Comparison of Efficacy of Probiotic Versus Racecadotril in Children with Acute Diarrhea Aged 2 to 59 Months

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ABSTRACT

Background: Diarrhea remains the second leading cause of death among children under five, contributing to 1.5 million deaths annually. In Pakistan, diarrhea leads to approximately 500 deaths daily, with children experiencing 5–6 episodes per year. While oral rehydration therapy (ORT) is the cornerstone of treatment, adjunct therapies such as probiotics and racecadotril require further evaluation.

Objective: To compare the efficacy of probiotics versus racecadotril in children aged 2 months to 59 months with acute diarrhea.

Methods: A randomized controlled trial was conducted at the Balochistan Institute of Child Health Services, Quetta, from November 2022 to May 2023. A total of 400 children were enrolled and divided equally into two groups. Group A received probiotics (Saccharomyces boulardii) and Group B received racecadotril, alongside ORT. Outcomes, including stool frequency improvement (<3 stools/day) and duration of diarrhea, were assessed on day 4. Data were analyzed using SPSS v25, with a significance level of $p \leq 0.05$.

Results: Improvement in stool frequency was observed in 70% of Group A and 45% of Group B ($p < 0.001$). The mean duration of diarrhea was 3.7 ± 2.43 days in Group A versus 6 ± 3.21 days in Group B ($p < 0.001$).

Conclusion: Probiotics significantly reduced diarrhea duration and stool frequency compared to racecadotril, supporting their use as an adjunct therapy in pediatric diarrhea management.

INTRODUCTION

Acute diarrhea remains one of the most significant global health challenges, particularly among children under the age of five, where it stands as the second leading cause of mortality. Annually, diarrheal diseases claim approximately 1.5 million lives worldwide, with developing countries bearing a disproportionate burden of these fatalities. In Pakistan alone, an alarming 500 deaths occur daily due to diarrhea, and on average, each child experiences 5–6 episodes annually. The primary mechanism underlying these deaths is dehydration caused by water and electrolyte loss, which particularly endangers infants due to their higher vulnerability and limited physiological reserves (1,2).

Rehydration therapy, particularly oral rehydration solution (ORS), is globally recognized as the cornerstone of diarrhea management and is recommended by major pediatric organizations, including the American Academy of Pediatrics, the Canadian Pediatric Society, and the European Society for Gastroenterology, Hepatology, and Nutrition. Despite the efficacy of ORS in mitigating dehydration, its role is limited to symptomatic relief, with no direct impact on the frequency or duration of diarrheal episodes.

Consequently, adjunctive therapies are being increasingly explored to optimize outcomes, reduce disease burden, and alleviate the associated healthcare costs (2-4).

Probiotics, defined as live microorganisms that confer health benefits when consumed in appropriate quantities, have gained significant attention as a promising therapeutic option in pediatric diarrhea. These microbial agents are thought to modulate host immunity, restore disrupted gut flora, and enhance the integrity of the intestinal barrier, all of which contribute to mitigating the clinical manifestations of diarrhea. Among probiotics, Saccharomyces boulardii has emerged as one of the most extensively studied strains, demonstrating moderate efficacy in reducing stool frequency, improving stool consistency, and shortening the duration of diarrheal episodes. Moreover, probiotics are well-tolerated, with minimal adverse effects, making them a favorable option in pediatric populations (3-7).

Racecadotril, on the other hand, is an antisecretory agent that reduces intestinal hypersecretion by inhibiting enkephalinase, thereby preserving endogenous enkephalins. While it has shown efficacy in decreasing stool output and diarrhea duration, its utility remains limited due to variability in clinical outcomes and a lack of consensus on its routine use. Comparative studies between probiotics and racecadotril in children with acute diarrhea have yielded mixed results, highlighting the need for well-designed randomized trials to establish their relative efficacy and guide clinical practice (8-12). The current study aims to fill this critical knowledge gap by evaluating and comparing the efficacy of probiotics and racecadotril in

children aged 2 months to 59 months presenting with acute diarrhea. By assessing key outcomes such as stool frequency and the duration of diarrhea, this study seeks to provide robust evidence to inform future treatment guidelines. The findings are expected to be particularly relevant in resource-limited settings like Pakistan, where the high burden of diarrheal diseases necessitates cost-effective and evidence-based therapeutic interventions. This study also underscores the need for larger trials to further validate the findings and explore the role of probiotics in pediatric diarrhea management, ultimately contributing to the reduction of morbidity and mortality associated with this preventable condition (13-18).

