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Safety and Efficacy of Racecadotril in Acute Watery Diarrhea: A Randomized Controlled Trial in Children Aged 3 –59 Months

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Abstract

Objective: To evaluate the efficacy and safety of racecadotril (1.5 mg/kg thrice daily) in combination with standard oral rehydration therapy (ORT) and compare with placebo plus ORT in 3 - 59 months old hospitalized children with acute watery diarrhea

Study Design and Setting: A randomized controlled trial having registration number NCT07392931 was conducted with 200 children aged 3-59 months hospitalized with AWD at the Punjab Rangers Teaching Hospital in Lahore, as a prospective, double-blinded study. Participant enrolment and follow-up covered six consecutive months (1st June to 30th November 2025). The study protocol was approved by the Institutional Review Board (IRB) of Punjab Rangers Teaching Hospital, Lahore (Ref: PRTH/IRB/2023/63).

Methodology: Children either received Racecadotril (1.5mg/kg three times a day) or a placebo, with standard oral rehydration therapy. The key outcomes were the number of stools in 24 hours and the length of stay of the children in the hospital.

Results: Day 1 (3.1 vs. 4.8) Racecadotril reduced the stool count. The proportion of children who achieved treatment success (a decrease in stools) on the drug compared to placebo was 82% and 48%, respectively (NNT=3). The children who were administered Racecadotril spent 26.4 hours less in the hospital. The adverse effects were rare (8% vs. 12%) and no drug-related or serious problems were observed. The cost analysis showed a savings of 6,230 PKR per patient.

Conclusion: Racecadotril is safe, effective, and cost-effective. It promptly reduces stool output and hospital stay of children with AWD regardless of their age and dehydration condition.

Keywords: Racecadotril; Acute watery diarrhea; Antisecretory; Oral rehydration therapy; Randomized controlled trial

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INTRODUCTION

Acute watery diarrhea (AWD) is one of the main reasons why children are brought to emergency rooms and hospitals worldwide, with a major toll on children and health-care systems.[1] The World Health Organization estimated that children under five have about 1.7 billion episodes of diarrhea each year, and this leads to 525,000 deaths (around 1,400 per day), despite the availability of low-cost interventions.[2] Nearly 90% of all these deaths occur in low- and middle-income countries (LMICs), where lack of sanitation, overcrowding, low parental education and delayed seeking of care combine to increase risk.[3] In fact, AWD is one of the leading causes of health-care use even in high-income countries. In Europe, any episode of gastroenteritis represents 5-10% of pediatric emergency consultations and 132 hospitalizations per 100 000 children annually.[4]

Most deaths related to diarrhea are due to dehydration and electrolyte imbalance, but the long-term sequelae (including growth faltering, cognitive impairment, and greater susceptibility to infection) affect human capital development as well.[5] For more than 4 decades, the mainstay of diarrheal disease management has been oral rehydration therapy (ORT), a simple solution that contains glucose and

electrolytes that replaces fluid losses and corrects hypovolaemia.[6] The universal coverage of ORT could prevent up to 93% of diarrhea related deaths.[7] ORT does not alter stool frequency or consistency. Thus, there is a recognized need for a safe adjunctive agent that will shorten the duration of illness without compromising the safety profile of ORT.[8-9]

Racecadotril, an orally active prodrug of enkephalinase inhibitor thiorphan is a rational therapeutic approach. By selectively blocking membrane-bound neutral endopeptidase in the intestinal mucosa, it also conserves endogenous enkephalins which physiologically inhibit the cyclic adenosine monophosphate cAMP-mediated secretory cascade elicited by the enterotoxins.[10] Unlike opioids, racecadotril has no effects on gastrointestinal (GI) motility or crosses the blood-brain barrier, avoiding centrally-mediated effects.[11] In adult volunteer studies using jejunal perfusion chambers, the presence of racecadotril was shown to induce a 45% lower secretion of fluid following a dose of toxin derived from cholera, within 90 minutes.[12]

