A Review of Probiotics: Are They Really “Functional Foods”?

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Probiotic therapy may be useful in the treatment or prevention of a number of disorders, particularly diarrheic disease. Practitioners should attempt to use probiotics that are accurately labeled (genus, species, and ideally strain), indicating the number of viable organisms. Ideally, only organisms that have been demonstrated to colonize the intestinal tract of horses and products for which efficacy has been shown clinically should be used. More research is needed, but equine doses of $1 \times 10^9$ to $1 \times 10^{10}$ CFU/50 kg per day seem reasonable at this point. Author’s address: Department of Clinical Studies, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada N1G 2W1. © 2001 AAEP.

1. Introduction

Probiotics are being used increasingly in both human and veterinary medicine. Appealing properties of probiotics include the ability to reduce antibiotic use, the apparently very high index of safety, and the public’s positive perception about “natural” or “alternative” therapies. Despite the rapid increase in interest in probiotics that has occurred over the last decade, there is still a paucity of basic and applied research in veterinary species. This review is intended to provide veterinarians with a basic understanding of probiotic properties, the principles of probiotic therapy, and a general overview of current research in order to allow them to approach probiotic therapy in a more informed and critical manner.

2. History

The concept of probiotics was first reported by Elie Metchnikoff in 1907. He postulated that consumption of fermented milk products was responsible for longevity of certain ethnic groups and suggested that these products manipulated the intestinal microflora to maintain the normal balance between pathogenic and non-pathogenic bacteria. The term probiotic was proposed initially in 1965 by Lilley and Stillwell, as an antonym to antibiotic, and used to describe substances favoring the growth of microorganisms. Fuller later described a probiotic as a “live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance.” The definition of probiotics was further refined in 1998 to “living microorganisms, which upon ingestion in certain numbers, exert health effects beyond inherent basic nutrition.”

3. Basic Concepts

Regardless of the definition used, there are certain criteria that have been developed to evaluate the potential of microorganisms to function as probiotics. Based on the definition reported by Guarner, it is clear that adequate numbers of viable organisms must reach the intestinal tract. To do this, probi-
otic organisms must be able to survive transit through the acidic environment of the stomach and resist bile digestion. Organisms that survive acid and bile must possess a variety of other properties, including the ability to adhere to intestinal epithelial cells, colonize the intestinal tract, produce an antimicrobial factor, and inhibit enteric pathogens.\textsuperscript{5–9} Other properties such as immunomodulation, modulation of metabolic activities, and inactivation of procarcinogens are also desirable.\textsuperscript{5,10} An organism can only be considered to be a probiotic after these properties have been identified and a positive health effect has been documented. Many authors state that probiotics should be native inhabitants of the target species,\textsuperscript{5,10,11} however across-species efficacy has been demonstrated for some probiotics.\textsuperscript{12} Commercial probiotics should also be safe, result in no undesirable effects on the host (i.e., excessive gas production), be robust enough to grow in commercial conditions, and survive during processing and storage.\textsuperscript{5}

Part of the reason that probiotic treatment is approached with scepticism by some is that the mechanism of action is not fully understood.\textsuperscript{13} The poor understanding of the mechanism of action is not, however, very surprising considering that we still do not have an accurate understanding of the composition of the intestinal microflora.\textsuperscript{13} Originally, it was thought that probiotic bacteria exerted their effects through competitive inhibition of enteric pathogens, however, further research, particularly studies involving viral or inflammatory enteric disease, has demonstrated that colonization resistance is only one possible mechanism. Other potential mechanisms that have been suggested or demonstrated include production of antimicrobial substances, competition for adhesion receptors, competition for nutrients, stimulation of immunity,\textsuperscript{3} and decreasing intestinal antigen absorption.\textsuperscript{14}

Most probiotic preparations are comprised of one or more lactic acid bacteria (LAB). Within this group, strains of Lactobacillus, Bifidobacterium sp. and occasionally Streptococcus are most commonly used.\textsuperscript{3,5} Certain strains of yeasts, most notably Saccharomyces boulardii, have also been evaluated.\textsuperscript{5,15}

Development of probiotics requires more than just selection of any Lactobacillus or Bifidobacterium isolate. Selection of probiotic organisms at the genus or species level is not adequate as only a few strains of certain bacterial species have positive health effects.\textsuperscript{7} One cannot assume that probiotic properties expressed by one member of a lactic acid bacteria species will be present in all related strains. As such, probiotic organisms must be identified to the strain level and testing must be performed on individual strains.\textsuperscript{10,11}

