Efficacy of Racecadotril in Acute Gastroenteritis in Children at Tertiary Care Hospital

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Abstract

Objective: To compare the mean reduction in number of stools in racecadotril group with placebo group in the management of acute gastroenteritis in children with some dehydration.

Material and Methods: It was Quasi experimental study conducted in the Department of Pediatric Medicine, Children Hospital and ICH, Pakistan. Duration was of this study six months from 01/08/2022 to 31/01/2023. A total of 60 patients presented with acute gastroenteritis were divided to 2 groups. Group A oral rececadotril in addition to standard WHO treatment for acute gastroenteritis and Group B only standard WHO treatment along with 5ml of distilled water in the form of placebo. After 3 days both the groups were contacted and asked about the number of stools. Drug was considered efficacious if the number of stools is ≤2 per day after three days.

Results: In our Mean No. of stools at baseline in Group A was 7.001.26 in Group B 7.30±1.09, p-value = 0.328, mean No. of stools after treatment in Group A was 2.47±0.77 and in Group B 4.63±0.67, p-value = 0.0001. Comparison of mean reduction in number of stools after treatment in Group A was 4.53±1.14 and in Group B 2.67±1.03, p-value=0.0001. Conclusion: Racecadotril is more effective when compared with placebo group in the management of acute gastroenteritis in children with some dehydration.

Keywords: acute gastroenteritis, children, management, racecadotril, effective.

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Introduction

Diarrhea typically refers to having three or more unusually loose or watery bowel movements in a day.[1] Acute gastroenteritis, as described by the American Academy of Pediatrics, is a type of diarrhea that comes on suddenly and may include other symptoms like nausea, vomiting, fever, and stomach pain.[2] An estimated 525,000 children under the age of five worldwide pass away from diarrheal illness each year.[3]

Acute diarrhea is infection of gastrointestinal tract caused by variety of viruses, bacteria and protozoa. Rota virus is being the most common cause of acute diarrhea in well nourished breastfed infants and children under the age of five years.[4] Treatment of acute gastroenteritis with ORS is the most effective and recommended intervention by the WHO for prevention and management of dehydration. Annually, 11 million child deaths occur, of which two thirds are avoidable due to the widespread use of zinc supplements and oral rehydration salts (ORS) for the treatment of diarrhoea.[5]

The use of Zinc has shown significant reduction in the duration and severity of diarrhea and is the essential component in the treatment of gastroenteritis according to the WHO recommendations.6 Racecadotril is a new addition for the treatment of acute gastroenteritis. Racecadotril (acetorphan) is an inhibitor of enkephalinase (endorphin-metabolizing enzyme neutral endopeptidase).[7] It is the specific inhibitor of the neutral endopeptidase present on the epithelium of kidney and small intestine.[8]

Rececadotril reduces the hypersecretion of water and electrolytes in the intestinal lumen by preventing the degradation of endogenous enkephalins.[4] In randomized double blind control trials rececadotril has proven effi-

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cacious than placebo in acute diarrhea in adolescents and adults.[9] A study was conducted by Sultana et al[5] on 100 children in 2020. Study was randomized controlled trial and rececadotril group showed significant reduction in stool frequency than the placebo group (11.95± 2.41 Vs 14.85±1.95, p=0.0001) on third day of admission. Diarrhea is major of cause of mortality, second to pneumonia in under 5 children and is common cause of hospitalizations due to dehydration and electrolytes imbalances. If the results of this study will be favorable, the drug will definitely help in reducing under 5 mortalities, malnutrition and need for hospitalizations due to diarrheal illness. Moreover, this study will also help to fulfill the gap in literature.

Material And Methods

A Quasi experimental designed, during the period from 01/08/2022 to 31/01/2023, the study was conducted at the Pediatric Medicine Department of Children hospital and ICH, involving 60 patients (30 in each group). After taking approval from IRB No. Ref No. 187-89 dated 07-10-2021. These patients were selected based on specific inclusion criteria: they pre-sented with acute gastroenteritis and some dehydration, were of either gender, and aged between 6 months and 14 years. Excluded were those with malnutrition, immu-nocompromised status, osmotic diarrhea, severe dehy-dration, bloody diarrhea, chronic diarrhea, or those with severe dehydration. Following approval from the ethical committee of Children Hospital and Institute of Child Health, Faisalabad, informed consent was obtained from guardians. Patient demographics (age, gender, weight, height) were recorded, along with their contact details. A thorough medical history was taken, and a standard physical examination was conducted upon admission, including assessing dehydration status. Patients were then randomly assigned to two groups using a blinded envelope system: Group A received oral racecadotril in addition to standard WHO treatment for acute gastroenteritis, while Group B received standard WHO treatment along with 5ml of distilled water as a placebo. After three days of intervention, both groups were contacted by phone to inquire about their stool frequency. The intervention was considered successful if the stool frequency was ≤2 per day after three days. Data were input and analyzed using SPSS version 23. Mean and standard deviation were computed for quantitative variables such as age and stool frequency. An independent sample t-test was utilized to compare stool frequency between the two groups. Effect modifiers like age, gender, weight, and disease duration were controlled by stratifying the data, followed by post-stratification independent sample t-tests. A p-value of ≤0.05 was deemed statistically significant.

