

Probiotic Safety and Risk Factors

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Probiotics are defined by the Food and Agriculture Organization of the United States as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.”¹ They are considered nutritional supplements and, as such, are classified as Generally Regarded as Safe (GRAS). Organisms of the probiotic groups are added to all sorts of foods, particularly yogurts, but are also found in drinks and other common food supplements. They are commonly sold as pills or powders, and there is no control on their quality other than control of any marketing claims. As a consequence, patients purchase probiotics and foods containing them over the counter. There is no government control. The probiotic industry is reaching almost \$20 billion a year² in the westernized world and it is growing extensively worldwide. Very few complications have been reported with their use. However, there are risks, particularly in immunocompromised patients.

In this issue, a case report has been published in which a 17-year-old with universal ulcerative colitis treated with both corticosteroids and antibiotics was given *Lactobacillus rhamnosus* GG by his parents.³ The authors carefully identified a case of sepsis. They identified, genetically and by culture, that the circulating organism was the same as from the probiotic Culturelle. The patient responded to antibiotic therapy, but there was some clinical question as to whether the septic symptoms could have been from a viral infection. The virus was identified before and after manifestation of symptoms. This case was reported as an immunocompromised patient and that appears to be a risk factor status for infection with probiotics, although the incidence is extremely low.⁴

As noted in our recent book “*Probiotics: A Clinical Guide*,” there are risk factors for possible infection that should be observed before probiotics are administered.⁵ The risk factors are clearly outlined by Boyle et al.⁶

Major risk factors are immunocompromised and premature infant patients.

Minor risk factors are presence of central venous catheters, impaired intestinal epithelial barriers, administration of probiotics by jejunostomy, concomitant administration of broad-spectrum antibiotics, to which probiotics are resistant, properties of high mucosal adherence of known pathogenicity, and cardiac valve disease. The cardiac valve disease risk factor appears to be only for *Lactobacillus* probiotics.

Although these risk factors are not widely used, Boyle and associates felt they were significant. This patient was both on antibiotics and on corticosteroids.

In 2010, Whelan and Meyers⁷ conducted an extensive systematic review of case reports, randomized controlled trials, and nonrandomized trials in patients administered probiotics while on nutrition support. There were 52 articles reporting 53 trials in which 4131 patients received probiotics. There were only 3 trials that showed increased complications, which were largely noninfectious in nature. In all, 20 case reports of adverse events in 32 patients were published. The organisms involved in the adverse reports were either *Lactobacillus rhamnosus* GG or *Saccharomyces boulardii*, and the risk factors of either the presence of central venous catheters or disorders associated with increased bacterial translocation were present. They felt that the very low incidence of complications in patients on nutrition support resulted in no contraindication to their use.

The use of probiotics should always be subjected to a risk/benefit analysis before they are administered. Healthy people do not face any risk. Regular surveillance for adverse events should always be carried out when probiotics are used in the presence of a central venous catheter. An extensive review of the literature by other authors is reassuring. There is a long history of safe use of probiotics in foods and as supplements, and they are generally regarded as safe by the Food and Drug Administration and by EFSA.⁸ Patients and physicians should feel comfortable in recommending the use of probiotics. However, risk factors should be evaluated, and when a patient is on significant antibiotic or immunocompromising medication

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or is immunocompromised or on a central venous catheter, risk analysis should be performed. If there are no risk factors, probiotic use can be considered GRAS.

REFERENCES

1. Report of joint FAO/WHO expert consultation on evaluation of health and nutritional properties of probiotics in food including powder milk with live lactic acid bacterial. October 2011.
2. Natural Products Insider. May 23, 2008.
3. Vahabnezhad E, Mochon AB, Wozniak LJ, et al. *Lactobacillus* bacteremia associated with probiotic use in a pediatric patient with ulcerative colitis. *J Clin Gastroenterol*. 2013;47:437–439.
4. Snyderman DR. The safety of probiotics. *Clin Infect Dis*. 2008;46:S104–S111.
5. Floch MH, Kim AS. *Probiotics—A Clinical Guide: Introduction*. Thorofare, NJ: SLACK Inc; 2010:pxw–xxi.
6. Boyle R, Robins-Bowne RM, Tang MLK. Probiotic use in clinical practice: what are the risks? *Am J Clin Nutr*. 2006;83:1256–1264.
7. Whelan K, Myers CE. Safety of probiotics in patients receiving nutrition support: a systemic review of case reports, randomized controlled trials, and nonrandomized trials. *Am J Clin Nutr*. 2010;91:687–703.
8. Ferreira CL, Magalhaes M, Gueimonde M, et al. Probiotics: from origin to labeling from a European and Brazilian perspective. In: Kneifel W, Salminen S, eds. *Probiotics and Health Claims*. Ames, IA: Wiley-Blackwell; 2011:75–87.