Trials in Europe and Latin America in the early years of treatment showed benefit. In a Peruvian study on 135 boys aged 3-35 months, 48 hour stool output was reduced by 45% ($p = 0.02$) and time to cure by 27 hours by racecadotril.[13] In a study, Racecadotril has a significant beneficial effect on acute gastroenteritis regardless of whether it is caused by rotavirus, with a number needed to treat (NNT) of about 3 to promote rapid clinical improvement (eg normalisation of stool frequency within 72 hours).[14] A randomised study (n=120, children 6 months-5 years) found that Racecadotril significantly decreased racecadotril significantly decreased the number of stools at 48 hours ($p=0.012$) and made the hospital stay shorter than placebo. The authors concluded that racecadotril is effective in the treatment of acute gastroenteritis in paediatric subjects.[15]

Pakistan has the fifth highest diarrheal mortality in the world with an estimated 41,000 under-five deaths every year.[16] National Demographic and Health Surveys show that only 46% of caregivers prepare ORT correctly, 38% withhold feeds during illness, and 28% first seek care from unqualified providers.[17] These factors may reduce the effectiveness in real-life practice in comparison to controlled trials. To date, the only open-label study from Karachi (n = 176) has evaluated the efficacy of racecadotril, revealing a reduction of 1 day of hospital stay; despite the lack of comparison with placebo and single center design, the study is limited. Therefore, high-quality evidence produced through the public-sector hospitals of Pakistan is necessary to inform decisions at the clinical and policy level.[18]

This study sought to assess the therapeutic benefit of racecadotril in routine clinical settings outside of the ambient conditions of tertiary care, but serving a population of low socio-economic standing and living in peri-urban areas. By using rigorous randomization, blinding the trials and using objective outcomes, it aims to offer actionable evidence for clinicians and policymakers. Demonstration of the benefits of an inexpensive oral adjunct safely reducing the duration of illness by 24 hours and resulting in hospital stay savings could improve child outcomes while also increasing hospital efficiency--an achievement with dual benefit in health systems under financial constraint.

METHODOLOGY

This prospective, double-blinded, placebo-controlled, parallel-group randomized controlled trial (RCT), with registration number NCT07392931, assessed the efficacy and safety of racecadotril as supplemental oral rehydration therapy (ORT) in children admitted for an episode of acute watery diarrhea (AWD). The study was conducted in the pediatric wards of the Punjab Rangers Teaching Hospital, Lahore.

Participant enrolment and follow-up covered six consecutive months (1st June to 30th November 2025). The participants were followed up until discharge; those hospitalized for longer than seven days were censured at seven days for length of stay analysis. Sample size was estimated using the WHO Sample Size Calculator (v2.0) assuming that the mean difference in stools per 24 hours (SD 3) in the racecadotril group compared to placebo would be two, $a = 0.05$ (two-tailed), 90% power and 5% attrition. Ninety-six participants were needed in each arm; the actual total was raised to 200 (100 in each group) for the potential for losses.

Simple randomization was achieved by lottery method. Two hundred opaque, sequentially numbered envelopes holding allocation cards on which the words "Racecadotril" or "Placebo" were printed as words were prepared by an independent statistician. Once eligibility confirmation and consent were obtained, the next envelope in sequence was opened by the study nurse. Allocation concealment was performed and blinding involved participants. Identical-appearing sachets that contained racecadotril 15 mg (Hidrasec(R)) or placebo (microcrystalline cellulose) were dispensed in sequentially numbered drug boxes. The participant flow through the trial is presented in the CONSORT diagram (Figure 1).

Eligible participants were children between 3 months and 59 months, of either sex, who had >3 loose or watery stools in the past 24 hours, was expected to last <72 hours and led to hospitalization, determined by the attending physician. Written informed consent was received from a parent or guardian with assent of children less than 5 years of age or younger. Exclusion criteria were less than 3 months or >60 months of age, stool containing visible blood or mucus, chronic diarrhea (>14 days), persistent diarrhea (7-14 days), severe dehydration requiring intensive care, severe acute malnutrition (weight-for-height z-score), and major comorbidities, e.g. pneumonia, sepsis, congenital heart disease, hepatic or renal impairment, known hypersensitivity to racecadotril.

Before enrolment, the principal investigator trained all ward nurses, residents, and data collection staff in eligibility determination, randomization, and stool grading and adverse-event documentation. Standardized case report forms (CRFs), Bristol Stool Chart cards, and calibrated tools of measuring were placed at each bedside.

