Review: *Saccharomyces boulardii* reduces risk for antibiotic-associated diarrhea

Szajewska H, Mrukowicz J. **Meta-analysis: non-pathogenic yeast *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea.** Aliment Pharmacol Ther. 2005;22:365-72.

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

QUESTION

Is use of *Saccharomyces boulardii* as an adjunct to antibiotics effective for preventing antibiotic-associated diarrhea (AAD)?

METHODS

Data sources: MEDLINE (1966 to March 2005), EMBASE/Excerpta Medica (1980 to March 2005), CINAHL (1982 to March 2005), Cochrane Database of Systematic Reviews (Issue 1, 2005), Cochrane Controlled Trials Register (Issue 1, 2005), bibliographies of relevant articles, and key experts in the field.

Study selection and assessment: Randomized controlled trials (RCTs) (published in any language) that compared *S. boulardii* with placebo or no additional intervention in adults and children who received antibiotics for any reason. Quality assessment of individual studies included allocation concealment, blinding, intention-to-treat analysis, and comprehensive follow-up.

Outcomes: Incidence of diarrhea or AAD. Secondary outcomes included incidence of *Clostridium difficile*–associated diarrhea (CDAD), mean frequency of bowel movements, mean duration of diarrhea, need for discontinuation of antibiotic treatment, hospitalization to manage the diarrhea, intravenous rehydration, and adverse effects.

MAIN RESULTS

5 RCTs (all placebo controlled) (n = 1076) met the selection criteria. Meta-analysis was done using a random-effects model. The incidence of AAD was lower in the *S. boulardii* group than in the placebo group (Table). The groups did not differ for incidence of CDAD (relative risk reduction 70%, 95% CI −4 to 90) (1 RCT). Data were insufficient for all other outcomes.

CONCLUSION

Use of *Saccharomyces boulardii* as an adjunct to antibiotics reduces the risk for antibiotic-associated diarrhea.

Source of funding: No external funding.

For correspondence: Dr. H. Szajewska, Medical University of Warsaw, Warsaw, Poland. E-mail hania@ipgate.pl.

Saccharomyces boulardii* vs placebo as an adjunct to treatment with antibiotics at 2 to 7 weeks

Outcome	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		S. boulardii	Placebo		
Antibiotic-associated diarrhea	5 (1076)	7.2%	17.2%	57% (22 to 77)	10 (7 to 16)
Clostridium difficile–associated diarrhea	1 (246)	{2.5%}†	{7.9%}†	70% (−4 to 90)	Not significant

*Abbreviations defined in Glossary; weighted event rates, RRR, and CI calculated from data in article using a random-effects model.
†Unweighted event rates obtained from Kotowska M, Albrecht P, Szajewska H. Aliment Pharmacol Ther. 2005;21:583-90.

COMMENTARY

AAD occurs in up to 30% of patients receiving antibiotics (1). The most serious form of AAD is mediated by *C. difficile* toxin (CDAD). Several antibiotics have been associated with AAD and CDAD. Those with greater potency against anaerobes may predispose to CDAD, which is potentially fatal when it escalates into *C. difficile*–associated colitis (CDAC) and toxic megacolon.

The incidence of CDAD is cyclical. This may relate to variations in antibiotic use, varying community colonization rates, and other factors external to the hospital setting. Heightened control of antibiotic use has been associated with reduced AAD and CDAD attack rates (2).

The use of probiotics to treat or prevent diarrhea has been promoted for some time in the complementary medicine literature, and more recently in traditional medical journals (3). One probiotic, *Saccharomyces boulardii*, seems to promote reconstitution of nonpathogenic bowel flora, as well as having other antidiarrheal effects, and has received considerable attention. The meta-analysis by Szajewska and Mrukowicz showed a reduction in AAD attack rates with the use of *S. boulardii* (i.e., for every 10 patients receiving daily *S. boulardii* with antibiotics, 1 fewer patient developed AAD). The CDAD attack rate was not significantly affected in the 1 small trial that had CDAD as an outcome measure included in this review.

This review and other encouraging reports support the continuing need to identify optimal bowel recolonization regimens in patients receiving antibiotics. However, because the fundamental cause of AAD and CDAD is the antibiotics themselves, it also remains paramount to eliminate the inappropriate use of antibiotics, particularly those closely associated with CDAD and its complications. One can envision that large-scale use of such probiotics as *S. boulardii* might reduce the rate of AAD, which is certainly a nuisance, but might not affect the more serious problem, CDAD and CDAC. Furthermore, it might pose risks to immunocompromised patients because of its known association with fungal superinfection, fungal sepsis, and death (4), and it is those patients who need protection most.

Thomas A. Parrino, MD
West Palm Beach Veterans Affairs Medical Center
West Palm Beach, Florida, USA

References

1. **McFarland LV, Surawicz CM, Greenberg RN, et al.** Prevention of beta-lactam-associated diarrhea by *Saccharomyces boulardii* compared with placebo. Am J Gastroenterol. 1995;90:439-48. 7872284.
2. **Gerding DN.** Clindamycin, cephalosporins, fluoroquinolones, and *Clostridium difficile*-associated diarrhea: this is an antimicrobial resistance problem. Clin Infect Dis. 2004;38:646-8. 14986247.
3. **Dendukuri N, Costa V, McGregor M, Brophy JM.** Probiotic therapy for the prevention and treatment of *Clostridium difficile*-associated diarrhea: a systematic review. CMAJ. 2005;173:167-70. 16027434.
4. **Enache-Angoulvant A, Hennequin C.** Invasive *Saccharomyces* infection: a comprehensive review. Clin Infect Dis. 2005;41:1559-68. 16267727.