Review: Probiotics are effective for prevention of antibiotic-associated diarrhea and treatment of *Clostridium difficile* disease

McFarland LV. **Meta-analysis of probiotics for the prevention of antibiotic associated diarrhea and the treatment of *Clostridium difficile* disease.** Am J Gastroenterol. 2006;101:812-22.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Hospitalists ★★★★★★☆ Gastroenterology ★★★★★★☆

QUESTION

Are probiotics effective for preventing antibiotic-associated diarrhea (AAD) and treating or preventing *Clostridium difficile* disease (CDD)?

METHODS

Data sources: MEDLINE and Google Scholar (2005), Cochrane Central Register of Controlled Trials, metaRegister of Controlled Trials, National Institutes of Health clinical trial register, conference abstracts, and bibliographies of relevant studies and books.

Study selection and assessment: Randomized, blinded, controlled trials (RCTs) published as full articles in peer-reviewed journals that assessed the efficacy of specific probiotics for prevention of AAD or treatment or prevention of CDD in patients of any age. 25 RCTs (n = 2810) for AAD (16 in adults and 9 in children) and 6 RCTs (n = 354) for CDD (all in adults, 5 treatment and 1 prevention) met the selection criteria. Methodological quality assessment of trials included randomization, study design, sample size, generalizability, study biases, and outcome assessment.

Outcomes: For AAD: diarrhea within 2 months of antibiotic exposure. For CDD: new episode of *C. difficile*–positive diarrhea within 1 month of antibiotic exposure or a previous CDD episode.

MAIN RESULTS

Probiotics, *Saccharomyces boulardii* and *Lactobacillus rhamnosus* GG in particular, reduced risk for AAD (Table). Probiotics reduced risk for recurrence or development of CDD (Table).

CONCLUSION

Selected probiotics can be effective for preventing antibiotic-associated diarrhea and treating *Clostridium difficile* disease.

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Probiotics for prevention of antibiotic-associated diarrhea (AAD) and treatment or prevention of *Clostridium difficile* disease (CDD) at 1 to 12 weeks*

Outcomes	Type of probiotic	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
			Probiotics	Control		
AAD	Overall	25 (2810)	12%	27%	57% (42 to 69)†	7 (6 to 9)
	SB	6 (1119)	7%	18%	63% (48 to 74)	9 (8 to 12)
	LRGG	6 (817)	8%	27%	69% (28 to 87)†	6 (5 to 14)
	Other single probiotics	6 (502)	15%	33%	54% (–3 to 79)†	Not significant
	Mixture of 2 probiotics	7 (372)	23%	45%	49% (32 to 62)	5 (4 to 7)
CDD	Overall	6 (354)	18%	31%	41% (15 to 59)	8 (6 to 22)

*SB = *Saccharomyces boulardii*; LRGG = *Lactobacillus rhamnosus* GG. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article using a fixed-effects model.
†A random-effects model was used.

COMMENTARY

During recent years, outbreaks of CDD of surprising severity, as well as cases of CDD that respond poorly to metronidazole, have been reported (1, 2). These reports have led to a search for new approaches to the treatment and prevention of AAD and CDD. Probiotic therapy, the use of nonpathogenic microorganisms to restore a normal intestinal flora, is an attractive alternative. The meta-analysis by McFarland indicates that probiotic treatment can be effective in the management of both CDD and AAD, although the effectiveness varies notably with different probiotic regimens.

So, how should probiotics be prescribed? Unfortunately, this is difficult to determine because major unanswered questions remain about the pathogenesis of AAD and CDD. Recent analysis of human intestinal microflora using molecular techniques has shown that the diversity of bacterial strains present is far greater than previously recognized, with a large percentage of species not yet cultivated (3). At this time, we understand neither how these microflora are affected by antibiotics nor how alterations in the flora contribute to AAD and CDD. Moreover, we do not understand how probiotic agents affect human intestinal flora to allow a rational approach to their use. This knowledge deficit is not a reason to avoid probiotics, but is a reason to restrict their use to specific indications and defined protocols for which there is objective evidence of efficacy, as noted in this review.

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References

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