Each eligible child was given a unique study code. Baseline demographic data, anthropometry and hydration status (as per the WHO criteria), vitals were noted. The allocated study medication was newly reconstituted in 10 mL of potable water by the hospital pharmacist just before dosing and was administered orally at 1.5 mg/kg every eight hours (maximum 30 mg per dose) for up to five days or until discharge, whichever happened first. All participants were rehydrated per standard care based on WHO recommendations: low-osmolarity oral rehydration solution (ORS) 50-100 mL/kg during 4-6 h for mild to moderate dehydration or isotonic intravenous fluids (0.9% saline with or without 5% dextrose).

During hospitalization, the nursing staff noted the amount of stool being produced each 24 hours (from 00:00 to 23:59). Stool frequency was established as the overall count for each 24 h period during which defecation/stool passage occurred. Time to first formed stool was the number of hours from the first dose until passage of a stool of a Bristol type 3 or 4. Duration of hospital stay was calculated as the number of whole hours between the electronic admission timestamp and the signed discharge order. Dehydration status was classified as none/mild (<5% weight loss), moderate (5-9%) or severe (>10%) (The latter was not considered in this study).

Compliance was taken to be ingestion of >90% of prescribed sachets, confirmed by reconciliation of returned doses. Any new symptom, including vomiting, abdominal distention, rash, lethargy, and/or constipation that lasts for >48 hours were considered a potential adverse drug event that was evaluated by the attending physician for potential relation to the study medication. Blinding was strictly maintained - drug boxes were annotated with only study ID and dosing time, and caregivers assessors were unaware of group assignment. Any refusal, regurgitation in 15 min. or incomplete dose was entered; if so, the dose was repeated once.

The study protocol was approved by the Institutional Review Board (IRB) of Punjab Rangers Teaching Hospital, Lahore (Ref: PRTH/IRB/2023/63). Data confidentiality was guaranteed by the use of anonymized study codes and by storing all records in password-protected servers only shared by the research team. Participation was voluntary and withdrawal was not related to standard medical care. Adverse events that could cause serious harm were to be reported to the IRB within 24 hours. This over Rigorous methodology ensured standardization of enrolment, allocation concealment, intervention delivery, and outcome measurement, which could robustly echo the therapeutic benefit of racecadotril as an adjuvant to ORT in hospitalized children with acute watery diarrhea.

All statistical analyses were performed using IBM Statistics: IBM Sure Statistics 26.0. Baseline demographic and clinical characteristics: age, gender, weight, duration of diarrhea, baseline stool frequency, dehydration state, vomiting and fever were compared between the two groups in order to assure initial equivalence. Independent-sample tests of the normally distributed variables were performed using t-tests. Categorical variables were compared using the Pearson's Chi-square test. A p-value < 0.05 was used to represent significance for all tests.

RESULTS:

Table 1 demonstrates that groups were similar in terms of baseline characteristics. The mean age was approximately 18 months, 40% of both were 3-12 months and males slightly out-numbered females. There were no significant differences between the Racecadotril and Placebo groups, with similar stool frequency, as well as length of diarrhea, dehydration status, vomiting and fever.

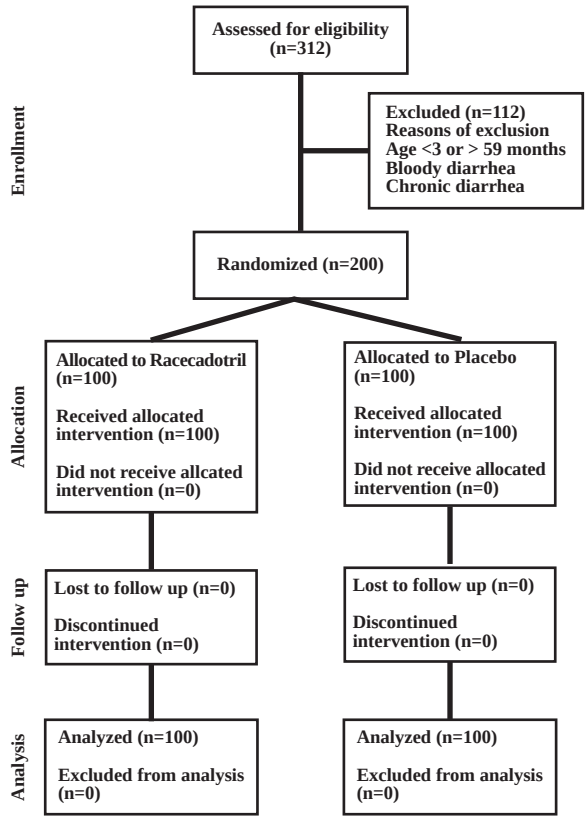
Table 2 shows the main efficacy results, which indicate a strong clinical benefit of Racecadotril compared with placebo. Stool frequency was similar at baseline and decreased faster in the Racecadotril group (3.1 ± 1.2) compared to the placebo group (4.8 ± 1.4, $p<0.001$) and remained so for the 3 days of the study. The absolute reduction in stool frequency was larger in the Racecadotril group (4.7 vs. 2.8 stools/day) and greater proportion of Racecadotril group achieved =50% reduction than placebo group (82% vs 48%, NNT = 3). Racecadotril also had a dramatic effect on the hospital stay as the treated group had an average hospital stay of 76.4 hours versus 102.8 hours in the placebo group ($p<0.001$), a mean difference of about 26 hours.

