Original Article

To Study the Efficacy of Racecadotril for Treatment of Acute Watery Diarrhea in Children

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ABSTRACT

Objective: To study the efficacy of racecadotril on decreasing no of stools in pediatric population presenting with acute watery diarrhea to decrease the length of hospital stay.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Pediatric Unit MTI, Mardan Medical Complex from April to August 2019.

Materials and Methods: 120 children, aged 6 months to 2 years, were included and placed on random basis in a racecadotril or placebo group. Criteria of inclusion was patients diagnosed with acute gastroenteritis. Patient having any other disease or allergy were excluded. Racecadotril and placebo were given at a dose of 10 mg p/o TDS for children below 1 year, 30mg P/O TDS for children above 1 year. Data were collected and analyzed in SPSS 20.

Results: Mean age was 9.8 months. Females were 45.8% whereas males were 54.2%. Stool frequency at 48 hours in Racecadotril group were significantly decreased with a (mean of 5.10/SD 2.589/ P-value 0.012 as compared to Placebo (mean of 7.22 /SD 2.835). Mean age was 9.8 months. females were 45.8% whereas males were 54.2%. Stool frequency at 48 hours in Racecadotril group were significantly decreased with a (mean of 5.10/SD 2.589/ P-value 0.012 as compared to Placebo (mean of 7.22 /SD 2.835). Length of hospital stay was lower in racedo category 76.40 hours /SD 31.08610/P – value: 0.029 as compared to placebo with a mean of.92.400 hours /SD 38.9816. Length of hospital stay was lower in racedo category 76.40 hours /SD 31.08610/P – value: 0.029 as compared to placebo with a mean of.92.400 hours /SD 38.9816.

Conclusion: We have concluded from this study that racecadotril can be effectively used for treating acute gastroenteritis in pediatric population. It decreases stool frequency that will reduce duration of hospital stay.

Key Words: Racecadotril¸ Treatment, Acute Watery Diarrhea, Children

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INTRODUCTION

In children, acute gastroenteritis is very common. Its characteristics are acute diarrhea with or without vomiting. It is defined by passing 3 or more loose stools in a day (or more than what is normal for that person), that lasts for no more than two weeks.[1,2]

Diarrhea is a major global issue that causes very huge impact on social and financial sector. About 1.9 million children die annually due to diarrhea.[3] One of the major causes of under nutrition in pediatric population below 5 years of age is diarrhea. [4]

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It is common cause of morbidity and mortality within pediatric population of under developed countries with estimated 2 million deaths annually.[5]

The causative organism is rotavirus. Treatment is primarily aimed at the correction of dehydration and electrolyte abnormality.[6]

Racecadotril (acetorphan) inhibits enkephalinase so that it dosenot allow splitting of endogenic opioids (enkephalins) which then acts on receptors in gastrointestinal tract thereby decreasing water and electrolytes secretion in intestines with no impact on intestinal motility.[7-10]

It is safe and effective to use orally in pediatric population as well as in adults diagnosed with acute gastroenteritis.[11]Racecadotril when given as adjunct therapy is more efficacious and less expensive in comparison to ORS used alone.[12-14] It is recommended to use racecadotril with oral rehydration therapy. According to the NICE guidelines.[15]

MATERIALS AND METHODS

It was cross sectional study with Non Probability Consecutive Sampling conducted at Pediatric Unit Mti

Mardan Medical Complex from April to August 2019. The study was approved by ethical committee.

Children aged 6 months to 2 years who had passed3 or more loose stools in a day (or more than what is normal for that person), lasting less than 2 weeks were included for the study. Written informed consent was taken from parents.

Exclusion Criteria: Severe dehydration[16].

Allergy to racecadotril

Children who had severe vomiting.

Patients in renal failure.

Patients in liver failure

Children who received probiotics/antibiotics or other anti diarrheal medications.

