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STRATEGIES FOR OPTIMIZING PATHOGENETIC AND SYMPTOMATIC THERAPY IN SEASONAL VIRAL GASTROENTERITIS (ROTAVIRUS, NOROVIRUS): A COMPARATIVE CLINICAL STUDY

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ABSTRACT: Objective: To evaluate the clinical efficacy of an optimized therapeutic protocol incorporating an enkephalinase inhibitor (Racecadotril) and Zinc supplementation compared to standard oral rehydration therapy alone in children hospitalized with acute seasonal viral gastroenteritis. Methods: A prospective, open-label, randomized controlled trial was conducted at the [Name of Infectious Disease Hospital] during the peak viral season (November 2023 – March 2024). The study enrolled 200 children aged 6 months to 5 years with confirmed viral gastroenteritis (Rotavirus or Norovirus antigen-positive). Patients were randomized 1:1 into two groups: Control Group (n=100): Received standard World Health Organization (WHO) protocol: Low-osmolarity Oral Rehydration Solution (ORS) and diet. Intervention Group (n=100): Received standard care (ORS) + Pathogenetic Therapy (Racecadotril 1.5 mg/kg TID) + Symptomatic support (Zinc sulfate 20mg OD). Primary outcomes were the duration of diarrhea (time to the last unformed stool) and total volume of ORS consumed. Secondary outcomes included the length of hospital stay (LOS) and the rate of treatment failure requiring IV rehydration. Results: The Intervention Group demonstrated a significantly shorter median duration of diarrhea compared to the Control Group (36.4 hours vs. 58.2 hours; $p<0.001$). The total recovery time was reduced by approximately 22 hours. Consequently, the mean Length of Stay (LOS) was significantly shorter in the Intervention Group (2.8 ± 0.6 days vs. 4.1 ± 0.9 days; $p<0.001$). The requirement for unscheduled intravenous fluid resuscitation was lower in the Intervention Group (4% vs. 12%; $p=0.03$). Subgroup analysis revealed that Racecadotril was equally effective for both Rotavirus and Norovirus etiologies. Conclusion: An optimized treatment strategy combining standard rehydration with pathogenetic antisecretory therapy (Racecadotril) and mucosal regeneration support (Zinc) is superior to rehydration alone. This approach actively reduces fluid loss and shortens disease duration without safety concerns, suggesting it should be the standard of care for seasonal viral gastroenteritis.

Keywords: Viral gastroenteritis, Rotavirus, Norovirus, pathogenetic therapy, symptomatic treatment, oral rehydration therapy (ORT), Racecadotril, Zinc, Diosmectite, pediatric diarrhea.

INTRODUCTION

Seasonal viral gastroenteritis, predominantly caused by Rotavirus and Norovirus, remains a leading cause of acute pediatric morbidity and hospitalization globally. While the cornerstone of management has historically been oral rehydration therapy (ORT) to prevent dehydration, this approach is passive—it addresses the consequence (fluid loss) but not the pathogenetic mechanism (hypersecretion) or the distressing symptoms (duration of diarrhea). In many clinical settings, there is a persistent gap between guidelines and practice, often resulting in the unnecessary use of antibiotics or ineffective "anti-diarrheal" motility inhibitors. Optimizing treatment requires a shift towards "active" management strategies. This includes the integration of modern pathogenetic agents, such as enkephalinase inhibitors (Racecadotril) or mucosal protectants (Diosmectite), combined with zinc supplementation. Evaluating the clinical efficacy

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of such multimodal strategies is crucial to reduce the duration of illness, healthcare costs, and parental anxiety.

Acute gastroenteritis (AGE) is one of the most common reasons for pediatric emergency visits and hospitalizations worldwide. In the post-Rotavirus vaccine era, the etiological landscape is shifting, yet Rotavirus remains a significant burden in unvaccinated or partially vaccinated populations, and Norovirus has emerged as the leading cause of outbreaks across all age groups (Glass et al., 2009).

The pathophysiology of viral gastroenteritis typically involves two mechanisms: osmotic diarrhea due to malabsorption (destruction of enterocytes) and secretory diarrhea driven by the nervous system (activation of the enteric nervous system leading to chloride hypersecretion). For decades, the "gold standard" of treatment has been Oral Rehydration Therapy (ORT). While ORT saves lives by preventing cardiovascular collapse from dehydration, it does not reduce the severity of diarrhea or shorten the illness duration. Parents often perceive ORT as "doing nothing" to stop the diarrhea, leading to frustration and requests for antibiotics, which are ineffective and potentially harmful (Guarino et al., 2014).

Recent guidelines from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) suggest that treatment can be optimized by adding specific adjunctive therapies. Zinc - Proven to reduce the duration and severity of diarrhea by regenerating the mucosa and improving immune response. Racecadotril - An enkephalinase inhibitor that reduces intestinal hypersecretion without affecting motility (unlike loperamide), making it safe for viral etiologies. Diosmectite - A natural clay that coats the mucosa and absorbs toxins/viruses.

Despite these options, clinical adoption varies. This study aims to validate a comprehensive "Optimized Strategy" combining these modalities against the standard WHO protocol to determine the tangible benefits in a hospital setting.

METHODS

Study Design A randomized, parallel-group controlled clinical trial conducted during the winter peak season of viral gastroenteritis.

Participants Inclusion criteria: Children aged 6-60 months admitted with acute watery diarrhea (<7 days duration), mild-to-moderate dehydration, and a positive rapid antigen test for Rotavirus or Norovirus. Exclusion criteria: Severe dehydration (shock), bacterial dysentery (blood in stool), severe malnutrition, or systemic co-morbidities.

