Review: probiotics are effective in preventing antibiotic associated diarrhoea

D'Souza AL, Rajkumar C, Cooke J, et al. *Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis. BMJ* 2002;**324**:1361-4.

QUESTION: In patients being treated with antibiotics, does co-administration with probiotics reduce the incidence of diarrhoea?

Data sources

Studies in any language (with English abstracts) were identified by searching Medline (1966-2000) with the terms probiotics, biotherapeutic agents, lactobacilli, antibiotic associated diarrhoea, and *Clostridium difficile*; the Cochrane Controlled Trials Register; and the Cochrane Database of Systematic Reviews.

Study selection

Studies were selected if they were randomised, double blind, placebo controlled trials of probiotic treatment given in combination with antibiotics and if diarrhoea prevention was reported. Studies of travellers' diarrhoea and infectious diarrhoea were excluded.

Data extraction

Data were extracted on sample size; type, dose, and duration of probiotic treatment; and antibiotic studied. The outcome of interest was prevention of diarrhoea. Diarrhoea was defined as a change from the normal bowel habit with ≥ 2 loose or watery stools for ≥ 2 days.

Main results

9 trials (1214 patients) met the selection criteria. 2 of the trials studied children. No statistical heterogeneity or publication bias was detected among the 9 trials. The pooled odds ratio (OR) showed that probiotic treatment was more effective than placebo in the prevention of diarrhoea (OR 0.37, 95% CI 0.26 to 0.53) (table). 4 trials that used *S. boulardii* (yeast trials) also favoured probiotic treatment (OR 0.39, CI 0.25 to 0.62) as did 5 that used lactobacilli or enterococci (non-yeast trials) (OR 0.34, CI 0.19 to 0.61).

Conclusion

In patients being treated with antibiotics, co-administration with probiotics reduces the incidence of diarrhoea.

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Probiotics v placebo to prevent antibiotic associated diarrhoea*

Outcome	Weighted event rates		RBI (95% CI)	NNT (CI)
	Probiotics	Placebo		
Proportion of patients without diarrhoea	90%	78%	15% (9 to 20)	9 (7 to 13)

*Abbreviations defined in glossary; RBI, NNT, and CI calculated from data provided by author using a fixed effects model.

COMMENTARY

It is well accepted that antibiotic associated diarrhoea occurs in 5-25% of treated patients and that 10-20% of these patients will have diarrhoea related to *Clostridium difficile*.¹ Most clinicians would also agree that antibiotic associated diarrhoea is a greater problem for certain patients, such as those < 6 years or > 65 years of age, or those being cared for in intensive care units. Antibiotic associated diarrhoea is also more likely to occur in patients receiving aminopenicillins, cephalosporins, or clindamycin. However, the value of probiotics in preventing antibiotic associated diarrhoea has only recently (since the early 1990s) been clinically addressed.

The study by D'Souza *et al* may be the only meta-analysis that attempts to clarify the usefulness of probiotics in preventing antibiotic associated diarrhoea in patients of varying ages using various antibiotics. As such, this review had the potential to provide community and hospital based clinicians with new information about whether to recommend or, in some cases, prescribe probiotics as concomitant treatment to antibiotic use.

The methods of the review were rigorous. Unfortunately, only 9 studies were included, and all had relatively small sample sizes. Furthermore, important characteristics of the interventions varied considerably. The studies differed in the type of probiotic studied, as well as the dosage and duration of administration. Characteristics of the antibiotics also varied across studies.

The findings lend some support to the use of probiotics. However, the review fails to provide new insights into which specific antibiotics should be targeted or which populations may benefit both in terms of health and cost outcomes from the use of a specific probiotic.

As a result, healthcare providers cannot be certain as to which probiotic to use with which antibiotic in which patient population to produce the best possible outcomes for the individual patient or the healthcare system in the long term. As indicated by D'Souza *et al*, a large, randomised trial of the efficacy of probiotic use in the prevention of antibiotic associated diarrhoea should be targeted to the elderly. Optimal probiotic dosages and cost-benefits should be addressed.

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1 Kelly CP, Pothoulakis C, Lamont JT. *Clostridium difficile* colitis. *N Engl J Med* 1994;**330**:257-62.