



Comparative efficacy of racecadotril versus loperamide and probiotics in acute diarrheal illness of adults.

Amar Nazir¹, Muhammad Mustafa Qamar², Fida Muhammad Sheikh³, Nighat Faima⁴, Shahzad Aslam⁵, Sheraz Saleem⁶

1. MBBS, FCPS
Associate Professor of Medicine
Sargodha Medical College.
2. MS (Special Medicine)
Assistant Professor
Sargodha Medical College.
3. MBBS, FCPS
Assistant Professor of Cardiology
Sargodha Medical College.
4. MBBS, FCPS
RMO Medicine
Sargodha Medical College.
5. MBBS, FCPS
Professor of Cardiology
Niazi Medical & Dental College,
Sargodha
6. MBBS, FCPS
Assistant Professor of Medicine
Sargodha Medical College.

Correspondence Address:

Dr. Amar Nazir
Department of Medicine
Sargodha Medical College.
amirnazir234@yahoo.com

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ABSTRACT... Objective: Main aim of this research is to evaluate and differentiate the safety, effectiveness and acceptability of racecadotril versus probiotics and loperamide in the out/inpatient management of adults with acute diarrheal illness. **Study Design:** Cross sectional study. **Setting:** Department of Medicine District Head Quarter Hospital Sargodha. **Period:** May 2019 to October 2019. **Material & Methods:** Patients over eighteen years of age (Males/females) having acute diarrheal illness were entitled for this study. Patients who have symptoms of at the minimum three watery stools per 24 hours with less than two weeks duration were considered having acute diarrhea. Acetorphan (100 mg 3 times/ 24hrs), probiotics and loperamide (2 mg succeeding every loose motion) were given orally in 100 adults with moderate severe diarrhea in three different groups of patients. Treatment plus oral rehydration therapy was continued for five days or uptill recuperation, if this sprung up prior. The patients were briefed (at the day one visit) to report during the succeeding visit about symptoms control. Patients were not clued-up that normal stool frequency was the main seek of the study, so there was no chance for Pygmalion effect. **Results:** Towards the end of study it was observed that the quantifiable accomplishment rates for loperamide, racecadotril and probiotics were 89.0%, 94.28% and 33.33% respectively. Denote diarrhea span was (16 +/-1.9h) with racecadotril, (15+/-1.1h) for loperamide and 26 +/- 4.5h) for patients using probiotics. **Conclusion:** In adult patients having acute diarrheal illness loperamide and racecadotril are expeditious, about equivalently effectual therapies. Probiotics are not as effective as other two drugs but have least side effects. Treatment relevant constipation was more in loperamide group as compare to two others.

Key words: Adults Acute Diarrhea, Loperamide, Probiotics, Racecadotril.

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INTRODUCTION

One of the most prevalent devastating disease of human gastrointestinal system is acute infectious diarrhea affecting people irrespective of age from childhood to adulthood around the globe.¹ Lot of deaths every year amid all age groups are due to acute infectious diarrhea and its complications especially in undersized countries.² Acute infectious diarrhea remains a considerable therapeutic predicament in children's as well as in adults especially in third world countries which is the reason for increased number of deaths due to fluid electrolytes imbalance, dehydration, acute renal failure (pre renal azotemia), metabolic acidosis, circulatory shock,

impaired consciousness and other complications of acute diarrhea.^{3,4} Comparative Data for acute diarrhea control by medication lacks in Pakistan predominantly for adult inhabitants. The wonted underlying cause of acute onset infectious diarrhea is escalated intestinal mucosal secretions. Edelman, R etal annotated that incorporated electrolytes and water substitution with a compound which restrains intestinal frenzied secretion and does not obtuse gastrointestinal tract movement is the best therapeutic treatment of choice for acute diarrhea in adults.⁵ Another anti-diarrheal agent is loperamide which reduces gut transportability by acting as agonist of u-opioid receptor (MOR) with high rapport for

enkephalins and beta- endorphin. Loperamide has crouch compassion for dynorphins. Imprudent constipation, abdominal bloating and hazardous microorganisms confinement are common superfluous side effects of loperamide.⁶ Racecadotril, Mechanism of accomplishment is that it causes specific deterrence of enkephalinase and by this way it impedes gut hypersecretion of water and electrolytes by not influencing the gut transit. Probiotics (*Saccharomyces boulardii* and *Lactobacillus rhamnosus*) are usual accompanied medicines for adult's acute diarrhea treatment. Probiotics acts by restraining metabolic bustle, augmentation and adhesions of enteromorbific bacterias (*shigella*, *salmonella* and *E coli*) to intestinal wall.^{7,8} In this study efficiency analysis of racecadotril (100mg three times daily) with loperamide (2mg after each loose stool) and probiotics were surveyed in 100 patients (3 groups) with acute diarrheal illness. Reduction of stool frequency after treatment beginning was the foremost efficiency decisive factor used.

