

## Management of Acute Diarrhea in Children: Systematic Literature Review

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### Abstract

This review is aiming to discuss the management of acute diarrhea in children, the presented review was conducted by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. were searched up to November 2018 for published and unpublished studies and without language restrictions, if several studies had similar findings, we randomly selected one or two to avoid repetitive results. On the basis of findings and results this review found Racecadotril, probiotics with standard rehydration therapy, Loperamide, human *Lactobacillus* strain (*Lactobacillus casei* sp strain GG, Gefilac), zinc supplementation.

**Keywords:** AManagement; Acute; Diarrhea; Children

### Introduction

Scientific research has been conducted and has demonstrated an inverse relationship between the spread of diarrhea! Disease and child development in the least developed countries [1,2]. In contrast to the more developed countries it is less pronounced for the developed population as a whole [3]. The failure of secondary growth of diarrhea is due to negative effects. Its effect on dietary intake [4,5] and also poor intestinal absorption during and after intestinal infections [6,7].

Oral rehydration therapy is the most effective treatment for dehydration in children with acute diarrhea and has been recommended by the World Health Organization for dehydration prevention and management [8,9]. But its use has significantly reduced both morbidity and mortality in diarrhea [10,11]. Therefore, the World Health Organization has recommended adding drug therapy to rehydration therapy, as long as the drug used has proven safe and effective among children [8,9].

16.5 million children suffer from acute diarrhea annually in the United States [12]. In developing countries, children usually experience up to seven acute episodes of diarrhea each year [13]. According to a recent report by the Centers for Disease Control and Prevention, diarrhea represents an annual rate of 1186 hospital treatments and 33,386 outpatient visits annually for children younger than 5 years in the United States [14].

Worldwide, children younger than 5y of age have approximately three cases of diarrhea annually and 1.6 - 2.5 million children younger than 5y die each year from diarrhea, as estimated from studies published between 1992 and 2000 [15]. The national health-care cost for diarrhea-associated disease in the United States was estimated to be US\$1.55 billion in 2002 [16]. In a 1997 survey, an estimated 34% of persons with a diarrheal illness in the United States reported taking anti-diarrheal medications [17]. Some review papers on the treatment of acute diarrhea in adults suggest loperamide as a first-line agent [18,19]. Although loperamide is widely used in adults, the World Health Organization and the American Academy of Pediatrics are concerned about its use in young children because of concerns over its efficacy and safety [20,21].

Probiotics are live microbial feeding supplements that beneficially affect the host animal by improving its microbial balance [22]. They are commonly used in the treatment and prevention of acute diarrhea. The rationale for using probiotics in acute infectious diarrhea is based on the assumption that they act against intestinal pathogens. However, the mechanism by which probiotics work is unclear. The possible mechanisms include the synthesis of antimicrobial substances [23,24], competition for nutrients required for growth of pathogens [25], competitive inhibition of adhesion of pathogens [26,27], modification of toxins or toxin receptors [28,29] and stimulation of nonspecific and specific immune responses to pathogens [30,31].

It was assumed that the risk factors and the duration of diarrhea were related to zinc deficiency, as it was found that children with zinc deficiency suffer from frequent diarrhea [32,33], as well as in animals with [34] zinc depletion; responds quickly to zinc supplements [35]. And that zinc deficiency can lead to underdevelopment, especially stunting [36] and weak immune function [37,38]. Finally, diarrhea leads to excess zinc loss and may contribute to zinc deficiency [39,40] and is therefore due to the scarcity of zinc in the limited diet [41,42].

### Methods

This review was conducted in November 2019 according to the preferred reporting clauses of systematic reviews and the PRISMA criteria for systematic reviews. All subjects related to management of acute diarrhea in children, such as Racecadotril, probiotics with standardized rehydration therapy, Loperamide, human *Lactobacillus* strain (*Lactobacillus casei* sp strain GG, Gefilac), zinc supplementation have been shown.

