Probiotics and Diarrhea

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Probiotics have become increasingly popular as a therapeutic strategy for diseases, especially those resulting from a disruption of normal microbiota [1]. The advantages of probiotics include multiple mechanisms of action, efficacy for a variety of diseases and conditions and a remarkable safety profile. Probiotics may act by producing bacteriocins against pathogens, or by competitively inhibiting the attachment of pathogens or their toxins, or by directly destroying pathogenic toxins, or by enhancing the host physiology or act as immune regulators. However, choosing the appropriate probiotic can be challenging for the physician and patient alike. The efficacy is dependent upon matching the correct probiotic strain with the appropriate indication, using sufficient doses and duration of treatment and selecting a probiotic with high quality control standards. The appropriate probiotic strain should be chosen based on evidence from well-designed randomized controlled trials (RCT).

Of over 300 RCT published in the literature on probiotics, 19% were for the treatment or prevention of pediatric diarrhea, 16% were on the prevention of antibiotic-associated diarrhea (AAD) and 6% were for the prevention of traveler's diarrhea (TD). Pediatric diarrhea occurs in 16.5 million children under the age of 5 years per year in the USA and is a significant cause of mortality in developing countries. Although oral rehydration is the

standard therapy, this does little to shorten the symptoms of diarrhea or restore the normal microbiota in the colon, which is important for the patient's recovery. Many strains of probiotics have been tested for pediatric diarrhea including *Lactobacillus rhamnosus* GG, *Saccharomyces boulardii* and mixtures of several probiotic strains. Of 54 RCT done testing 8 different single strains and different mixtures of 2–4 strains, 78% found significant effects for pediatric diarrhea. As shown in table 1, the strength of the clinical evidence supports the use of several types of probiotic for pediatric diarrhea. For example, Pedone et al. [2] enrolled 287 children (7–32 months old) in 12 day care centers suffering from acute diarrhea and randomized them to either Actimel (*L. casei* DN-114 001, *L. bulgaricus*, *Streptococcus thermophilus*) or control milk formula or control yogurt for 1 month. The duration of diarrhea was significantly shortened in the probiotic group (4.3 days, $p < 0.05$) compared to the control milk formula (8 days) and a trend was found for the control yogurt (5.3 days, $p = 0.06$).

The incidence of AAD may range from 5 to 25% depending upon the type of antibiotic and risk factors of the host. The consequences of AAD may include dehydration, longer hospitalizations, increased risk of other nosocomial infections, reduced antibiotic compliance and higher healthcare costs [3]. Of 41 RCT, 58% showed sig-

Table 1. Strength of evidence for probiotic therapy for 3 types of diarrheal diseases

Type of disease	<i>L. casei</i> DN-114 001	<i>L. rhamnosus</i> GG	<i>S. boulardii</i>	<i>L. acidophilus</i>
Pediatric diarrhea	+++	++++	++++	0
AAD	+	+++	++++	+
TD	none	+	+++	0

Significant efficacy from: >3 RCT with >100 subjects (++++), 2–3 RCT with >100 subjects (+++), ≥2 RCT with <100 subjects (++) and only 1 RCT with >100 subjects (+); no significant efficacy found in any RCT (0) or no published RCT (none).

nificant prevention of AAD by probiotics. Table 1 shows the most promising probiotic strains for the prevention of AAD. For example, Hickson et al. [4] randomized 135 inpatients given antibiotics to Actimel or placebo milkshake for the duration (plus 1 week) of the antibiotic. Significantly fewer given the probiotic mixture developed AAD (12.3%) compared to the controls (33.9%).

TD may also be common, especially for high-risk destinations. It can affect travelers and have a severe economic impact on tourist-related industries. Of 13 RCT for TD, 38% showed significant prevention of TD by probiotics. For example, Kollaritsch et al. [5] randomized 3,000 Austrian tourists travelling to Turkey to either a low dose (250 mg/day) or a high dose (1,000 mg/day) of *S. boulardii* or placebo for the duration of their trip. Significantly fewer given the high probiotic dose developed TD (29%, $p < 0.05$) compared to the controls (39%), but no effect of the low dose was found (34%).

The use of probiotics has an excellent safety profile, as none of these RCT documented any serious adverse reactions associated with the probiotic treatment and probiotics have been used in a wide variety of patients.

Diarrhea is a global problem and many types are amenable to probiotic therapy. However, the efficacy is both strain and disease specific. Future research should confirm small studies and expand our exploration of newer probiotic strains and mixtures.

Disclosure Statement

L.V.M. is employed by the VA Puget Sound Health Care System, Seattle, Wash., USA. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government. L.V.M. has received lecture fees from Acambis, Biocodex, Danone, Massachusetts Biologic Laboratory and Osel.

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