The results of safety and tolerability are summarized in table 3; Racecadotril was equally safe when compared to placebo. Adverse events occurred in 8% of Racecadotril group and in 12% of placebo group, the difference between the two groups did not reach statistical significance ($p=0.34$, RR=0.67). There were low and similar rates of specific events (persistent vomiting, abdominal distention, skin lesions, and constipation) in each group. There were no serious adverse events; and no drug-related adverse events were reported. No significant difference between groups in treatment compliance (96% from Racecadotril group and 98% from placebo group with at least 90% of treatment taken, $p=0.41$). Racecadotril had a favourable and well-tolerated safety profile overall.

Table 4 shows the result of the cost-effectiveness analysis, which revealed that Racecadotril, although it was more expensive in terms of drug cost (450 PKR vs. 50 PKR), eventually led to overall cost savings as it resulted in faster recovery and reduced hospital resource use. The reduced

length of stay in hospitals reduced the bed and nursing care cost (11,460 PKR) as compared to 15,420 PKR and consequently reduced total direct medical cost by 4,580PKR per patient. Indirect costs also were reduced with the caregivers of Racecadotril treated children missing fewer work days (3.2 vs. 4.3) with additional savings of 1,650 PKR. The cost per patient of Racecadotril was 19,730 PKR, while that of placebo was 25,960 PKR; and resulted in a saving of 6,230 PKR per patient and 623000rs saving in costs for treatment group. Therefore, Racecadotril was found to be a cost-effective strategy as it cuts down on both direct and indirect costs.

Figure 1: Consort Flow Diagram



DISCUSSION

This double blinded randomized controlled trial findings indicate that racecadotril together with conventional oral rehydration therapy (ORT) has significant clinical and economic advantages in children with acute watery diarrhea. The great reduction in the stool frequency and the time span of hospital stay and disappearance of symptoms observed in our study is in line with the increasing amount of evidence that indicates the effectiveness of racecadotril as an antisecretory agent. These results are of particular interest in the area of paediatric gastroenterology where safe and effective treatment of acute watery diarrhea is the main issue of public health, especially in the low and middle-income countries, where the disease rate is catastrophically

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Racecadotril (n=100)	Placebo (n=100)	P-value
Age (months)			
Mean ± SD	18.4 ± 12.6	17.9 ± 13.1	0.78
3-12 months, n (%)	38 (38.0%)	41 (41.0%)	0.68
13-24 months, n (%)	34 (34.0%)	32 (32.0%)	0.76
25-60 months, n (%)	28 (28.0%)	27 (27.0%)	0.88
Gender			
Male, n (%)	58 (58.0%)	56 (56.0%)	0.78
Female, n (%)	42 (42.0%)	44 (44.0%)	0.78
Weight (kg) (Mean ± SD)	10.2 ± 2.8	10.4 ± 2.9	0.62
Diarrhea Duration (hours)	36.2 ± 18.4	34.8 ± 17.9	0.58
Baseline Stool Freq. (24h)	7.8 ± 2.1	7.6 ± 2.3	0.52
Dehydration Status			
Mild, n (%)	42 (42.0%)	45 (45.0%)	0.68
Moderate, n (%)	58 (58.0%)	55 (55.0%)	0.68
Vomiting present, n (%)	64 (64.0%)	62 (62.0%)	0.77
Fever present, n (%)	48 (48.0%)	51 (51.0%)	0.68

