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Effect of dietary modulation of intestinal microbiota on reproduction and early growth

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Abstract

An optimal balance of intestinal microbiota is necessary for digestive and immune health. Poor performance, susceptibility to infections, and decreased growth rate can be signs of an imbalanced microbiome. Dietary strategies to establish and maintain an optimal balance of microbiota include prebiotics (food for indigenous microbiota in the gastrointestinal tract) and probiotics (beneficial microbiota consumed by the animal). Recent research regarding use of probiotics and prebiotics in reproducing and growing livestock and companion animals is summarized. Documented benefits include prevention of diarrhea, decreased mortality, establishment of a healthy microbiota balance, and improved immune function.

Keywords: Intestinal microbiota; Probiotic; Prebiotic

1. Introduction

Intestinal microbiota are essential for the development of a healthy, stable intestinal tract, and a healthy immune system. Beneficial bacteria, such as bifidobacteria, lactobacilli, and some species of enterococci, provide nutrients for intestinal cells, promote absorption of nutrients, create a healthy intestinal environment, and promote a healthy immune system [1,2].

The intestinal microbiome, the community of microbiota residing in the intestinal tract, consists of a balance of beneficial and potentially harmful microbiota. This microbiome is established early in life. Disruption of the microbiome, or failure to establish a healthy microbiome, can result in intestinal upset and poor immune function. However, the signs can be much more subtle than diarrhea, and can include decreased growth rate, poor skin and coat quality, exacerbation of inflammatory conditions, susceptibility to infections, and a failure to thrive. Stress, travel, aging, changes in the environment, and long-term antibiotic therapy can disturb the balance of microbiota within the microbiome.

A comprehensive review of all the literature is beyond the scope of this manuscript. However, recent research regarding the effects of dietary modulation of intestinal microbiota on reproductive performance and early growth will be highlighted, with a focus on probiotic (beneficial bacteria) and prebiotic (food for beneficial bacteria) usage in livestock and companion animals.

2. Dietary modulation of intestinal microbiota

2.1. Probiotics

Probiotics, otherwise known as ''live active cultures'' or ''direct fed microbials'', are defined as ''live microorganisms which when administered in adequate amounts confer a health benefit on the host'' [3]. Specific probiotic microbiota include bifidobacteria

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species and lactic acid bacteria such as *Lactobacillus*, *Enterococcus*, *Pediococcus* and *Bacillus*. Some of the most commonly fed probiotics include *Enterococcus faecium* SF68, *Lactobacillus acidophilus*, *Pediococcus acidilacticii*, and *Bacillus subtilis*. Certain yeast species also have been used as probiotics. A complete list of probiotics approved for use in livestock and companion animals in the USA is included in the Association of America Feed Control Officials official publication [4].

Several excellent reviews have recently been written concerning the health benefits of probiotics [5–7]. Probiotics are often consumed to help restore and maintain microbiota balance during times of stress. Doctors recommend probiotics to help establish a healthy microbiota balance in infants, treat acute and chronic diarrhea, prevent traveler's diarrhea, and prevent diarrhea associated with long-term use of broad-spectrum antibiotics. Recent research with humans has linked probiotic use to decreased allergies and atopic dermatitis in infants, and fewer sick days in both infants and adults. Probiotics currently are being used in livestock feed as a substitute for growth-promoting antibiotics.

2.2. *Prebiotics*

A prebiotic is defined as a "nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, that can improve the host health" [8]. Therefore, prebiotics provide nourishment for the beneficial bacteria already present in the gastrointestinal tract. Insulin, short chain fructo-oligosaccharides and galacto-oligosaccharides have been the most extensively studied prebiotics [9]. Benefits of prebiotics in humans include establishment of a healthy gut microbiome in infants, production of beneficial short chain fatty acids, improved mineral absorption, lowering intestinal pH, decreased intestinal concentration of potential pathogens, and modulation of immune function. Prebiotics are consumed by humans to establish a healthy microbiome, to prevent gastrointestinal disturbances, and to maintain regularity. As with probiotics, prebiotics are viewed as a potential substitute for growth-promoting antibiotics in livestock feed.

3. Recent research in livestock and companion animals

3.1. *Swine*

Numerous studies have evaluated beneficial effects of probiotics and prebiotics on weanling and early-weaned piglets. Maternal probiotic ingestion resulted in increased food intake, litter size, and maternal body weight during lactation in first-litter sows [10]. Benefits extend beyond those apparent in the sow. Supplementation of the maternal diet with probiotics improved immune function in the resulting piglets [11]. Probiotic ingestion by piglets improved post-weaning weight gain, improved intestinal immune function, and increased villus height and crypt depth [12]. These alterations in intestinal cell morphology may beneficially affect nutrient absorption. Tako et al. [13] demonstrated that the prebiotic inulin increases expression of iron transporter genes in both the duodenum and colon of weanling piglets.

Establishment of healthy microbiota balance is also enhanced by probiotic [14] and prebiotic [13,15,16] ingestion. Increased concentrations of beneficial bacteria are often associated with increased short chain fatty acid concentration and decreased fecal pH, resulting in an intestinal environment that is less conducive to growth of potentially pathogenic bacteria. Scouring and mortality due to *Escherichia coli* infection [17] and intestinal *E. coli* content [18] were decreased in piglets fed probiotics. A combination of prebiotics and probiotics decreased adherence of *E. coli* to piglet intestinal mucosa [19].

