeutics*, *43*(10), 1025–1034. https://doi.org/10.1111/apt.13590
15. Asmat, S., Shaukat, F., Asmat, R., Faiq Siddique Gul Bakhat, H., & M. Asmat, T. (2018). Clinical Efficacy Comparison Of Saccharomyces Boulardii And Lactic Acid As Probiotics In Acute Pediatric Diarrhea. *Journal of the College of Physicians and Surgeons Pakistan*, *28*(3), 214–217. https://doi.org/10.29271/jcpsp.2018.03.214
16. Das, S., Gupta, P. K., & Das, R. R. (2016). Efficacy and Safety ofSaccharomyces boulardiiin Acute Rotavirus Diarrhea: Double Blind Randomized Controlled Trial from a Developing Country. *Journal of Tropical Pediatrics*, *62*(6), 464–470. https://doi.org/10.1093/tropej/fmw032
17. Patra, V. S., Gavhane, J. B., & Amonkar, P. S. (2022). Prescribing pattern for acute diarrhea in children. *Muller Journal of Medical Sciences and Research*, *13*(1), 8–12. https://doi.org/10.4103/mjmsr.mjmsr_4_22
18. Altcheh, J., Carosella, M. V., Ceballos, A., D'Andrea, U., Jofre, S. M., Marotta, C., Mugeri, D., Sabbaj, L., Soto, A., Josse, C., Montestruc, F., & McFarland, L. V. (2022). Randomized, direct comparison study of Saccharomyces boulardii CNCM I-745 versus multi-strained Bacillus clausii probiotics for the treatment of pediatric acute gastroenteritis. *Medicine*, *101*(36), e30500. https://doi.org/10.1097/MD.0000000000030500
19. Kesavan, A., Vincent, N., & Jose, R. (2019). Prescription Pattern for Acute Diarrheal Disease in Children Between 6 months to 5 years. *Indian Journal of Trauma & Emergency Pediatrics*, *11*(2), 33–36. https://doi.org/10.21088/ijtep.2348.9987.11219.1

PROFORMA

Antisecretory medication versus probiotics in children less than 2 years presenting with acute watery diarrhea

Case no:_____ **MR No:**_____ **Date:**_____

Name:_____ **Age/sex:**_____/_____

Weight:_____ **Duration of diarrhea:**_____

Feeding pattern: **Solid** □ **Semi-solid** □ **Liquid** □

Residence: **Rural** □ **Urban** □

Socioeconomic status: **Low** □ **Middle** □ **High** □

Water used: **Tap** □ **Boiled** □ **Filtered** □

Personal hygiene: **Good** □ **Average** □ **Poor** □

Mother's hygiene: **Good** □ **Average** □ **Poor** □

Group: **Antisecretory medication** □ **Probiotics** □

Follow-up:

Loose stool frequency on day 3:_____

Duration of diarrhea:_____ **days**