Probiotics: Preventing Antibiotic-Associated Diarrhea

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PURPOSE. *Probiotics are live microorganisms that offer a health benefit to the host. Found typically in dietary supplements, probiotics can be safely used in the treatment of acute diarrheal disease, inflammatory bowel disease, and antibiotic-associated diarrhea. They can be found in milks, yogurt, powders, and pills.*

CONCLUSIONS. *Research has shown that several strains of probiotics are helpful in the prevention and treatment of antibiotic-associated diarrhea. The most commonly studied probiotics are* Lactobacillus *GG and* Saccharomyces boulardii.

PRACTICE IMPLICATIONS. *By understanding the uses, dosages, and safety of common probiotics, nurses can help educate patients and their families on the benefits of probiotics.*

Search terms: *Antibiotic-associated diarrhea*, Lactobacillus *GG*, *probiotics*, Saccharomyces boulardii

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Probiotics have become increasingly popular in the United States over the last 10 years, but they have been studied for many years. In 1908, Dr. Eli Metchnikoff won the Nobel Prize in medicine for his research on probiotics. Dr. Metchnikoff was the first to officially propose that ingesting certain bacteria could help replace harmful microbes in the body. He proposed that increasing the amount of sour milk consumed, or dairy drinks with live bacteria, was associated with increased longevity (Isolauri et al., 2002). This concept is believed to be the beginning of the evolution of the study of probiotics. Probiotics are "live microorganisms" that, in certain dosages, can result in a health benefit to the host. Probiotics modify the microflora of the intestine, which results in antibacterial substances being secreted, and then, the probiotics compete with pathogens to prevent adherence to the intestinal epithelium (Land & Martin, 2008; Michail, Sylvester, Fuchs, & Issenman, 2006).

The gastrointestinal tract of a newborn baby, at birth, is sterile. Bacteria that are ingested during the birthing process colonize the gastrointestinal tract. Subsequently, our intestinal flora is most similar to our mother's intestinal flora. In addition, the intestinal tract has 10 times as many bacteria as cells in the human body. It is these bacteria that are responsible for priming the immune system. Without these bacteria, the immune system would not function properly (Vanderhoof & Young, 2002). Isolauri and colleagues (2002) referred to the gastrointestinal tract as the most metabolically active organ in the human body.

The types of bacteria that colonize the infant depend on several things, such as the type of delivery (vaginal vs. Cesarean section), age at birth, and the type of feeding (breastfeeding vs. formula feeding; Kligler, Hanaway, & Cohrssen, 2007). Infants born via Cesarean section appear to have delayed colonization with *Bifidobacterium* and *Bacteroides* (Vael & Desager, 2009). Breast-fed infants appear to have intestinal tracts that primarily contain bifidobacteria. This is thought to have an effect on the occurrence and virulence of intestinal pathogens (Isolauri et al., 2002; Saavedra, 2001). The food that humans ingest travels through the intestines and interact along the way. Our environment is heavily colonized with many microorganisms. In the modern movement to

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sterilize the environment and protect the host, many nonpathogenic bacteria, which are actually helpful to the host, are being destroyed (Saavedra, 2001).

Probiotics are thought to contribute to intestinal homeostasis in the midst of this modern invasion of sterility. They are used in the treatment of acute infectious diarrhea, irritable bowel syndrome, antibiotic-associated diarrhea (AAD), inflammatory bowel disease, and allergic disease. In the past 10 years, the amount of research on probiotics has dramatically increased (Land & Martin, 2008).

AAD

Probiotics are used in the prevention of AAD. Antibiotics are commonly prescribed in the treatment of children with illnesses such as otitis media, streptococcal pharyngitis, pneumonia, and cellulitis. Children are estimated to use three times more antibiotics than adults (Szajewska, Ruszczynski, & Radzikowski, 2006). While these antibiotics may cure disease, they can result in unwanted side effects like diarrhea. Antibiotics, such as aminopenicillins, cephalosporins, and clindamycin, that fight anaerobes more often cause diarrhea. These antibiotics alter the intestinal microflora of the patient, leading to crampy abdominal pain and diarrhea (Johnston, Supina, Ospina, & Vohra, 2007).

Diarrhea is defined by the World Health Organization (2009) as three or more loose or liquid stools in a 24-hr period or more frequent stool than is normal for the individual. AAD is thought to occur in 11–40% of children between the initiation of antibiotics and 2 months after their completion (Szajewska et al., 2006).

Administration of *Lactobacillus* GG (LGG) has been shown to reduce AAD risk by 75% in children in the United States (Vanderhoof & Young, 2002). *Saccharomyces boulardii*, a yeast, has also shown the ability to reduce the risk of AAD (Vanderhoof & Young, 2002).