To achieve this goal, we searched Medline, Embase, Web of Science, Science Direct, and Google Scholar for, researches, the Cochrane Central Register of Controlled Trials, bibliographies of known clinical trials, review articles, and reports, published over the past 15 years.

The examination was completed without language restrictions. Then data were extracted from the year of study, study design and major outcomes of diabetes. Selected studies were summarized and unproductive studies were excluded. The data specified is shown in table 1.

### Inclusion criteria

Inclusion criteria were management of diarrhea in children, acute.

### Exclusion criteria

Irrelevant articles [not related to the aim of this review and articles that did not meet the inclusion criteria in this review.

Author and year	Sample	Management	Key point
Jean P, 2001 [43]	172 patients	Racecadotril	This study demonstrates the efficacy (up to 50% reduction in stool output) and tolerability of racecadotril as adjuvant therapy to oral rehydration solution in the treatment of severe diarrhea in infants and children.
Jeannie S, 2002 [44]	18 eligible studies	Probiotics with standard rehydration therapy	Bacterial probiotic therapy shortens the duration of acute diarrheal illness in children by approximately one day.
Su-ting- T, 2007 [45]	345 articles	Loperamide	In children who are younger than 3y, malnourished, moderately or severely dehydrated, systemically ill, or have bloody diarrhea, adverse events outweigh benefits even at doses $\leq 0.25$ mg/kg/d. In children who are older than 3y with no/minimal dehydration, loperamide may be a useful adjunct to oral rehydration and early refeeding
Erika I, 1990 [46]	71 well-nourished patients (56% male)	Human <i>Lactobacillus</i> strain ( <i>Lactobacillus casei</i> sp strain GG, Gefilac)	<i>Lactobacillus</i> GG in the form of fermented milk or freeze-dried powder is effective in shortening the course of acute diarrhea.
Sunil S, 1995 [47]	937 children	Zinc supplementation	For infants and young children with acute diarrhea, zinc supplementation results in clinically important reductions in the duration and severity of diarrhea.

Table 1: Results from sequencing studies.

Data extraction and analysis

Information relating to each of the systematic review question elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of management of acute diarrhea in children.

Results and Discussion

Double blind clinical trial on 172 patients who are divided into two groups of (89 in racecadotril group and 83 in placebo group), “primary efficacy criterion was stool output (grams per hour) during the first 48 hours of the study. Secondary efficacy criteria were stool output during the first 24 hours, Na1/K1 ratio of urine, duration of diarrhea, and number and characteristics of stools”. the patient who are stool weight wasn’t recorded had been dismissed from the study (about 6) and recorded as missing [43]. Study showed significant difference between the two groups in the 48 in which racecadotril recorded significant ability to lower stool output another significant records showed at time of 24 hours’ interval [44].

Systematic review and meta-analysis of randomized controlled trials to assess the efficacy and the adverse effect of the loperamide of children data had been collected from reports of the clinical trials on the and duration and the severity of the diarrhea in addition to the side effect of the loperamide children younger than 12 years old with acute onset of diarrhea had been included, “Serious adverse events, defined as ileus, lethargy, or death, were reported in eight out of 927 children allocated to loperamide (0.9%, 95% CI: 0.4% to 1.7%)”. About 927 of the children of placbo have no adverse effect been recorded, on the other hand, the loperamide show its adverse effect in the children younger than 3 years old [45].

Rotavirus was the etiological agent in 82% of the cases, and it was found equally often in the study groups: 92% in group 1, 74% in group 2, and 79% in group 3 ( $\times 2.63$ ,  $P = .27$ ). There were no cases of bacterial diarrhea [46].