Table 2: Primary Outcome Measures

Outcome Measure	Racecadotril (n=100)	Placebo (n=100)	Mean Diff. (95% CI)	P-value
Stool Frequency (24h)				
Day 0 (Baseline)	7.8 ± 2.1	7.6 ± 2.3	0.2 (-0.4 to 0.8)	0.52
Day 1	3.1 ± 1.2	4.8 ± 1.4	-1.7 (-2.1 to -1.3)	<0.001**
Day 2	1.8 ± 0.9	3.2 ± 1.3	-1.4 (-1.7 to -1.1)	<0.001**
Day 3	1.2 ± 0.6	2.1 ± 1.1	-0.9 (-1.2 to -0.6)	<0.001**
Reduction from Baseline				
Absolute reduction	4.7 ± 1.8	2.8 ± 1.6	1.9 (1.4 to 2.4)	<0.001**
Percentage reduction	60.3 ± 15.2%	36.8 ± 14.8%	23.5% (19.1–27.9)	<0.001**
Achieved =50% reduction	82 (82.0%)	48 (48.0%)	NNT = 3	<0.001**
Hospital Stay (hours)				
Median (IQR)	72 (60-84)	96 (84-120)	-24 (-32 to -16)	<0.001**
Mean ± SD	76.4 ± 18.2	102.8 ± 24.6	-26.4 (-32 to -20)	<0.001**

Table 3: Safety Profile and Adverse Events

Adverse Event	Racecadotril	Placebo	P-value	Risk Ratio (95% CI)
Any adverse event, n (%)	8 (8.0%)	12 (12.0%)	0.34	0.67 (0.28-1.58)
Persistent Vomiting, n (%)	3 (3.0%)	5 (5.0%)	0.48	0.60 (0.15-2.46)
Abdominal distension, n (%)	2 (2.0%)	4 (4.0%)	0.41	0.50 (0.09-2.68)
Skin rash, n (%)	1 (1.0%)	1 (1.0%)	1.00	1.00 (0.06-15.77)
Constipation (=48h), n (%)	2 (2.0%)	2 (2.0%)	1.00	1.00 (0.14-6.96)
Serious adverse events	0 (0.0%)	0 (0.0%)	-	-
Drug-related events	0 (0.0%)	0 (0.0%)	-	-
Discontinuations, n (%)	0 (0.0%)	0 (0.0%)	0.32	-
Compliance (=90%), n (%)	96 (96.0%)	98 (98.0%)	0.41	0.98 (0.93-1.03)

Table 4: Cost-Effectiveness Analysis (PKR)

Parameter	Racecadotril	Placebo	Difference
Direct Medical Costs			
Drug cost per patient	450	50	+400
Hospital bed cost (150/hr)	11,460	15,420	-3,960
Nursing care cost	2,400	3,200	-800
ORS/IV fluid cost	620	840	-220
Subtotal Direct Costs	**14,930**	**19,510**	**-4,580**
Indirect Costs			
Work days lost (Mean)	3.2	4.3	-1.1
Productivity loss (PKR)	4,800	6,450	-1,650
Total Cost Per Patient	**19,730**	**25,960**	**-6,230**
Total Savings (n=100)	-	-	**623,000**

PKR = Pakistani Rupees (1 USD ˜ 280 PKR). Racecadotril demonstrates clear cost-effectiveness through reduced hospital stay despite higher drug acquisition costs

predominant and affordable treatment options are frequently accessible. The size of the morbidity and mortality burden associated with the acute form of the gastroenteritis disease in the pediatrics sets the size of the problem as one of the most urgent ones to the healthcare systems of the developing world, and the discovery of the pharmacological agents that could allow reducing the clinical course and severity of the disease safely and meaningfully constitutes a significant challenge to both the clinical practice and the healthcare policy of the population.