Several randomized controlled trials have been conducted to assess the influence of probiotics on AAD. All of them have shown a statistically significant reduction in AAD in those patients taking probiotics compared with placebo. In a meta-analysis by Szajewska et al. (2006), six randomized controlled trials were included. Probiotics decreased the risk of AAD from 28.5% to 11.97%. Thus, for every seven patients taking probiotics with their antibiotics, one less patient developed diarrhea. In these same studies, LGG, *S. boulardii*, and *Bifidobacterium lactis* with *Streptococcus thermophilus* were associated with decreasing AAD. In general, the length of diarrhea in the study participants was decreased by a total of 1 day (Szajewska et al., 2006).

In another meta-analysis by Johnston et al. (2007), 10 randomized controlled studies were evaluated. According to the authors, probiotics significantly decreased the incidence of diarrhea. The mean decrease in duration of diarrhea because of probiotics in these studies was three quarters of a day. A limitation in these studies was that the dose of probiotics used varied between the studies, thus making it difficult to determine the dosage of probiotics necessary.

Dosage

Probiotic products come in many preparations. They are available in milk, infant formula, and yogurt as well as in powders and pills. The most common probiotics are bifidobacteria and lactobacilli. The standard accepted dosing is between 1 and 10 million colony-forming units (CFU) daily (Saavedra, 2001). According to a meta-analysis by Johnston et al. (2007), the evidence suggested that a dose of 5–40 billion CFU/day of LGG or *S. boulardii* had the most promise of decreasing AAD. Few studies have been completed to determine the exact dosage required to colonize the intestine, but most researchers agree that the dose should likely be greater than or equal to 5 billion CFU per day (Boyle, Robins-Browne, & Tang, 2006; Johnston et al., 2007).

Two popular over-the-counter preparations are Florastor® (Bicodex, San Bruno, CA) and Culturelle® (Amerifit Brands, Inc., Cromwell, CT). Florastor® is composed of the yeast *S. boulardii*. It is dispensed as a powder or capsule. The dose recommended by the manufacturer for AAD is one to two capsules twice a day. Each capsule contains 5 billion CFU (Bicodex, 2009). Culturelle® is a newer probiotic composed of LGG. LGG is the best studied and most documented probiotic strain available. Each capsule of Culturelle® contains 10 billion CFU of LGG and is recommended for once-a-day dosing (Amerifit Brands, Inc., 2009).

The large number of probiotic preparations on the market makes it more difficult to create generalized recommendations for probiotic use. Many of the products found in pharmacies and health food stores are neither reliable nor effective, and consumers need to understand that all probiotics are not created equal. For example, many probiotics are ineffective because they are unable to survive gastric and bile acids, unable to colonize the intestine, and ineffective at binding to epithelial cells in the intestine. Those probiotics strains showing the most promise are LGG, bifidobacteria, and *S. boulardii* (Saavedra, 1999; Vanderhoof et al., 1999).

Safety

Probiotics, in the powder or the pill form, are classified as a dietary supplement. Thus, they fall under different regulations than medications. Based on the Dietary Supplement Health and Education Act of 1994, supplements that existed prior to 1994 are not required to be reviewed by the U.S. Food and Drug Administration (FDA). Products marketed after 1994 must provide the FDA with information showing that the supplement/product is safe for use in humans. The

manufacturers do not have to provide factual evidence that these products are effective and safe, although they are not permitted to market products that are not safe and effective (National Institutes of Health Office of Dietary Supplements, n.d.). Once the supplement makes it to the marketplace, the FDA must prove that the product is unsafe or ineffective to have it removed from the market. Product labels should be truthful and not misleading (National Institutes of Health Office of Dietary Supplements, n.d.).

While probiotics are generally considered very safe, there are several case reports of sepsis in adults and children after the ingestion of probiotics. All cases of bacteremia and fungemia in children have occurred in premature infants, those children with underlying immune compromise, and children with central venous catheters (Boyle et al., 2006). In addition, there was a study conducted by Besselink and colleagues (2008) that recommended that probiotics not be administered routinely in patients with severe acute pancreatitis. An increase in mortality rates was observed in the adult patients they studied.

Future Research

With their good safety profile and studies proving their efficacy, probiotics will continue to be used. In addition, their effect on the immune system interests many researchers. Many future uses of probiotics have been suggested. These include: control of inflammatory diseases, treatment and prevention of allergies, cancer prevention, immune stimulation, and reduction of respiratory disease.

How Do I Apply This Evidence to Nursing Practice?

By understanding the uses, dosages, and safety of probiotics, nurses can give their patients accurate information on another way to improve their health. In addition, probiotics can help patients avoid the unwanted side effects, such as AAD, of certain medical therapies. Many parents stop treatment with antibiotics against their medical provider's recommendations in order to avoid diarrhea. Probiotic use may be one way to achieve greater compliance with antibiotic treatment in the pediatric population.

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