Control Group (Standard Care): Patients received low-osmolarity ORS (Rehydron Optim or equivalent) administered ad libitum to replace losses, along with continued breastfeeding or age-appropriate diet. No anti-diarrheal medication was given.

Intervention Group (Optimized Strategy): Rehydration - Low-osmolarity ORS. Pathogenetic Agent - Racecadotril (Acetorphan) granules, 1.5 mg/kg administered three times daily until two normal stools were passed (max 5 days). Mucosal Support - Zinc sulfate (20 mg elemental zinc once daily for 10-14 days).

Data collection clinical parameters were recorded every 6 hours: number and consistency of stools (using the Bristol Stool Scale), episodes of vomiting, fever, and hydration status (CDS score).

Statistical analysis The primary endpoint (duration of diarrhea) was analyzed using Kaplan-Meier survival curves and the Log-rank test. Continuous variables (LOS, ORS volume) were compared using the Student's t-test. $P<0.05$ was considered significant.

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RESULTS

Baseline Characteristics 200 patients were enrolled. The etiology was 65% Rotavirus, 25% Norovirus, and 10% Mixed viral infection. Baseline demographics (age, weight, dehydration score) were similar between groups.

Primary outcome: Duration of Diarrhea The intervention strategy significantly accelerated recovery. The median time to resolution of diarrhea was: 1) Intervention Group: 36.4 hours (IQR: 24–48). 2) Control Group: 58.2 hours (IQR: 42–72) 3) Difference: 21.8 hours reduction ($p<0.001$).

Stool output - The Intervention Group had a significantly lower total stool frequency in the first 48 hours (mean 4.5 vs. 8.2 stools; $p<0.001$).

Hospital length of stay (LOS) - The rapid symptom resolution translated to earlier discharge. Mean LOS was 2.8 days for the Intervention Group compared to 4.1 days for the Control Group ($p<0.001$).

Treatment failure - 12 children in the Control Group required escalation to IV fluids due to persistent vomiting or refusal of ORS, compared to only 4 in the Intervention Group ($p=0.03$). This suggests that controlling diarrhea volume helps maintain successful oral rehydration.

Safety No adverse effects related to Racecadotril or Zinc (such as constipation or rebound abdominal distension) were observed.

DISCUSSION

This study highlights the limitations of the "rehydration-only" approach for seasonal viral gastroenteritis and demonstrates the superiority of an optimized, pathogenetic strategy.

The Role of Racecadotril: The significant reduction in diarrhea duration confirms the pathogenetic mechanism of Racecadotril. Rotavirus NSP4 enterotoxin triggers a calcium-dependent chloride secretion. Racecadotril inhibits the breakdown of enkephalins, which naturally inhibit this secretion. By targeting the hypersecretion without paralyzing the gut (as loperamide does), it prevents fluid loss "upstream," making rehydration "downstream" much easier. This is particularly valuable in Norovirus infections, where vomiting can make retaining large volumes of ORS difficult; reducing the stool output reduces the obligatory ORS volume needed [4].

The Role of Zinc: While the acute effect of Zinc is less dramatic than Racecadotril over 24 hours, its role is vital for mucosal repair. Zinc deficiency is common in developing regions and is exacerbated by diarrhea. Supplementation likely contributed to the prevention of protracted diarrhea in our study cohort.

Economic and Social Impact: Reducing hospitalization by an average of 1.3 days has profound implications. For the healthcare system, it increases bed turnover during peak epidemic seasons [5]. For parents, it reduces lost workdays and the psychological stress associated with caring for a sick child. The "Optimized Strategy" transforms the management of viral gastroenteritis from "waiting it out" to "active treatment," which also improves compliance and reduces the demand for inappropriate antibiotics.

CONCLUSION

The findings of this comparative clinical study strongly support a paradigm shift in the management of seasonal viral gastroenteritis from a passive "rehydration-only" approach to an active, multimodal therapeutic strategy. We have demonstrated that while Oral Rehydration

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Therapy (ORT) remains the cornerstone of safety, it is insufficient on its own to address the morbidity burden of the disease.

The optimized protocol, which integrates the enkephalinase inhibitor Racecadotril and Zinc supplementation, proved superior to standard care across all key clinical metrics. Specifically:

Pathogenetic efficacy - Racecadotril effectively targets the secretory mechanism of Rotavirus and Norovirus, significantly reducing fluid loss and the duration of diarrhea by nearly 24 hours. Crucially, this was achieved without the safety risks (e.g., ileus, bacterial overgrowth) associated with traditional antimotility drugs like loperamide.

Clinical efficiency - The reduction in stool output directly translated to a significantly shorter length of hospital stay (2.8 vs. 4.1 days) and a reduced need for invasive intravenous rehydration. This represents a substantial efficiency gain for hospital wards during peak viral seasons.

Holistic recovery - The addition of Zinc ensures not just symptom relief but active mucosal regeneration, likely reducing the risk of persistent diarrhea syndromes.

Therefore, we conclude that the "Optimized Strategy" represents a safe, effective, and economically viable standard of care. We strongly recommend the revision of national pediatric clinical guidelines to include Racecadotril and Zinc as mandatory adjunctive therapies for acute watery diarrhea in children. This proactive approach will not only improve clinical outcomes but also significantly alleviate parental anxiety and reduce the societal costs associated with pediatric gastroenteritis.

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