Results

Our study observed that 63.33% of patients in Group A and 53.33% in Group B were aged between 1-7 years, while 36.67% in Group A and 46.67% in Group B were aged between 8-14 years. The mean age was 7.13±3.03 years in Group A and 7.40±2.71 years in Group B. Regarding gender distribution, 56.7% of patients in Group A and 53.3% in Group B were male, while 43.3% in Group A and 46.7% in Group B were female. The mean duration of the disease was 1.23±0.43 days in Group A and 1.20±0.41 days in Group B, with a non-significant p-value of 0.759. The table presents a comprehensive comparison between Group A and Group B concerning the number of stools before and after treatment, as well as the mean reduction in stool frequency post-treatment. At baseline, there was no statistically significant difference in the mean number of stools between the two groups, with Group A having a mean of 7.00 stools and Group B having a mean of 7.30 stools, both with relatively similar standard deviations. After treatment, however, notable distinctions emerged. Group A exhibited a substantial reduction in stool frequency, with a mean of 2.47 stools post-treatment, whereas Group B showed a less pronounced decrease, with a mean of 4.63 stools. This discrepancy in post-treatment stool frequency was highly significant, as indicated by the p-value of 0.0001. Furthermore, analyzing the mean reduction in stool frequency after treatment revealed a stark contrast between the groups. Group A demonstrated a substantial mean reduction of 4.53 stools, while Group B exhibited a lesser mean reduction of 2.67 stools. This difference was also highly significant, underscoring the efficacy of the intervention in Group A compared to the control group.

Table 1: *Comparison of two groups regarding number of stools*

	Group A(n=30)		Group B(n=30)		P value
	Mean	SD	Mean	SD	
At baseline	7.00	1.26	7.30	1.09	**0.328**
After treatment	2.47	0.77	4.63	0.67	0.0001
Mean reduction after treatment	4.53	1.14	2.67	1.03	0.0001

Discussion

Each year, around 2 billion cases of acute diarrhea affect children, primarily in underdeveloped countries, according to the World Health Organization. This disease accounts for about 18% of deaths among children under five years old. Globally, diarrheal illnesses are a leading cause of both illness and death in children. Dehydration results from the loss of water and electrolytes due to intestinal issues like malabsorption and excessive secretion. The main treatment approach for children with watery diarrhea is to administer oral rehydration solutions to replace the ongoing fluid losses. Oral rehydration therapy remains the primary and recommended treatment for acute diarrhea in children, according to the World Health Organization. While this approach has significantly reduced morbidity and mortality rates associated with diarrhea, it has limited impact on reducing stool volume or frequency.

Recognizing this limitation, the World Health Organization has proposed the use of pharmacological treatments alongside rehydration therapy, provided these medications are proven safe and effective for pediatric patients. Racecadotril is one such medication that works by inhibiting intestinal hypersecretion without significantly affecting motility. Studies have shown that oral racecadotril is safe and effective in treating acute watery diarrhea in both children and adults. This study aims to evaluate the efficacy of racecadotril as an additional treatment, which could potentially contribute to reducing mortality rates, malnutrition, and the need for hospitalization among children under five years old due to diarrheal illnesses. Additionally, this research may help fill gaps in existing literature regarding the management of acute diarrhea in pediatric patients.

In our study, Group A had a mean age of 7.13±3.03 years, while Group B had a mean age of 7.40±2.71 years. In terms of gender distribution, 56.7% of Group A and 53.3% of Group B were male, with 43.3% and 46.7% being female, respectively. The mean duration of disease was similar between Group A (1.23±0.43 days) and Group B (1.20±0.41 days), with a non-significant p-value of 0.759. At baseline, the mean number of stools was 7.00±1.26 in Group A and 7.30±1.09 in Group B, with a p-value of 0.328. After treatment, Group A showed a mean of 2.47±0.77 stools, significantly lower than Group B's 4.63±0.67 stools (p-value=0.0001). The mean reduction in stool frequency after treatment was 4.53±1.14 in Group A and 2.67±1.03 in Group B, also significant at p=0.0001.

Sultana et al[5] conducted a randomized controlled study on 100 children in 2020, finding a significant reduction in stool frequency in the control group compared to the placebo group (11.95±2.41 vs. 14.85±1.95, p=0.0001) on the third day of admission, supporting our findings on racecadotril's efficacy.

Quantitative analysis of racecadotril's effect in placebo-controlled and add-on studies has been performed previously, with meta-analysis focusing on placebo control studies due to heterogeneity in active controls. Nine studies reported a reduction in mean stool number on the second day post-racecadotril administration, contrasting with our study's significant reduction after 3 days. Two larger studies found no statistically significant difference, yet meta-analysis demonstrated racecadotril's benefit in reducing stool frequency.

Numerous studies assessed racecadotril's efficacy based on various criteria, including the national diarrhea prevention and treatment commission's parameters in China.[13] Meta-analyses[14] consistently showed racecadotril's benefits in terms of efficacy, whether categorized by improvement, cure rates, or global efficacy scales.

Considering this evidence, racecadotril emerges as an efficacious and well-tolerated treatment for reducing stool frequency compared to placebo, as supported by multiple studies.

Considering all these evidence we come to conclusion that rececadotril is efficacious and more tolerable then placebo in reducing mean number of stools.[15]

Conclusion

We concluded that the mean reduction in number of stools was significantly lower in racecadotril group when compared with placebo group in the management of acute gastroenteritis in children with some dehydration.

Conflict of Interest: *None*

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Authors Contribution

ZMA: Conceptualization of Project
AK: Data Collection
AK: Literature Search
MIK: Statistical Analysis
AI: Drafting, Revision
AM: Writing of Manuscript