Probiotic Selection Based on Level of Evidence

Options for Probiotics for Prevention of Diarrhea in Children Taking Antibiotics [1]

Probiotic Species	**Prevention of Antibiotic-associated Diarrhea**	**Prevention of *Clostridium Difficile*-associated Diarrhea**	**Typical Dose**
Lactobacillus rhamnosus (GG strain) (Culturelle)	Effective (level 1 [likely reliable] evidence)	May be ineffective (level 2 [mid-level] evidence)	1010 CFU/capsule once or twice daily
Saccharomyces boulardii (Florastor)	Effective (level 1 [likely reliable] evidence)	May be effective (level 2 [mid-level] evidence)	250-500 mg/day

Alternatives with Less Robust Evidence of Efficacy (DynaMed Level 2)

- Combination: *Lactobacillus casei, Lactobacillus acidophilus, L. reuteri, Lactobacillus bulgaricus, Streptococcus, Bifidobacterium bifidum, Bifidobacterium infantis*
- Combination: *Bifidobacterium lactis* and *Streptococcus thermophilus*
- *Lactobacillus sporogenes*
- Combination: *Clostridium butyricum* and *Bifidobacterium combination*

[1] DynaMed. Acute Diarrhea in Children. EBSCO Information Services. Accessed July 11, 2021. https://www.dynamed.com/approach-to/acute-diarrhea-in-children

Assessing Clinical Relevance

Lactobacillus GG in the prevention of antibiotic-associated diarrhea in children

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Objective: The objective of this study was to determine the efficacy of *Lactobacillus casei sps. rhamnosus (Lactobacillus GG)* (LGG) in reducing the incidence of antibiotic-associated diarrhea when coadministered with an oral antibiotic in children with acute infectious disorders.

Study design: Two hundred two children between 6 months and 10 years of age were enrolled; 188 completed all phases of the protocol. LGG, $1 \times 10^{10} - 2 \times 10^{10}$ colony forming units per day, or comparable placebo was administered in a double-blind randomized trial to children receiving oral antibiotic therapy in an outpatient setting. The primary caregiver was questioned every 3 days regarding the incidence of gastrointestinal symptoms, predominantly stool frequency and consistency, through telephone contact by blinded investigators.

Results: Twenty-five placebo-treated but only 7 LGG-treated patients had diarrhea as defined by liquid stools numbering 2 or greater per day. *Lactobacillus GG* overall significantly reduced stool frequency and increased stool consistency during antibiotic therapy by the tenth day compared with the placebo group.

Conclusion: *Lactobacillus GG* reduces the incidence of antibiotic-associated diarrhea in children treated with oral antibiotics for common childhood infections. (J Pediatr 1999;135:564-8)

Outpatient use of antibiotics is common in pediatrics, most often for a variety of minor infections of the respiratory tract, integument, and urinary tract. Certain antibiotics, especially those with a relatively broad spectrum, frequently result in diarrhea.[1] The incidence of antibiotic-associated diarrhea in children ranges from 20% to 40% of those receiving broad-spectrum antibiotics.[2]

The mechanism by which antibiotic-associated diarrhea occurs most likely relates to disturbances of microbial flora in the gastrointestinal tract. More than 500 species of bacteria inhabit the gut, and a balance of these organisms is crucial to normal gastrointestinal function.[3,4] Disruption of the microbial flora may result in the overgrowth of pathogenic organisms such as *Clostridium difficile* or may disturb the metabolism of carbohydrates, resulting in malabsorption of osmotically active particles.

See editorial, p. 535.

Recently, probiotic organisms have been advocated for use in stabilizing gut microflora in conditions where disturbances of normal bacterial flora result in gastrointestinal symptoms.[5,6] Because antibiotic-associated diarrhea is such a condition, use of a probiotic would seem appropriate in this situation. Unfortunately, many purported probiotics are not effective because of their inability to survive in gastric and bile secretions, inability to colonize the gastrointestinal tract, and ineffective binding to intestinal epithelial cells.[7-9] *Lactobacillus casei sps. rhamnosus (Lactobacillus GG)* has been shown to do all 3

LGG *Lactobacillus GG*

and consequently would seem to be a suitable probiotic in this situation.[10-12] Consequently, we elected to initiate a randomized, double-blind, placebo-controlled trial of coadministration of *Lactobacillus GG* with antibiotics in children being treated for a variety of minor infections to assess the efficacy of this bacterium as a probiotic in the prevention of antibiotic-associated diarrhea.

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For one RCT within systematic review:

- diarrhea in 8% vs. 26% ($p < 0.001$, NNT 6)
- mean duration of diarrhea 4.7 days vs. 5.9 days ($p = 0.05$)

[1] Vanderhoof JA, Whitney DB, Antonson DL, Hanner TL, Lupo JV, Young RJ. Lactobacillus GG in the prevention of antibiotic-associated diarrhea in children. J Pediatr. 1999 Nov;135(5):564-8. doi: 10.1016/s0022-3476(99)70053-3. PMID: 10547243.