Critical Appraisal Topic: Probiotics and Antibiotic Associated Diarrhea in Pediatrics

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Clinical Scenario:

A 4 year old otherwise healthy male, accompanied by his mother presents to the clinic with diarrhea (4 episodes in past 24 hours) after starting amoxicillin 80 mg/kg/day PO divided BID two days ago for acute otitis media.

Clinical Question:

In the pediatric population with antibiotic associated diarrhea, does the concurrent use of probiotics and oral antibiotics decrease the incidence of antibiotic associated diarrhea compared to taking antibiotics independently?

Articles:


Search Terms: Probiotics, Diarrhea, Antibiotic Associated Diarrhea, Pediatrics, and Children

Critical Review of Study:

Johnston, Goldenberg, Vandvik, Sun, and Guyatt (2011), performed a systematic review of 16 studies (3432 participants), using randomized, parallel, controlled trials in children (0 to 18 years) receiving antibiotics, that compare probiotics (Bacillus spp., Bifidobacterium spp., Lactobacilli spp., Lactococcus spp., Leuconostoc cremoris, Saccharomyces spp., or Streptococcus spp) to placebo, active alternative prophylaxis, or no treatment and measured the incidence of diarrhea secondary to antibiotic use. (Level 1 evidence, Grade A). Patients were diagnosed with upper and lower respiratory tract, ear, gastrointestinal, dermatological, or other infections and meningitis or septicemia and overall the trials provided between 3 and 30 days of antibiotic therapy, with most trials providing oral antibiotics. In 10 studies, the probiotic(s) intervention was compared to a placebo control group, two trials compared probiotics to conventional care including formula and diosmectite, two trials compared probiotics to no treatment, one trial compared a live probiotic drink to a heat-killed probiotics drink and one trial
used three arms: ‘bioyogurt,’ commercial yogurt, and no yogurt. There were varying definitions of “diarrhea”. In eight studies they defined diarrhea as ≥ 3 loose/watery/liquid stools per day for at least 2 consecutive days, two trials defined diarrhea as ≥ 3 watery/liquid stools per 24 hours, one defined diarrhea as one or more abnormally loose bowel movements per 24 hours, one defined diarrhea as at least two liquid bowel movements per 24 hour period, and one defined diarrhea as two or more loose stools on two or more occasions throughout the study period.

Szymański, Armańska, Kowalska-Duplaga, and Szajewska (2008) performed a double-blind, randomized, placebo-controlled clinical trial intended to evaluate the efficacy, safety, and tolerability of a mixture of three probiotic strains (Bifidobacterium longum PL03, Lactobacillus rhamnosus KL53A, and Lactobacillus plantarum PL02) in the prevention of antibiotic associated diarrhea in children aged 5 months to 16 years. (Level 2 evidence, Grade B). Patients with acute otitis media, and/or a respiratory tract infection, and/or a urinary tract infection who started short-term treatment with oral or intravenous antibiotics within 24 hours of enrollment were included. Both the active treatment and placebo were taken orally twice daily for the duration of the antibiotic treatment. Diarrhea was defined as 3 loose or watery stools per day for a minimum of 48 hours, occurring during and/or up to 2 weeks after the end of the antibiotic therapy.

Both studies included all types of antibiotics, with no exclusions.

Results:

Johnston et al. (2011) found the overall pooled results using an available case analysis showed that the use of probiotics produced a statistically significant reduction in the incidence of antibiotic associated diarrhea. The incidence of antibiotic associated diarrhea in the probiotic group was 9% compared to 18% in the active, placebo or no treatment control group.

Szymański et al. (2008) found no significant difference between the study groups with respect to the incidence of diarrhea, however; the stool frequency was statistically significantly lower in the probiotic group than in the placebo group.

No adverse effects from probiotics were found in either study. Limitations in the study by Johnston et al. was the pooling of the probiotic species, the varying definitions for diarrhea, and conference proceedings or dissertation abstracts were not used in the systemic search. Limitations in the study by Szymański et al. is the low number of the antibiotic associated diarrhea among the patients. Only 3 of 78 (3.8%) patients developed antibiotic associated diarrhea despite the intake of high-risk antibiotics by the majority of the children.

Clinical Bottom Line:

Both studies found some statistical significance in the use of probiotics taken concurrently with antibiotics in the pediatric population; however the study by Johnston et al. found a decrease in the incidence in diarrhea while the study by Szymański et al. found a decrease in the frequency of diarrhea. Both prove a benefit to the patient population, but are difficult to compare. The recommended dosage and type of probiotics was not well defined or consistent in either study and future studies would be beneficial in determining the dosage and type of probiotic.