MATERIAL & METHODS

A cross-sentential study of one hundred well collaborative patients (over eighteen years of age, Males/females) having acute diarrheal illness were incorporated in this study. Patients who have symptoms of at the minimum three watery stools per 24 hours with less than two weeks duration were considered having acute diarrhea. Study was conducted in Medicine Department of District Head Quarter Hospital Sargodha and University Medical Diagnostic Centre, period May 2019 to October 2019.

Loperamide (4mg stat then 2 mg after each loose stool and maximum of 16mg/ 24 hrs), Racecadotril (100 mg three times/ 24hrs) were given in 35 patients each and probiotics in 30 patients of acute diarrheal illness along with rehydration therapy. Patients treatment was continued for 5 days or until recuperation, if this sprung up prior. Improvement in symptoms of acute diarrhea after commencing treatment was the foremost efficiency measure used. Patients having acute diarrhea were treated in anticipation of revival, distinct as passing two normal stools per 24 hrs. Patients on antidiarrheals not ameliorating after

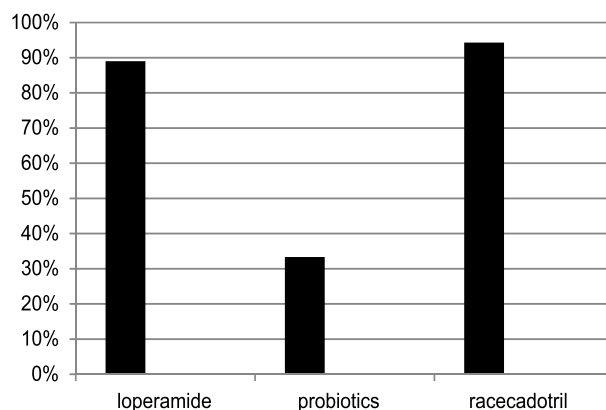
mentioned time period were prescribed other treatment options to improve diarrheal symptoms. At the initial visit patients were briefed to inform on the succeeding visit about control of diarrheal symptoms, constipation or other symptoms if they have. To avoid Pygmalion effect patients were not clued up that normal stool frequency was the main seek of study.

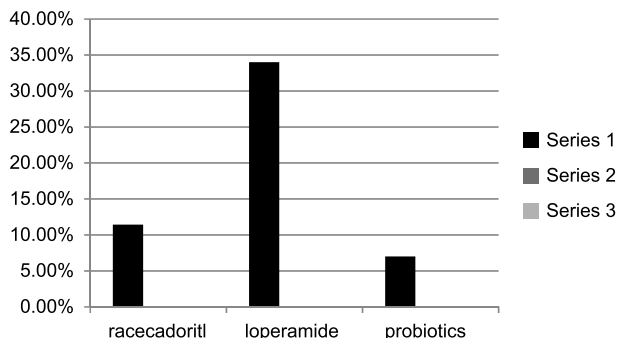
Patients having (i) Lactation or gestation (ii) Immune deficient states (iii) Severe associated infections (iv) Renal or hepatic failure (v) Chron's disease and ulcerative colitis (vi) Chronic, bloody or drug induced (pseudomembranous colitis) diarrhea and patients who received diarrhea treatments (antibiotics or antidiarrheal) within seven days before advent were excluded from the study.

RESULTS

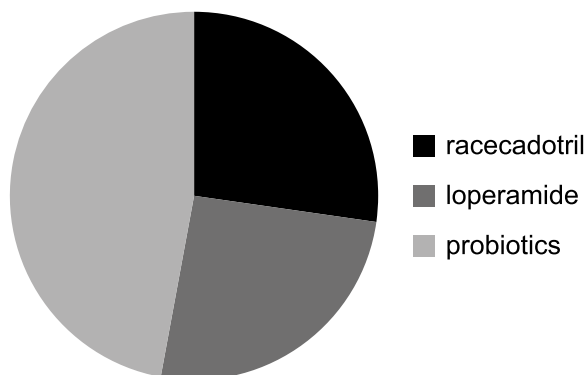
Towards the end of study it was observed that the quantifiable accomplishment rates for loperamide, racecadotril and probiotics were 89.0%, 94.28% and 33.33% respectively. Totally 100 submissive patients took part in the study and each one at least got sole dosage in hospital under observation. Racecadotril and loperamide were given in 35 patients each and probiotics in 30 patients of acute diarrhoeal illness. Denote diarrhea span was (16 +/-1.9h) with racecadotril, (15 +/-1.1h) for loperamide and 26 +/- 4.5h) for patients using probiotics.

Patients group on loperamide got side effect of constipation in 33% of patients.