3.2. *Cattle*

Several studies have evaluated the effect of probiotics on health of calves. Timmerman et al. [20] evaluated efficacy of probiotics of either human or calf origin on health of veal calves. Probiotics, regardless of source, improved average daily gain and feed efficiency and tended to decrease mortality. The percentage of calves requiring treatment for respiratory or digestive conditions was also lower in the probiotic group. The synergistic effect of cow vaccination and calf probiotic supplementation was studied by Avila et al. [21]; a combination of maternal vaccination and calf probiotic supplementation was more effective at controlling calf diarrhea than either the vaccination or probiotic alone. Galvao et al. [22] also detected a beneficial effect of probiotic supplementation on feed intake, pre-weaning weight gain, plasma glucose concentration, and diarrhea incidence.

The effects of probiotic supplementation on milk yield and reproduction have also been studied in dairy cows. Researchers in Japan [23] reported higher milk production and total amounts of fat protein and non-fat solids in milk of dairy cows supplemented with a prebiotic/probiotic combination than in control dairy cows. Somatic cell counts were higher in control cow milk than probiotic cow milk during summer months. Researchers in the United States observed similar effects for a probiotic blend [24]. Dairy cows fed the probiotic blend had higher milk production than control cows. Although milk lactose and glucose were greater in the probiotic cows, milk fat was greater in the control cows. Probiotic intake was associated with higher plasma insulin concentrations. The researchers hypothesized that the probiotic combination may have enhanced glucose uptake by the mammary gland and gluconeogenesis.

3.3. Sheep

Feeding a probiotic blend to ewes during late pregnancy and lactation decreased mortality in their lambs [25]. Mortality was related to diarrhea in both groups, and *E. coli* was isolated from the feces of the dead lambs. Similar to the results of dairy cow research, milk yield was increased in probiotic-supplemented ewes. Milk fat and protein content were also higher in the supplemented ewes.

3.4. Horses

There is a paucity of data on the benefits of prebiotic and probiotic ingestion in reproducing or growing horses [16]. Feces from foals fed a prebiotic had lower pH and decreased *E. coli* when compared to feces from control calves [26]; the decreased pH was most likely due to increased fecal concentrations of the short-chain fatty acids acetate, propionate and butyrate in the supplemented foals. Fecal quality was similar in all groups of foals, regardless of prebiotic intake.

3.5. Dogs

Although numerous studies have evaluated the efficacy of prebiotics in adult dogs [16,27,28] few studies have studied prebiotic or probiotic efficacy in reproducing dogs or growing puppies. Apanavicius et al. [29] evaluated the effect of prebiotic ingestion on severity of *Salmonella* infection. Puppies fed a prebiotic had increased fecal lactobacilli concentrations, total short-chain fatty acids and acetate, all indicators of a healthy intestinal environment. Indicators of severity of *Salmonella* infection were reduced in puppies fed the prebiotic. These indicators included enterocyte sloughing, ileal Na+-dependent glucose transport, and food intake reduction. Therefore, ingestion of the prebiotic helped protect the puppies against *Salmonella* infection.

Adogony et al. [30] fed bitches a control or prebiotic-supplemented diet throughout the second half of gestation and lactation. The prebiotic-supplemented bitches had higher colostrum and milk IgM than the control bitches. The mechanism was not determined, but was hypothesized to contribute to immune protection in the offspring.

Higher food intake and growth rate were observed by Pasupathy et al. [31] in puppies fed a probiotic supplement. This effect was only apparent during the early part of the growth phase. When a probiotic was fed to neonatal puppies [32], fecal concentrations of lactobacilli were increased and *Clostridium perfringens* decreased. In addition, IgA increased in the puppies fed the probiotic. Benyacoub et al. [33] observed similar effects in weaned puppies. Puppies fed the probiotic had increased fecal IgA and a higher proportion of mature B cells (Cd21(+)/major histocompatibility complex class II(+)). These puppies also had significantly higher canine distemper virus vaccine-specific circulating IgG and IgA. Thus, the probiotic enhanced specific immune response in the puppies, without causing over-stimulation of the immune system.

3.6. Cats

The effect of probiotics on immune function in growing cats has also been evaluated. Veir et al. [34] observed higher CD4+ lymphocytes in kittens fed a probiotic. Czarnecki-Maulden et al. [35] observed increased fecal bifidobacteria concentrations and decreased fecal *C. perfringens* concentration in weanling kittens fed a probiotic when compared to weanling kittens fed the control. The probiotic-supplemented kittens had higher serum IgA than the control kittens. The improved intestinal environment and immune status of the probiotic kittens helped protect them from a natural outbreak of diarrhea. Although 60% of the control kittens were treated for intestinal symptoms, only 10% of the probiotic-supplemented kittens had symptoms severe enough to be treated. Duration of treatment was also shorter in the probiotic-supplemented kittens. The authors hypothesized that this effect was due to improved immune function and intestinal environment in the kittens fed the probiotic.

4. General considerations when evaluating probiotics

A good probiotic should be safe, stable until consumed, survive in the gastrointestinal (GI) tract and promote a normal, balanced microbiome. Safety studies need to prove that the probiotic does not acquire antibiotic resistance, transmit antibiotic resistance to other microbiota, or produce pathogenic factors [3]. Stability studies must prove that the probiotic survives typical manufacturing, shipping and storage conditions. Because probiotics are live microorganisms, keeping them stable prior to consumption is one of the biggest barriers to producing an effective probiotic. Use of microencapsulation technology can help improve stability of probiotics. Manufacturers should guarantee that an effective concentration of live probiotic microbiota remain in the product at the end of the product's shelf life.

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