Probiotic organisms are classified by the FDA and other regulatory bodies as generally regarded as safe (GRAS),\textsuperscript{16,17} a property that has lead to frequent use of these organisms without standard efficacy or safety studies. Lactobacilli have been implicated in cases of bacteremia and endocarditis in people,\textsuperscript{18–20} although probiotic organisms were not thought to be involved. A liver abscess in a person was found to contain the probiotic Lactobacillus rhamnosus strain GG (LGG).\textsuperscript{21} However, the incidence of adverse effects is exceedingly low, in contrast to the well-known side effects of antibiotics. It has been suggested that unlimited use of probiotics may lead to adverse effects in “at risk” groups.\textsuperscript{4} Particular “at risk” groups have not been identified, but it has been questioned whether the stimulation of the immune system by probiotics could be detrimental in autoimmune disease and whether the possibility of transfer of antibiotic resistance from probiotics to virulent microorganisms exists.\textsuperscript{4} Certain LAB species possess atypical resistance to certain antimicrobials and may have the potential for plasmid-mediated transfer of antimicrobial resistance.\textsuperscript{22,23} Additionally, 3 species of bifidobacteria are associated with dental caries in people, therefore these species cannot be considered for use in people.\textsuperscript{23}

Yogurt has been used by medical doctors, veterinarians, and lay people for the treatment of a variety of conditions with varying degrees of anecdotal success. It is important to remember that the potential for yogurt to be a probiotic revolves around the bacterial strains in the yogurt and the numbers of viable bacteria that are present. Yogurt can be an effective delivery vehicle for probiotic organisms,\textsuperscript{9} but not all strains of lactobacilli in yogurt possess probiotic properties. Some yogurts are prepared with probiotic strains; however, common yogurt products contain strains of L. delbrueckii and/or S. thermophilus,\textsuperscript{24} which have no demonstrable probiotic effect.\textsuperscript{6,25,26} Clinical trials using standard yogurt have been disappointing.\textsuperscript{27,28} Yogurt manufacturers recommend that 2 × 10^6 CFU/ml of probiotic organisms be present in yogurt at the end of shelf-life, which is not always achieved, and which may not be adequate for clinical effect based on probiotic concentrations used in clinical studies.\textsuperscript{24}

4. Probiotics in Human Medicine

Despite the widespread availability of commercial probiotic preparations containing a variety of bacterial species, extensive research has only been performed on a small number of probiotic organisms. Some studies evaluating probiotics have used combinations of organisms, making it difficult to ascribe effects to individual organisms. Therapeutic effects of most commercial preparations are unsubstantiated.

Strains of Lactobacillus rhamnosus (particularly L. rhamnosus strain GG [LGG]), L. salivarius, L. reuteri, L. johnsonii, L. acidophilus, Bifidobacterium lactis, B. bifidum, B. longum, Enterococcus faecium, and Saccharomyces boulardii are the most extensively tested probiotic organisms in people.\textsuperscript{13,15,29–32} Among these, LGG is probably the best understood probiotic organism and has been shown to possess probiotic properties in vitro and in vivo. Lactobacillus GG has been shown to be effective in the
5. Commercial Products

Quality control is a concern with commercially available probiotics due to the lack of regulatory oversight. Misidentification of probiotic bacteria is common in commercial preparations. A number of studies have been performed evaluating probiotics available for human use and all have reported disappointed results. In a survey of probiotics from a number of countries, Canganella et al reported that some products did not contain the claimed organisms, and some species of lactobacilli, bifidobacteria and streptococci were not viable. Similarly, Hamilton-Miller et al reported that the composition of only 2 out of 13 British probiotic preparations matched their label claims. The other 11 brands did not contain the listed species, contained other species, or contained less than one-tenth of the stated concentrations. Gilliland and Speck in 1977 reported that many commercial supplements claiming to contain L. acidophilus either had no growth or growth of other species. Preliminary results evaluating commercial veterinary probiotic products have been similarly disappointing.

Dose is very important when developing or evaluating a probiotic preparation. In humans, doses of 1 x 10^10 to 1 x 10^11 CFU/day are generally used in efficacy studies. Kailasapathy et al have suggested that the minimum therapeutic dose of 1 x 10^8 to 1 x 10^10 CFU/d in people while others have claimed that at least 1 x 10^9 to 1 x 10^10 viable organisms must reach the intestinal tract to be effective.