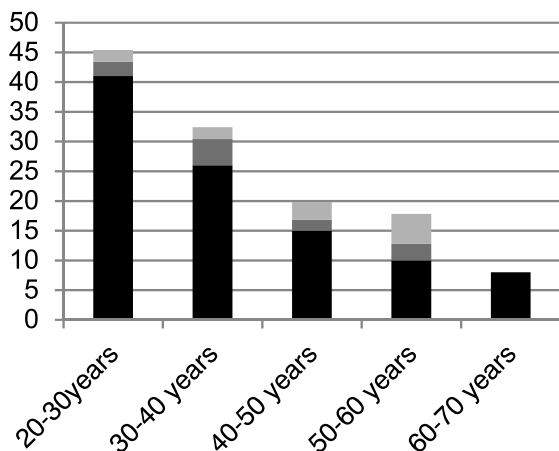




Constipation (Side effect) Comparison of three drugs used.



Denote diarrhea span 16.5, 15.5 & 28.5 hrs. in racecadotril loperamide and probiotics



Patient's Age.

About 11.4% patients using racecadotril got issue of infrequent or difficult bowels evacuation and 7% patients on probiotics got considerable constipation. 10 patients were given antibiotics and other medications within 5 days of treatment due to non-improving symptoms especially in

probiotics group.

DISCUSSION

Intestinal viral infection frequently is the reason of acute diarrhea in adult patients. Taking Oral rehydration therapy, foods containing probiotics, proper soft diets and copious amount of fluids is generally sufficient to be recovered from mild diarrheal illness.⁹ Nevertheless the unambiguous therapy is needed in moderate to severe acute adult diarrhea as the illness may become serious or even life threatening due to complications of severe acute diatthea.¹⁰ Inhibition of enkephalinase is the way by which racecadotril acts and by this way it protracts the antiscriptural action of endogenous enkephalinase.¹¹

Loperamide hydrochloride is agonist of kappa opiod receptor in intestinal wall, affects electrolytes and water movement through the bowel by decelerating gut agitation. These antidiarrheals are effectual in decreasing diarrhea symptoms, continuation, frequency, abdominal discomfort and other diarrhea associated complications.¹² Also these intestinal opiod sensory receptor synergists setbacks fluid conveyance through gut giving ample time for electrolytes and water to be engrossed though intestine.¹³ Hazardous microorganisms encampment (colonization), constipation and liquids amalgamating in bloated bowel lumen are commonest side effects of loperamide hydrochloride which necessitate the use of drug having antisecretory effect with no detrimental effect on intestinal peristalsis like racecadotril.^{14,15}

The best probiotics are lactobacilli (used in this study) and saccharomyces boulardii for treating acute diarrhea. Mechanism of action of Probiotics is by combating the hazardous microorganisms in gut improving diarrhea symptoms. Different studies demonstrate that probiotics are well endured with least after effects when used in patients of acute diarrhea.¹⁶ Comparative efficacy of race+cadotril, loperamide and probiotics in adult's acute diarrhea was observed in this cross sectional study.

According to an aforesaid multinational study

by Hwang et al the efficacy of loperamide and racecadotril in adults acute diarrhea was 92.0% and 95.7% which is quiet comparable with our results.¹ Another double blind, randomized study by J.M. Vetel and H. Berard revealed bit low efficacy of racecadotril as compare to this study. This may be due poor drug compliance, prolong study duration, dissimilar race and big set of patients.¹⁷ Cologne et al showed acute diarrhea responded in 29% patients after using probiotics which is compareable with our study as well.¹⁸ Towards the end of study it was observed that the quantifiable accomplishment rate for racecadotril was 94.28%, loperamide 89.0% and probiotics was 33.33%. The initial diarrhoeal symptoms, duration, frequency and amount was about analogous in patients using these three medicines separately.

In our study racecadotril demonstrates superior diminution in diarrhea persistence and symptoms as compare to loperamide and probiotis albeit they were used in about same quantity of patients. Rapid post treatment Constipation occurrence was noticed more in loperamide group as compare to two other drug category groups. Impulsive recovery in nausea & abdominal discomfort was there with racecadotril and loperamide groups. No significant concomitant side effects were perceived in patients using pobiotics and in general these were well endured. But yeast and bacteria in probiotics may be the source of infrequent infections among these patients particularly in serious and immunodeficient states.¹⁹

CONCLUSION

Abdominal ache, distension, infrequent or difficult bowels evacuation are the usual side effects of conventional antidiarrheal drugs, which confines their use. This study exposed that racecadotril and probiotics for acute diarrhea carries least side effects but racecadotril is far more efficacious. Mentioned side effects were more common with loperamide group especially constipation. As probiotics contain yeast and certain microorganisms so they may occasionally lead to infections in in immune compromised patients or patients with serious illnesses. Racecadotril

was efficacious and prudently endurable drug in solving the signs and manifestations of acute adult diarrheal illness.






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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Amar Nazir	Correspondence Author.	
2	M. Mustafa Qamar	Statistical analysis.	
3	Fida Muhammad Sheikh	Data collection.	
4	Nighat Faima	Data collection.	
5	Shahzad Aslam	Literature review.	
6	Sheraz Saleem	Drafting.	