Probiotics for the prevention of *Clostridium difficile*

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Clinical question

Do probiotics prevent *Clostridium difficile*–associated diarrhea (CDAD) in patients taking antibiotics?

Bottom line

Probiotics reduce the incidence of CDAD in patients taking antibiotics, with a number needed to treat (NNT) of 26. However, in a recent, high-quality, publicly funded study, probiotics were not beneficial in elderly inpatients. The influence of funding on study results, as well as the ideal product, duration of therapy, and safety of probiotics (particularly in immunocompromised patients), are unknown.

Evidence

Meta-analysis[1] of 20 RCTs examined 3818 mostly adult inpatients using a variety of probiotics for different lengths of time (usually for the duration of antibiotic use and up to 14 days after finishing antibiotics).

- Incidence of CDAD was reduced: placebo = 5.9%, probiotics = 2.0% (absolute risk reduction = 3.9%, NNT = 26).
- Results were similar for high-quality studies, adults and children, different probiotic species (*Bifidobacterium*, *Lactobacillus*, *Saccharomyces*, or *Streptococcus*), and single and multiple species.

Limitations:

- Thirteen trials reported some missing CDAD rates. Even with worst-case-scenario analysis, probiotics were still beneficial.
- Potential funding bias: most studies were funded by probiotic manufacturers.

Other systematic reviews[2,3] found similar results, and that outpatients and inpatients had similar relative benefits.[3]

Context

- Risk factors for CDAD are primarily antibiotic use and hospitalization, but also advanced age, concurrent diseases (especially inflammatory bowel disease), gastrointestinal surgery, nasogastric feeding, and acid suppressants (proton pump inhibitors and H_2 receptor antagonists).[4-6]
  -Any antibiotic might be associated with CDAD, but clindamycin, cephalosporins, and quinolones might convey the highest risk.[4]
- Probiotics also decrease antibiotic-associated diarrhea in adults[2] (NNT = 13) and children[7] (NNT = 7).
- Cases of fungemia and bacteremia in immunocompromised patients using probiotics have been reported,[8] but overall rates of adverse events (including serious events) seem similar to placebo.[1,8] More data are needed.
- Current American CDAD clinical practice guidelines[6] and the Canadian Paediatric Society[9] do not endorse using probiotics for the prevention of CDAD but they do not cite the systematic reviews discussed here.

Implementation

The approximate 14-day cost of probiotics for which there is evidence of efficacy and that are available in Canada varies: Bio-K+ ($13), TuZen ($37), Florastor ($45), and VSL#3 ($112). The mainstay of CDAD treatment is infection control (hand hygiene, gloves, and gowns), stopping associated medications if possible (eg, antibiotics and proton pump inhibitors), and using metronidazole or vancomycin.[6]

A recent, high-quality, placebo-controlled RCT of lactobacilli and bifidobacteria in 2941 inpatients 65 years of age and older who were given antibiotics demonstrated that probiotics did not reduce antibiotic-associated diarrhea or *C difficile* rates.[10] Additional high-quality, publicly funded studies, along with a meta-analysis evaluating the role of funding on results, are needed.

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