MATERIAL AND METHODS

This randomized controlled trial was conducted in the Department of Pediatrics at the Balochistan Institute of Child Health Services, Quetta, from November 29, 2022, to May 29, 2023. The study aimed to compare the efficacy of probiotics and racecadotril in managing acute diarrhea in children aged 2 months to 59 months. A total of 400 children meeting the inclusion criteria were enrolled, with 200 participants assigned to each treatment group using a lottery method for randomization. Group A received probiotics, while Group B was treated with racecadotril. Both groups were also provided standard oral rehydration therapy (ORS), in line with established guidelines for diarrhea management (1,2).

The inclusion criteria comprised children aged 2 months to 59 months presenting with acute watery diarrhea of less than 14 days' duration, with no signs of severe dehydration or comorbid conditions such as malnutrition or chronic illness. Exclusion criteria included children with bloody diarrhea, antibiotic-associated diarrhea, or known hypersensitivity to probiotics or racecadotril, as well as those with incomplete follow-up data. Written informed consent was obtained from the parents or guardians of all participants before enrollment in the study. The study was conducted in accordance with the Declaration of Helsinki, ensuring ethical principles were upheld, and approval was obtained from the institutional ethical review board (3,4).

Baseline data, including demographic details, clinical history, and initial stool frequency, were collected at the time of enrollment. Treatment was initiated immediately following randomization. Participants in Group A were administered a standard dose of probiotics (Saccharomyces boulardii), while those in Group B received racecadotril in age-appropriate doses. Both groups were followed for four days after the initiation of treatment, and outcomes were assessed during a follow-up visit or via telephonic communication if in-person visits were not feasible.

The primary outcomes included the duration of diarrhea, defined as the number of days from the initiation of treatment until the cessation of loose stools, and the frequency of stools per day, assessed on day four of treatment. Improvement in stool frequency was categorized as passing fewer than three stools per day. Secondary outcomes included the proportion of children with stool consistency returning to normal and the safety profile of the interventions, assessed through parental reporting of adverse events. All clinical assessments were performed by trained pediatricians to ensure consistency and minimize bias (5,6).

Data were recorded on standardized case report forms and subsequently entered into a secure database for analysis. Data were analyzed using SPSS version 25. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables such as age and duration of diarrhea were reported as means with standard deviations, while categorical variables such as gender and stool frequency were expressed as percentages. The chi-square test was used to compare categorical outcomes between groups, and an independent sample t-test was employed for continuous variables. Stratified analyses were performed based on age, gender, and baseline stool frequency to explore potential subgroup differences. A p-value ≤ 0.05 was considered statistically significant (7,8).

The study ensured strict adherence to ethical principles throughout its course. Confidentiality of participant data was maintained, and no identifying information was disclosed. Any adverse events reported during the study were managed according to clinical guidelines and recorded for analysis. The findings of this study are expected to provide valuable insights into the comparative efficacy of probiotics and racecadotril in managing acute diarrhea in children, with the potential to inform evidence-based treatment recommendations for clinicians working in similar resource-constrained settings (9,10).

RESULTS

A total of 400 children, equally divided into two groups, were included in the study. Group A comprised participants receiving probiotics, while Group B received racecadotril. The demographic and clinical characteristics of the study population are summarized in Table 1. The mean age of children in Group A was 2 years (SD ± 2.77), while in Group B, it was 2 years (SD ± 3.12). Gender distribution was comparable between groups, with males accounting for 53% in Group A and 55% in Group B (p = 0.688).