6. Probiotics in Equine Medicine

Despite the widespread and increasing use of probiotics in equine medicine, there is a paucity of research evaluating the efficacy of these products. One study evaluating two commercial probiotic preparations reported that there was no influence on shedding of Salmonella sp., prevalence of post-operative diarrhea, length of antimicrobial therapy, and length of hospitalization in horses with colic. This study evaluated one preparation claiming to contain L. plantarum, L. casei, L. acidophilus, and Streptococcus faecium and one claiming to contain L. acidophilus, S. faecium, Bifidobacterium thermophilum and B. longum at total daily doses of 3 x 10^8 CFU and 4.1 x 10^8 CFU, respectively. A second study evaluated a commercial product claiming to contain 5 x 10^9 CFU each of L. lactis and E. faecium, and 1 x 10^8 live yeast cells. This study reported no effect on Salmonella shedding in hospitalized horses with colic. Unfortunately, no indication was given whether these strains were able to colonize the equine intestinal tract or whether the doses were adequate. Another study evaluated the effect of a commercial “probiotic” on cardio-respiratory, hematonological, and biochemical parameters during exercise and suggested that it could modify the physiological effects of training. The supplement used in this study contained “a biologically active complex of metabolites of the intermediary metabolism,” yeast-RNA and nucleic acid bases, and oligonucleotides. Because this product did not contain live microorganisms it cannot be, by definition, a probiotic. Dietary yeast cultures have been studied as a means of increasing digestible energy content of feeds, however these products are nutritional supplements rather than probiotics.

As stated above, the dose of viable organisms is critical. The dose of probiotic organisms required to ensure colonization of the intestinal tract in a horse in unknown. Extrapolating from recommendations in people, an average (~450 kg) horse would likely require at least 1 x 10^10 to 1 x 10^11 CFU/day (10–100 billion CFU/day) of an organism able to colonize the intestinal tract. This may be difficult to achieve with some commercial probiotic preparations.

7. Clinical Use of Probiotics in Horses

Based on extrapolation from research in other species, it seems likely that probiotics have a role in equine medicine. Which probiotics, and which roles, however, have yet to be determined. One must remember that probiotics are specific tools, not “cure-alls.” Antibiotics have revolutionized medicine, but the right antibiotic must be used for the right condition, or treatment will fail. Probiotic administration should be considered in the same context. Probiotics will not be efficacious in the treatment of all conditions, and all probiotics will not be equally effective in treating all probiotic-treatable conditions.

Selection of probiotics for use in equine practice is difficult at this point due to the paucity of objective research. Many commercial preparations do not list the organisms that are present. Some products list additional ingredients such as “special proteins” and “immune factors.” These should be approached with scepticism if more detailed explanations, including indications of efficacy, cannot be provided. For critical evaluation of a product, it is essential to know the species and strain of the organism(s), the concentration, and whether colonization and efficacy studies have been performed. Testimonials are not acceptable for demonstration of efficacy. New probiotic products should be evaluated by practitioners in a manner similar to that taken for any pharmaceutical product.

Despite the scarcity of objective research, a variety of conditions have been suggested to be probiotic-responsive. One lay author listed the indicated conditions for probiotic treatment as: hard keepers; horses greater than 18 yrs old; those with a poor appetite, loose manure, or chronic diarrhea;
large amounts of undigested material in manure; other signs of digestive diseases such as recurrent colic, stress from shipping, racing, showing, recovering from surgery, or stressed by veterinary treatment such as floating teeth or vaccination; those that have recently been treated with antibiotics or anthelmintics; had recent feed or environment changes; horses struggling to adapt to extremes of temperature; new-born foals; horses losing weight or condition or horses appearing unthrifty. While probiotics could be helpful in some of these situations, this list encompassed the vast majority of horses.

Probiotics may have the greatest utility in the prevention and treatment of antimicrobial associated diarrhea, treatment of clostridial colitis, treatment of chronic diarrhea and prevention of nosocomial diarrhea, and prevention of acute infectious (especially rotaviral) diarrhea in foals. Certain probiotics have been shown to affect antigen transport in the small intestine people, thereby being useful for the treatment of food allergy. It has been postulated that these organisms may close large molecule transport pores. While this has not been evaluated in foals, one must wonder whether probiotics should be avoided in foals less than 24 h of age due to the potential to affect absorption of maternal antibodies.

Hopefully, future research studies will provide insight allowing for more specific selection of probiotic preparations. In the meantime, an understanding of the general principles of probiotics and of their application in other species can allow the practitioner to make reasonable choices.

8. Conclusion

It is too early to determine whether probiotics will make a profound impact on the practice of veterinary medicine. One must remember that just as all antibiotics are not effective against all bacterial infections, all probiotics will not be effective for all conditions. It is a logical to assume that certain probiotics will be effective in the treatment or prevention of certain conditions. Which probiotics and which conditions have yet to be determined. In the interim, practitioners should consider the general properties of probiotics and probiotic therapy when choosing and prescribing probiotic preparations.

References and Footnote

30. Orrhage K, Sjostedt S, Nord CE. Effect of supplements with Lactobacillus bifidum and Streptococcus thermophilus to...


*Weese, unpublished data.