Racecadotril has a therapeutic action premised on the selective inhibition of an enzyme enkephalase that breaks down the endogenous enkephalins at the intestinal mucosa. Racecadotril maintains the levels of these endogenous opioid peptides thus decreasing hypersecretion of water and electrolytes into the intestine lumen without negatively impacting the intestinal motility. This process is pharmacologically different as compared to the antimotility agents and is the basis behind the desirable safety profile that has been evidently apparent among a wide range of clinical trials in very different geographical and demographic settings. Such specificity of this enzymatic inhibition is clinically important, it is not only that unlike the agents with general effects on the gastrointestinal system, racecadotril acts specifically on the secretory activity, but also, the enteric nervous system and intestinal wall musculature associated with the action of the agent is referred to in detail. This specificity also helps to take into consideration the preservation of physiological intestinal functioning which is especially important in paediatric groups in which protracted gastrointestinal stasis poses a high clinical risk due to bacteria overgrowth, toxic build-up, and systemic dissemination of enteric pathogens.

According to Aziz et al., racecadotril was found to be reported as being similar to loperamide in reducing the length and incidence of acute infectious diarrhea among the adult population, with a better safety profile, especially in terms of no constipation and rebound effects, as described in nutrients.[19] The clinical value of preventing such adverse effects cannot be overestimated, taking into account that patients may already be in the physiologically poorly condition because of dehydration and electrolyte imbalance. This but constipation and rebound diarrhoea, which are sufficiently described (sequelae of loperamide use), inconvenient at best, but capable of contributing to the complexity of an already complicated presentation, potentially increasing hospitalization time and burden of care. Moreover, racecadotril with antisecretory therapy produced a faster rate of reduction in the number of stools and reduced length of diarrhoea than probiotic therapy in children less than two years of age with acute watery diarrhoea thus supporting the idea of better short-term effectiveness with antisecretory therapy in this most at risk group of children.[20] Such comparative advantage over probiotics is interesting given the prevailing and increasing interest in probiotic interventions in the management of diarrhoea in children; although probiotics hold mechanistic plausibility by regulating intestinal microbiome homeostasis, the urgency of the racecadotril antisecretory effect seems to have a clinically significant impact in the acute diarrhoeal treatment environment. Such findings are correlated with the current findings, in which the period of recovery in the post-racecadotril treatment group (about one day less than that in the control group) was statistically significant, which

implies that within the framework of clinical practice at the level of the personal patient of an individual patient, and, consequently, at the level of healthcare resource consumption.

Zulfiqar et al. compared the efficacy of racecadotril added to oral rehydration solution in children with acute gastroenteritis and found that oral rehydration solution with racecadotril was more effective than use of oral rehydration solution alone in reducing the number of stools and decrease in duration of diarrhoea, as well as the overall rate of clinical recovery.[21] The following findings have a significance in that they support the additive therapeutic effect of racecadotril in adjunction with ORT and reaffirm the theory that combination interventions focusing on both fluid replacement and intestinal hypersecretion may achieve better results than either one of the therapeutic approaches alone. The symbiosis of these two therapies is due to a physiologically sensible model of therapeutic action: ORT replenishes fluid and electrolytes losses, whereas racecadotril is an upstream control requiring less secretory action to be inhibited, which decreases the losses that ORT has to counter. The same was found in another study held in Pakistan by Anwer et al. in 2024 comparing racecadotril and ORT to probiotics alone, with symptoms being resolved almost 30-times faster with the former.[22] All these similar conclusions, based on a series of independent study populations, performed in diverse clinical settings, all indicate that racecadotril is a better supportive treatment modality in acute watery diarrhoea management, and point to its generality as a treatment with a generalisable, and not situation-specific, therapeutic application.

The results of a relatively low incidence of adverse events (less than 10 per 100,000-1) and none of the severe adverse reactions reported by Manfredi et al. (2025) are similar to our own safety data.14 Racecadotril has an excellent safety profile with a limited risk of constipation or abdominal stretching.[23] Tolerability data in our study are of special interest due to the fact that the population of the study was young children that drug safety is subject to the highest levels of rigour set and whose outcomes of an iatrogenic damage are most likely to be the most severe. The low rates of adverse events reported in the studies conducted in various countries and healthcare facilities consistently lend some level of external validity to the safety observations that enhance the degree of confidence in their clinical generalizability. No changes to the central nervous system which, when associated with our hypothesis that a local action of racecadotril might be responsible in the intestinal hypersecretion without any abnormal effect on motility, is in line with the pharmacological evidence that racecadotril does not cross the blood-brain barrier.[24] This property contributes further to its applicability in paediatric practice where their applicability in clinical practice among children has traditionally been constrained by the possibility of CNS-mediated side effects of the other antidiarrhoeal agents. Not only does the lack of neurological involvement separate racecadotril activity in comparison to older generations of antidiarrhoeal agent, but also it offers a mechanistic explanation of why intestinal motility is predictably preserved and no sedation or change in behaviour is reported in any paediatric cohort undergoing administration of racecadotril.