Among the children who received zinc supplementation, there was a 23 percent reduction (95 percent confidence interval, 12 percent to 32 percent) in the risk of continued diarrhea. Estimates of the likelihood of recovery according to the day of zinc supplementation revealed a reduction of 7 percent (95 percent confidence interval, -9 percent to +22 percent) in the risk of continued diarrhea during days 1 through 3 and a reduction of 38 percent (95 percent confidence interval, 27 percent to 48 percent) after day 3. When zinc supplementation was initiated within three days of the onset of diarrhea, there was a 39 percent reduction (95 percent confidence interval, 7 percent to 61 percent) in the proportion of episodes lasting more than seven days. In the zinc-supplementation group there was a decrease of 39 percent (95 percent confidence interval, 6 percent to 70 percent) in the mean number of watery stools per day ( $P = 0.02$ ) and a decrease of 21 percent (95 percent confidence interval, 10 percent to 31 percent) in the number of days with watery diarrhea. The reductions in the duration and severity of diarrhea were greater in children with stunted growth than in those with normal growth [47].

After clinical trials, this study demonstrated the efficacy of cadcotril as an adjunct to oral rehydration therapy and early continuous feeding in infants and children with acute diarrhea. Patients who received racecadotril had a significant reduction in stool excretion compared to those who received placebo; the mean reduction in stool excretion using racecadotril was 50% of the population per protocol and 40% in the complete data set. The speed of effect on stool excretion is illustrated by the fact that there was a significant difference between treatments seen during the first 24 hours of treatment ( $P = 0.026$ ). The effect on stool outputs was the main criterion identified by the World Health Organization to conclude that the drug has efficacy in acute diarrhea. In fact, this effect indicates that treatment with the use of anti-cadotril reduces electromagnetic losses in children [43].

An analysis summary of the 18 eligible publications showed that co-administration of probiotics with standard oral rehydration therapy reduced the duration of acute diarrhea by approximately one day. Due to the homogeneity of the reports, restricting the analysis to double-blind studies, studies conducted on children in hospitals and studies evaluating lactobacilli (especially LGG) significantly reduced measured heterogeneity [44].

Loperamide appears to decrease diarrhea duration and frequency in children when used as an adjunct to oral or intravenous rehydration. Compared with patients given placebo, patients who were randomized to loperamide were 34% less likely to have had diarrhea 24 after initiation of therapy and 41% less likely to have had diarrhea 48 h after initiation of therapy, had 0.8 fewer days of diarrhea, and had a 16% reduction in diarrheal stools within the first 24h of treatment. Serious adverse events of death, ileus, or lethargy were reported only in children younger than 3 y of age [45].

The current results confirmed previous results that early food pty is safe and beneficial in patients with acute diarrhea. In addition to it, nutritional treatment for watery diarrhea. Controversy exists over the most appropriate method for oral re-feeding in children with acute diarrhea. The diarrhea approach has long been complete withdrawal from oral administration for a viable period followed by the gradual restoration of nutrition. Fasting has been suggested to reduce abnormal losses of water and electrolytes. On the contrary, continuous eating was associated with deformation of bowel function and damage to the mucous membrane of acute gastroenteritis [46].

This study, conducted in New Delhi, also confirmed the effectiveness of zinc supplementation as an adjunct to oral rehydration therapy and early continuous feeding among preschool children with acute diarrhea. Zinc supplementation was associated with a clinically significant and statistically significant overall decrease of 23 percent in the risk of persistent diarrhea and a 39 percent decrease in the frequency of seizures lasting more than seven days after the start of treatment. This resulted in a 21 percent decrease in the number of days with stools. Watery and 39% decrease in the average number of watery stools per day. Reducing the frequency of prolonged diarrhea and the number of days with watery stools may reduce the risk of dehydration and the need to replace fluids and electrolytes. We were

unable to measure the effect of zinc supplementation on dehydration because the oral rehydration solution was provided from the day of registration. Reductions in the frequency of diarrhea may also improve growth [47].

### Conclusion

These studies showed that the management of acute diarrhea in children. Based on the findings and results, this review found Racecadotril, probiotics with standardized rehydration therapy, Loperamide, human *Lactobacillus* strain (*Lactobacillus casei* sp strain GG, Gefilac), zinc supplementation.

### Conflict of Interest

The authors of this article hasn't receive and support for this work and it was completely self-funded.

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