Table 1: Demographic and Baseline Characteristics

Variable	Group A (Probiotic)	Group B (Racecadotril)	p-value
Mean Age (Years ± SD)	2 ± 2.77	2 ± 3.12	1.000
Male (%)	106 (53%)	110 (55%)	0.688
Female (%)	94 (47%)	90 (45%)	

The primary outcome measures were the improvement in stool frequency and the duration of diarrhea. A significantly higher proportion of children in Group A (70%) achieved stool frequency of less than three stools per day by day four

compared to Group B (45%), as shown in Table 2 ($p < 0.001$). Similarly, the mean duration of diarrhea was significantly shorter in Group A (3.7 ± 2.43 days) compared to Group B (6 ± 3.21 days) ($p < 0.001$).

Table 2: Primary Outcomes

Outcome	Group A (Probiotic)	Group B (Racecadotril)	p-value
Improvement in Stool Frequency (<3 stools/day) (%)	140 (70%)	90 (45%)	<0.001
Mean Duration of Diarrhea (Days ± SD)	3.7 ± 2.43	6 ± 3.21	<0.001

Stratification of outcomes by age and gender revealed consistent findings across subgroups. Among children aged 6 months to 2 years, 66% in Group A achieved stool frequency improvement compared to 45% in Group B ($p = 0.007$). In the 3 to 5 years age group, improvement was observed in 72% of Group A and 45% of Group B participants ($p < 0.001$). Gender-wise stratification indicated that 68% of males in Group A showed improvement compared to 45% in Group B ($p < 0.001$), while 72% of females in Group A improved compared to 44% in Group B ($p < 0.001$).

Table 3: Stratification of Stool Frequency Improvement

Subgroup	Group A (Probiotic)	Group B (Racecadotril)	p-value
Age 6 months to 2 years	37 (66%)	27 (45%)	0.007
Age 3 to 5 years	103 (72%)	63 (45%)	<0.001
Male	73 (68%)	50 (45%)	<0.001
Female	68 (72%)	40 (44%)	<0.001

The mean number of days diarrhea persisted was stratified by age, gender, and duration of illness at presentation. In children aged 6 months to 2 years, the mean duration of diarrhea was significantly shorter in Group A (4 ± 2.98 days) compared to Group B (5.8 ± 3.30 days) ($p < 0.001$). Similar differences were observed in the 3 to 5 years age group, with a mean duration of 3.5 ± 2.57 days in Group A versus 5.7 ± 3.28 days in Group B ($p < 0.001$). These results are summarized in Table 4.

Table 4: Duration of Diarrhea Stratified by Subgroups

Subgroup	Group A (Probiotic) (Mean ± SD)	Group B (Racecadotril) (Mean ± SD)	p-value
Age 6 months to 2 years	4 ± 2.98	5.8 ± 3.30	<0.001
Age 3 to 5 years	3.5 ± 2.57	5.7 ± 3.28	<0.001
Male	4 ± 2.98	6 ± 3.25	<0.001
Female	4 ± 2.91	6 ± 3.27	<0.001

Adverse events were minimal and comparable between the groups. No serious adverse events were reported in either group. Mild gastrointestinal complaints were noted in 5% of children in Group A and 6% in Group B, with no significant difference ($p = 0.752$).

The findings of this study demonstrate that probiotics are significantly more effective than racecadotril in reducing both stool frequency and the duration of diarrhea in children with acute watery diarrhea. These results are consistent across various subgroups and provide robust evidence to support the use of probiotics as a preferred adjunctive therapy alongside ORS in this population.

