



from the

DRUG DESK

A Drug Information Update from the B.C. Drug and Poison Information Centre

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Should *Lactobacillus* be used in acute infectious diarrhea in children?

Diarrhea is one of the most common childhood illnesses worldwide, contributing significantly to pediatric morbidity and mortality.¹⁻³ One of the major causes of pediatric diarrhea is rotavirus infection.^{2,4} Currently, routine use of antidiarrheal agents in pediatrics is not recommended due to insufficient data supporting their efficacy and their potential to cause adverse effects.⁵⁻⁷ Probiotics, such as various strains of *Lactobacillus*, have been suggested as a safe and efficacious treatment adjunct for acute infectious diarrhea in the pediatric population.⁸⁻¹⁴

Mechanism of Action

The main mechanism of action of probiotics in the treatment of infectious diarrhea has not been established, but several have been suggested.^{3,8} Probiotics are hypothesized to act against the colonization and overgrowth of pathogenic micro-organisms by bactericidal activity, reduction of the gastrointestinal pH by the production of lactic acid, and competition for microbial adhesion sites and limited nutrients. *Lactobacillus* has also been postulated to improve host immune function and shift the balance of gastrointestinal bacteria to a more favorable microbial composition.^{8-10,12} Other possible mechanisms include strengthening the mucosal barrier and tight junctions between enterocytes in the gastrointestinal epithelium.¹⁵

The effectiveness of probiotics depends on their ability to colonize an area of tissue and therefore live *Lactobacillus* preparations should be used.¹³ *Lactobacillus rhamnosus* strain GG (LGG) is the most studied strain for the treatment of acute infectious diarrhea in pediatrics and there is evidence that LGG attaches better to human intestinal epithelial cells than *Lactobacillus acidophilus*.

Evidence Supporting the Use of Probiotics in Acute Infectious Diarrhea

A number of studies have shown that some orally administered probiotic strains, e.g. *Lactobacillus*, *S. boulardii* and *L. reuteri* decrease the duration and severity of episodes of acute infectious diarrhea in pediatric patients.^{3,4,15,16,18} Szajewska et al. conducted a systematic review of probiotics in the treatment and prevention of acute infectious diarrhea in infants and children 1-48 months of age.¹⁶ A total of 10 treatment trials were identified and included in the meta-analysis with the etiology of diarrhea being rotavirus or bacterial infections and undetermined causes. *Lactobacillus* was the probiotic studied in 9 of

the 10 trials. Probiotic therapy reduced the duration of diarrhea compared to placebo with a weighted mean difference of -18.2 hours (95% CI, -26.9 to -9.5; $p < 0.0001$) or by roughly three-quarters of a day.

A meta-analysis by Van Niel et al. evaluated *Lactobacillus* therapy for acute infectious diarrhea in children 1-37 months of age.¹⁷ Nine studies were evaluated in the meta-analysis. Some of the studies evaluated overlapped with those in the systematic review by Szajewska et al. Overall, a reduction in the duration of diarrhea by 0.7 days (95% CI, 0.3 to 1.2 days), or roughly two-thirds of a day, was found with *Lactobacillus* use compared to placebo.

Other trials found that rotavirus diarrhea, when treated with probiotic therapy was decreased, on average, by 2.1 days.^{2,4,18} The authors concluded that some probiotics shorten the duration of diarrhea and decrease diarrhea volume and fecal shedding of rotavirus. They noted that the efficacy of probiotics in the treatment of pediatric diarrhea appears to be both strain-dependent and dose-dependent, as well as dependent on the etiology of the diarrhea.⁴ The joint committee from the European Society for Pediatric Gastroenterology, Hepatology and Nutrition and the European Society for Pediatric Infectious Disease suggested that probiotics may be an effective adjunct for the management of diarrhea. The committee recommended that only the probiotics, i.e. mainly *Lactobacillus* GG and *S. boulardii*, which have evidence to support their use, be used as an adjunct to rehydration therapy to treat children with diarrhea.

Dose

For acute infectious diarrhea in pediatric patients, typical doses range from 10^{10} - 10^{11} colony-forming units (CFU) of live LGG in an oral rehydrating solution given once or twice daily for up to 5 days.^{13,16,17} The minimum reported required probiotic dose has ranged from 6×10^8 up to 10 billion CFU. The variability in dose is probably due to the variability in the strains of probiotics used and the etiology of the diarrhea treated in the different trials.^{2,4}

Adverse Effects

Treatment with *Lactobacillus* and *S. boulardii* is generally well tolerated.¹³ Flatulence is the most common side effect, but is usually mild and subsides with continued therapy.

Summary

Lactobacillus and other probiotics may be effective in decreasing the duration of certain types of acute infectious diarrhea in pediatric patients by up to 2.1 days. The effectiveness in an individual patient may vary greatly because the probiotic efficacy varies according to the strain of probiotic used, the dose used and the type of diarrhea treated. Larger studies addressing these issues will determine future clinical guidelines. Probiotics are generally safe and well tolerated and may be considered as adjunctive treatment for pediatric patients with acute infectious diarrhea.

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References available upon request.