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Probiotics probably reduce antibiotic-associated diarrhoea in children

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Clinical question

Do probiotics reduce the risk of antibiotics-associated diarrhoea in children and are they safe?

Context

Antibiotics change the microbial balance in the gut and often cause antibiotic-associated diarrhoea (AAD). Probiotics contain potentially beneficial bacteria or yeast, which may restore the natural balance of bacteria in the intestinal tract.

The review describes 33 trials including a total number of 6352 children, aged 3 days to 17 years, who received antibiotics. Studies compared probiotics with placebo, active alternative treatment i.e. diosmectite or infant formula or no treatment. All types and doses of probiotics were included. The studies used the following strains: *Bacillus spp.*, *Bifidobacterium spp.*, *Clostridium butyricum*, *Lactobacilli spp.*, *Lactococcus spp.*, *Leuconostoc cremoris*, *Saccharomyces spp.*, or *Streptococcus spp.*, alone or in combination. Outcomes were incidence of diarrhoea, number and type of adverse events, duration of diarrhoea and follow-up varied from 5 days to 12 weeks.

Summary of the results

After follow-up, 8% of the probiotic group had diarrhoea compared to 19% in the control group (RR 0.45, 95% CI 0.36 to 0.56; 6352 participants; NNTB 9, 95% CI 7 to 13). High dose probiotics (≥ 5 billion CFUs (colony forming units) per day) were more effective than low probiotic dose (< 5 billion CFUs per day). For the high dose studies, the incidence of diarrhoea in the probiotic group was 8% compared to 23% in the control group (RR 0.37; 95% CI 0.30 to 0.46; NNTB 6, 95%CI 5 to 9, 4038 participants). For the low dose studies the incidence of diarrhoea in the probiotic group was 8% compared to 13% in the control group (RR 0.68; 95% CI 0.46 to 1.01; 2214 participants).

None of the 24 trials (4415 participants) that examined adverse events reported any serious adverse events attributable to probiotics. Adverse event rates were low. After 5 days to 4 weeks follow-up, 4% of children who took probiotics had an adverse event compared to 6% of children in the control groups (RD 0.00; 95% CI -0.01 to 0.01; 4415 participants). Common adverse events included rash, nausea, gas, flatulence, abdominal bloating, and constipation.

Eight studies recorded data on the mean duration of diarrhoea. Probiotics reduced duration of diarrhoea by almost one day (mean difference -0.91; 95% CI -1.38 to -0.44; 1263 participants).

Remarks

Quality of evidence was moderate for incidence of diarrhoea, and low for adverse events and duration of diarrhoea. Some studies had important methodological problems such as lack of blinding, inadequate randomization, high loss to follow-up and commercial sponsorships. The authors performed separate analyses to evaluate the impact of these methodological problems. For all analyses, the results remained significant. The results of the subgroup on dose were judged to be credible based on 5 criteria, including a test for subgroup differences. Studies examined mostly otherwise healthy children. Some observational studies (not included in this review) reported serious adverse events in severely debilitated or immuno-compromised children with underlying risk factors.

Conclusion:

Probiotics probably decrease AAD in children. High doses are probably most effective with a NNTB of 6, meaning that 6 children need to be treated to prevent one case of diarrhoea. Probiotics seem to be safe and may reduce the duration of diarrhoea by almost 1 day.

Implications for practice:

Probiotics probably benefit otherwise healthy children who are prescribed antibiotics. *Lactobacillus rhamnosus* or *Saccharomyces boulardii* at 5 to 40 billion colony forming units per day appear most appropriate.

REFERENCE:

Guo Q, Goldenberg JZ, Humphrey C, El Dib R, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database of Systematic Reviews 2019, Issue 4. Art. No.: CD004827. DOI: 10.1002/14651858.CD004827.pub5.

Access the full text of these reviews via the Cebam Digital Library for Health (www.cebam.be/nl/cdlh or www.cebam.be/fr/cdlh)

[^] **CI:** confidence interval

^{*} **NNTB:** number needed to treat to be beneficial