Clinical parameters like height and weight of the patients were noted by attending physician. Patient Hydration status were classified according to WHO scale[16], after initial treatment recommended by who for mild to moderate dehydration, patients were categorized in a random way into two categories, one being racecadotril and the other placebo .patients in the racedo group received racecadotril dissolved in ORS at a dose recommended by the manufacturer: 10 mg per dose three times a day for children below 12 months of age and 30 mg thrice a day for those over 12 months of age. the placebo group received placebo(ORS without racecadotril) at equal doses to the racecadotril group. Patients were instructed to dissolve one sachet in a cup of water having ORS and drink thrice a day.

Patients were daily enquired about the number of stools and consistency of stools, treatment was continued till the cessation of diarrhea.

The criteria of cessation of diarrhea was passing of two formed stools successively or if the patient didn't pass any stool for 12 hours.[7,15]

Primary outcome was no of stools during the 72 hrs period, secondary outcome was length of hospital stay.

Descriptive statistics for age, gender were documented in the form of mean, standard deviation, percentages. To compare results of both groups cross tabulations, bar charts andchi-square test were used. SPSS 20 was used for the analysis of data. The P-value of <0.05 was considered as statistically significant.

RESULTS

120 patients were enrolled for research and were randomly assigned into two groups, one group received Racecadotril and the other group received Placebo.

Mean age was 9.8 months. Females were 45.8% whereas Males were 54.2%.

The baseline features like demographics and clinical presentation had no major differences. After receiving Racecadotril frequency of stools at 48 hrs decreases significantly with a (mean of 5.10) SD 2,589 P-value 0.012 as compared to Placebo where the mean no stools at 48 hrs is significantly higher than the Racecadotril group having mean of 7.22 SD 2.835.

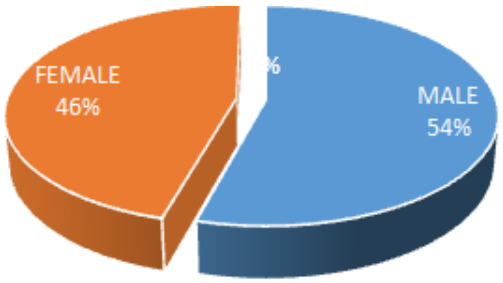

Figure No.1: Male female ratio.

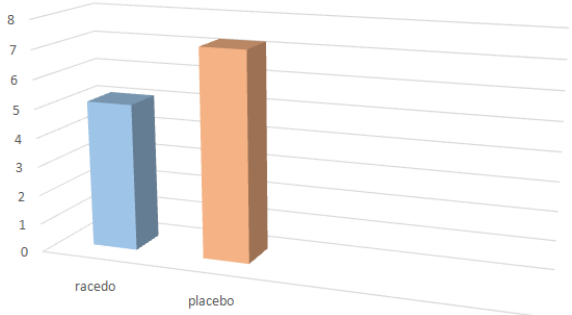

Figure No.2: Mean no. of stools at 48 hrs. for Racedo / Placebo

Above figure is a graphical presentation of effect of Racecadotril Vs Placebo on stool frequency at 48 hours of administration

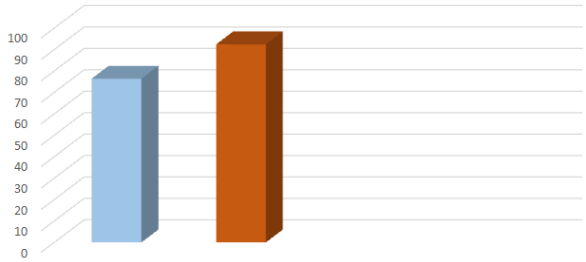

Figure No.3: Mean Hospital Stay after Treatment with Racedo /Placebo

Above figure is a graphical presentation of effect of Racecadotril Vs Placebo on duration of hospital stay after administration of drug/placebo.