Economic analysis studies have shown that racecadotril is cost-effective in numerous health care facilities and economic conditions. In a cost-utility model based on multinational analysis, Rautenberg and colleagues demonstrated that adjunctive racecadotril showed low overall treatment costs as measured by a reduced length of hospitalisation and costs related to resource use.[25] The practical implications of the finding are of significant importance to healthcare settings with limited budget where achieving the best clinical outcomes at the least possible cost is a primary policy goal. The dependence between clinical benefit and economic worth are most directly related in the scenario of acute diarrhoeal disease wherein the main determinants of the costs of health care such as, length of hospital stays, the intensity of nursing care, and the amount of intravenous fluid and electrolyte replacement needed are all directly regulated by the rate and extent of clinical healing. Our costing study also showed that there was a major saving and an average of 6,230 PKR per patient which this figure was comparable to the southeast Asian studies that had attributed the reduced recovery to the use of the racecadotril to lower hospital expenses.[26] These savings need to be put into context in terms of generally addressing healthcare economics, where even small cash reductions per-capita can result into significant systemic savings if brought together over large numbers of patients, which may allow the redirection of resources elsewhere to address clinical need gaps. Moreover, indirect economic recovery benefits linked to a lower illness period such as the lower opportunity cost that caregivers would otherwise face by having to stay out of the labor force, constitute yet another form of economic value that costing studies focused on direct healthcare spending alone are likely to underestimate systematically.

Moreover, a review of the world networks has demonstrated that racecadotril is among the most effective and safe approaches to cure diarrhea in children. Florez et al. considered the results by finding that racecadotril could not establish a difference in clinical recovery that might be linked to a greater chance of potential adverse events than did other antidiarrhoeal agents.[27] The strength of this conclusion based on an in-depth synthesis of the evidence base present, which includes information on randomised controlled trials different types of clinical populations and geographic locations, attests to the high level of confidence in the clinical recommendations to be made based on these results. Network meta-analytic techniques are especially appropriate in answering comparative effectiveness questions that emerge in areas of therapeutic interest typified by the

availability of multiple agents, and the racecadotril positioning that persistently appears favourable in these studies, in particular, is thus of particular value. In addition, Lukasik J expressed that the advantageous use of racecadotril was particularly evident in developing and middle-income nations where bacterial diarrhoeas are more prevalent, and in which the resources to rehydrate are scarce.[28] This finding highlights the possibility that racecadotril may have a role other than as a pharmacological adjunct, but rather as a strategically relevant part of the diarrhoea management systems, in which the coinciding clinical and logistical challenges of managing acute gastroenteritis in children are greatest, and where the instances of poor management, such as severe dehydration, electrolyte imbalance, and diarrhoea-related mortality.

Limitations: However, there are some limitations to this study. Being a single center trial, the results may not be applicable to outpatient or community-based cases. Stool output was measured in terms of frequency and not total volume and therefore may not reflect reductions in fluid loss. Importantly, microbiological testing was not done which restricts pathogen-specific assessment of treatment effects. Lastly, the follow-up period was completed at discharge and late recurrences or post-discharge complications were not assessed.

CONCLUSION

Racecadotril is safe, effective and economical. It reduces the stool quantity and the hospitali stay of children with AWD promptly and irrespective of their age and dehydration condition.

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Authors Contribution:
Own Abbas: Data collection and article drafting
Ayesha Nousheen: Article drafting
Abdullah Ali: Introduction and methodology
Syed Khuzaima Arslan Bokhari: Results analysis and write-up
Shazia Naz: Results analysis
Muhammad Ali Khan: Proof-reading and final refining

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