CHEST Special Features

Probiotics for Preventing and Treating Nosocomial Infections*

Review of Current Evidence and Recommendations

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Objective: **To review the available clinical data supporting the use of probiotics in preventing and treating serious nosocomial infections.**
Data source: **A Medline database from 1996 to July 2006 and references from identified articles were used to perform a literature search relating to the clinical applications of probiotics in preventing and treating *Clostridium difficile*-associated diarrhea (CDD) and prevention of hospital-associated pneumonia (HAP).**
Conclusion: **Nosocomial infections like HAP and CDD contribute significantly to health-care costs in the United States. These clinical problems are associated with prolonged hospital stays and increased mortality in critically ill patients. The emergence of multidrug-resistant pathogens in cases of HAP and the recent description of an epidemic, toxin gene-variant strain of *C difficile*, combined with the anticipated lack of new antimicrobial agents in the near future emphasize the need for new, innovative strategies to prevent and treat these diseases. Probiotics normally function as colonizers and contribute to the overall health of their hosts by multiple mechanisms including immune and antibacterial effects. There is no current clinical evidence to support the use of probiotics to restore the normal human flora in critically ill patients and reduce HAP rates. Probiotics can prevent episodes of antibiotic-associated diarrhea, but their utility in treating and preventing CDD requires demonstration of benefit in multicenter clinical trials, preferably sponsored by the National Institutes of Health.** ***(CHEST 2007; 132:286–294)***

Key words: *Clostridium difficile*; hospital-associated pneumonia; lactobacillus, probiotics; ventilator-associated pneumonia

Abbreviations: CDD = *Clostridium difficile*-associated diarrhea; HAP = hospital-associated pneumonia; RCT = randomized controlled trial

Patients admitted to hospitals and ICUs become susceptible to multiple nosocomial infections that significantly increase morbidity, mortality, and add to hospital costs. The normal flora in hospitalized patients is eradicated by broad-spectrum antibiotic therapy that creates an environment in which a pathogen not susceptible to the antibiotics can flourish, since the normal bacterial colonizers contribute to an unfavorable local milieu for pathogens. Hospital-associated pneumonia (HAP) is the leading cause of mortality attributed to nosocomial infections.[1,2] The incidence of HAP is from 5 to 10 cases per 1,000 hospital admissions. While the incidence of ventilator-associated pneumonia is difficult to determine due to differences in the case definition, it is

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estimated that 9 to 27% of patients receiving mechanical ventilation for > 48 h are affected.[3,4] HAP prolongs hospital stays for an average of 7 to 9 days and adds excess medical costs ranging from $12,000 to $40,000 per patient.[3–5] "Attributable mortality" from HAP is estimated to be between 33% and 50%, with the higher mortality occurring in patients with bacteremia or infections with *Pseudomonas aeruginosa* or Acinetobacter species.[6–9] Antibiotic-associated diarrhea results from an imbalance in the endogenous flora as a result of antibiotic therapy. Some cases of antibiotic-associated diarrhea are related to overgrowth of *Clostridium difficile*, a Gram-positive, spore-forming anaerobe. The incidence of *C difficile*-associated diarrhea (CDD) is increasing in US hospitals, occurring in up to 1.2% of hospitalized patients and causing life-threatening disease in 3.2% of patients.[10,11] The excess health-care costs associated with this illness amount to > 1 billion dollars per annum in the United States. This article will review some basic concepts relating to probiotic products and assess the evidence supporting their roles in preventing and treating these two important clinical problems.

Definition of Probiotics

Probiotics are viable microorganisms that colonize the host GI tract by adhering to the intestinal mucosa,[12] and each strain has unique characteristics with potentially different beneficial health effects on different organ systems (Table 1).[13]

Normal GI Flora and Its Benefits on Immune Function

The normal human GI tract flora is a complex ecosystem that in normal health maintains balance between commensals and pathogens. Normal human GI flora has many roles, including immune modulation, digestion, metabolic activity, and a competitive effect on other GI microbes. A healthy flora promotes the integrity of the gut defense barrier by normalizing intestinal permeability. The immune benefit is manifested by modulation of intestinal secretory Ig function and control of intestinal inflammatory responses by balancing the release of cytokines. By preventing excessive generation of inflammatory mediators in the GI tract that have the potential to extend the immune response systemically, the normal flora contributes to the overall immune function of its host.[14] Oral probiotic intake and maintenance of the normal GI flora microecology therefore has clinical effects at distant sites on an immunomodulatory basis. Additionally, these effects persist beyond the duration of actual colonization by the probiotic strain due to the memory capacity of the immune system.[15]

Probiotics: Antibacterial Effects

In addition to the immune and barrier function benefits noted above, probiotics are able to compete with the adhesion of pathogens to epithelial binding sites in the GI tract. These antibacterial and immune mechanisms are summarized in Table 2 and contribute to creating an unfavorable local milieu for pathogen colonization.[16–32]

Probiotics: Clinical Applications

Currently, probiotic products have been shown to be of some benefit in the following diseases: acute infectious diarrhea in children,[33–39] prevention of

Table 1—*Common Commercially Available Probiotic Products (This List Is Not All-Inclusive)*

Probiotic Species	Product
Lactobacillus rhamnosus GG	Culturelle (Amerifit Nutrition; Bloomfield, CT)
Bifidobacterium breve, *Bifidobacterium longum*, *Bifidobacterium infantis*, *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Streptococcus thermophilus*	VSL#3 (VSL Pharmaceuticals; Gaithersburg, MD)
L acidophilus	Acidophilus Pearls (Enzymatic Therapy; Green Bay, WI); Nature Made (Nature Made; Mission Hills, CA); Acidophilus Extra Strength (Nature's Bounty; Bohemia, NY); DDS-Acidophilus (UAS Labs; Eden Prairie, MN); Florajen (American Lifeline; North Freedom, WI); Kyo-Dophilus (Wakunuga of America; Mission Viejo, CA); Lactinex (BD; Franklin Lakes, NJ)
Bifidus regularis	Activia yogurt (Dannon; White Plains, NY)
Lactobacillus fermentum	GI48 (Lane Labs; Mahwah, NJ); ProBio PCC (Pharmanex; Provo, UT)
Bifidobacterium lactis, *L acidophilus*, *Lactobacillus brevis*, *L bulgaricus*, *L casei*, *Lactobacillus rhamnosus*, *streptococcus*	iFlora 4-women (SedonaLabs; Cottonwood, AZ)
Streptococcus salivarius	Aktiv-K12 (Therabreath; Los Angeles, CA)
Saccharomyces boulardii	Florastor (Biocodex; Seattle, WA)