Table No.1: Effect of Racecadotril on Frequency of Stools and Length of Hospital Stay: Descriptive Statistics

	No. of patients	Mean value	Std. Deviation
Length of hospital stay	60	76.4000	31.08610
Stool frequency	60	5.10	2.589

Secondary outcome was the duration of hospital stay 'that is lower with Racecadotril. Class in comparison to placebo with mean 76.40 hours /SD 31.08610/P –

value: 0.029. In the placebo group mean duration of hospital stay was 92.400 hours /SD 38.98161.
No adverse effects were noted.

Table No.2: Effect of Placebo on Frequency of Stools and Length of Hospital Stay: Descriptive Statistics

	No. of patients	Mean value	Std. Deviation
Stool frequency	60	7.22	2.835
Length of hospital stay	60	92.4000	38.98161

H0: No association between no. of stools at 48hrs /duration of hospital stay and drug utilized
H1: There is association between no. of stools at 48hrs /duration of hospital stay hospital stay and drug
Chi-Square shows the goodness of fit between the observed values and those expected theoretically. From the analysis of the given data set, the chi square value is greater than p value therefore it leads us to rejection of null hypothesis that is no association between hospital stay and drug.

P-Value (.012) was statistically significant for effect of racecadotril on the frequency of stools.

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	25.578[a]	12	.012
Likelihood Ratio	29.841	12	.003
Linear-by-Linear Association	15.931	1	.000
N of Valid Cases	120		

P-Value (.029) was statistically significant for effect of racecadotril on the length of hospital stay.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	12.477[a]	5	.029
Likelihood Ratio	15.269	5	.009
Linear-by-Linear Association	5.921	1	.015
N of Valid Cases	120		

DISCUSSION

This study on children having watery diarrhea is a comparison between Racecadotril and Placebo in reducing stool frequency and consequently hospital stay. Racecadotril not only decreases the severity but also the length of hospital stay.
When a comparison was made between racecadotril and placebo categories, former group hadpromising (P<0.012) decrease in stool output of 48 hours and a promising decrease In the length of hospital stay (p<0.029).
Racecadotril (acetorphan)inhibits enkephalinase so that it dosenot allow splitting of enkephalins which then acts on receptors in gastrointestinal tract thereby decreasing water and electrolytes secretion in intestines with no impact on intestinal motility.[8]
120 patients were enrolled in this study conducted at paediatric unit of MMC Mardan. The criteria of inclusion was passing 3 or greater than 3 unformed stools in a day for less than 14 days.
Individuals with severe dehydration or allergy to racecadotril were excluded. Also patients with comorbid conditions were excluded as they may have had effects on the results of the study
Oral dose of 10 mg for children less than 12 months and 30 mg for those above the age of 12 months was prescribed in TDS. The patient was considered to have improved after passsing formed stools at least twice. The primary outcome was the reduction in number of stools with the use of racecadotril (mean 5.10) as compared to the placebo group(mean 7.22) and secondary being reduction of hospital stay with a mean 76.4 hrs with racecadotril and 92.4 hrs with placebo.
the results were in accordance with the other studies carried out on the same topic.previous studies show the safety and efficacy of racecadotril in both children and adults.[11]
Other studies conducted on this topic compared the use of racecadotril with zinc and ORS. we conducted this study solely on racecadotril effects to determine its clinical significance. Also other studies lack information on comparison between hospital stay.

CONCLUSION

We have concluded from this study that racecadotril can be effectively used for treating acute gastroenteritis in pediatric population. It decreases stool frequency that will reduce duration of hospital stay.

Author's Contribution:

Concept & Design of Study:	Nafees Khan
Drafting:	Muhammad Qasim Khan, Kiramat Ullah
Data Analysis:	Muhammad Fazil, Ammad Ali, Rifayat Ullah Afridi
Revisiting Critically:	Nafees Khan, Muhammad Qasim Khan
Final Approval of version:	Nafees Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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