DISCUSSION

This study compared the efficacy of probiotics and racecadotril in managing acute diarrhea in children aged 2 months to 59 months. The findings demonstrated a significant reduction in the duration of diarrhea and improvement in stool frequency with the use of probiotics compared to racecadotril. The mean duration of diarrhea was shorter in the probiotic group (3.7 ± 2.43 days) compared to the racecadotril group (6 ± 3.21 days), and 70% of children in the probiotic group achieved an improvement in stool frequency (<3 stools per day) compared to 45% in the racecadotril group. These results align with previous studies, including those by Khan et al. and Guandalini et al., which highlighted the potential of probiotics, particularly Saccharomyces boulardii, in reducing the duration and severity of diarrhea in pediatric populations (13,14).

The observed efficacy of probiotics may be attributed to their ability to restore gut microbiota balance, enhance intestinal barrier integrity, and modulate immune responses. Saccharomyces boulardii and other probiotics are known to promote the production of short-chain fatty acids, which help in reducing intestinal motility and water loss, while also providing a protective effect against pathogenic bacteria. These mechanisms likely explain the superior outcomes in the probiotic group compared to racecadotril, which primarily functions as an antisecretory agent by inhibiting enkephalinase activity (15,16).

Stratified analyses further revealed that the benefits of probiotics were consistent across different age groups and genders. Children aged 6 months to 2 years and 3 to 5 years both showed significant reductions in stool frequency and duration of diarrhea in the probiotic group compared to the racecadotril group. These findings are consistent with the results of randomized trials conducted by Htwe et al. and Agustina et al., which also demonstrated that probiotics were effective across various demographic subgroups

(17,18). This highlights the broad applicability of probiotics in pediatric diarrhea management, irrespective of age or gender.

While the study provided robust evidence supporting the efficacy of probiotics, it also had certain limitations. The short follow-up period restricted the ability to assess long-term outcomes, such as recurrence rates or sustained benefits of probiotic therapy. Additionally, the study did not evaluate the impact of nutritional status, which may influence the efficacy of both probiotics and racecadotril. Previous research has shown that malnutrition can alter gut microbiota and immune responses, potentially modifying the therapeutic effects of probiotics (19). Future studies with a longer follow-up period and consideration of nutritional status are warranted to address these gaps and provide a more comprehensive understanding.

Another limitation was the lack of a placebo group, which would have allowed for a clearer differentiation of the effects of probiotics and racecadotril from the natural resolution of diarrhea. Moreover, the study relied on parental reporting for some outcomes, such as stool frequency, which could have introduced reporting bias. Despite these limitations, the randomized design, adequate sample size, and rigorous statistical analysis strengthen the reliability of the findings.

The safety profile of probiotics observed in this study, with minimal adverse events, further supports their use as a first-line adjunctive therapy alongside ORS in acute pediatric diarrhea. Racecadotril, while effective, was associated with a longer duration of diarrhea and lower improvement rates, suggesting it may have a more limited role in clinical practice. The absence of severe adverse events in either group reflects the overall safety of these interventions when used appropriately.

In light of these findings, it is recommended that probiotics, particularly Saccharomyces boulardii, be considered as a preferred adjunctive treatment for acute watery diarrhea in children, especially in resource-limited settings where reducing the burden of disease is critical. Further research should focus on the comparative cost-effectiveness of these therapies, the exploration of different probiotic strains, and their long-term impact on gut health and immunity. Policymakers should also consider integrating probiotics into national diarrhea management guidelines to optimize outcomes and reduce childhood morbidity and mortality associated with diarrheal diseases.

CONCLUSION

This study concluded that probiotics, particularly Saccharomyces boulardii, are significantly more effective than racecadotril in reducing the duration and frequency of diarrhea in children aged 2 months to 59 months with acute watery diarrhea. The findings underscore the potential of probiotics as a safe, effective, and well-tolerated adjunctive therapy alongside oral rehydration solutions, with broad applicability across various demographic subgroups. Incorporating probiotics into routine pediatric diarrhea management can improve clinical outcomes, reduce healthcare costs, and alleviate the burden of diarrheal diseases, particularly in resource-limited settings, ultimately contributing to better child health and survival worldwide.

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