NUTRITIONAL CONSIDERATIONS FOR THE GASTROINTESTINAL PATIENT

CONSIDÉRATIONS DIÉTÉTIQUES POUR DES PATIENTS ATTEINTS D’AFFECTIONS GASTROINTESTINALES

By Denise A. ELLIOTT (1)

SUMMARY

Nutrition is a fundamental component in the management of gastrointestinal disease. However, the diverse nature of gastrointestinal disease clearly indicates that different nutritional strategies need to be applied according to the pathophysiology of the underlying disease process. It is beneficial to approach the nutritional management of gastrointestinal disease by considering four approaches – diseases that respond to novel or hydrolyzed protein, diseases that respond to low dietary fat, diseases that respond to high energy, and diseases that respond to fiber. This review will address each of these key areas. In addition, emerging nutrients of interest to the management of gastrointestinal disease such as probiotics, long-chain omega-3 fatty acids and prebiotic fibers will be discussed.

Key words: nutrition, inflammatory bowel disease, fructooligosaccharides, hydrolyzed protein, gastrointestinal disease, fiber, protein, prebiotics, probiotics, glutamine, arginine.

(1) BVSc PhD Dipl ACVIM Dipl ACVN, Royal Canin USA, Inc.

RÉSUMÉ

La diététique est un aspect fondamental de la gestion des patients atteints d’affections gastrointestinales. Différentes stratégies nutritionnelles sont à utiliser selon la physiopathologie des processus pathologiques sous-jacents et la revue porte sur les quatre approches à prendre en considération : les maladies réagissant à de nouvelles protéines ou à des protéines hydrolysées ; celles réagissant à un régime à faible taux de matières grasses ; celles traitées par un régime riche en énergie et celles répondant à un régime riche en fibres. Un point sera en outre fait sur les nutriments émergents tels que les probiotiques, les acides gras oméga-3 à longue chaîne et les fibres prébiotiques.

Mots-clés : diététique, affections intestinales inflammatoires, fructooligosaccharides, protéine hydrolysée, maladies digestives, fibre, protéine, prébiotiques, probiotiques, glutamine, arginine.

(1) BVSc PhD Dipl ACVIM Dipl ACVN, Royal Canin USA, Inc.
COMMUNICATION

INTRODUCTION

Dietary therapy is an important aspect of the management of gastrointestinal (GI) disease in dogs and cats. Therapeutic recommendations have classically focused on dietary rest followed by implementation of a highly digestible or “bland” diet. However, as our understanding of the pathophysiology of gastrointestinal disease unfolds, it is clear that no single diet is likely to be effective for every patient. A surprising result is the strong interest in nutrients such as protein source, fat concentration, prebiotics, probiotics, omega three fatty acids, short chain fatty acids, glutamine, arginine, nucleotides, zeolite, and other nutraceuticals to optimize gastrointestinal tract (GIT) function. The purpose of this review is to review the function and application of these emerging nutrients for the management of patients with gastrointestinal disease. The overall objectives of dietary modification are to enhance digestion and absorption of nutrients, overcome potential nutrient deficiencies associated with mucosal damage, support the mucosal barrier function, promote normal GIT motility and function, decrease inflammation, and aid healing.

DIETARY REST

Traditionally, patients with vomiting and/or diarrhea have been managed with dietary rest followed with small amounts of highly digestible “bland” diets. However, recent evidence suggests that the presence of food in the GIT provides trophic signals in addition to direct nutrition to the enterocytes. The trophic signals increase mesenteric blood flow, stimulate the release of digestive enzymes and enterohormones which influence intestinal cell proliferation, differentiation, and the rate of mucosal cell turnover. Studies in piglets have suggested that small bowel atrophy begins within days of nil per os (Remillard et al, 1998a, b). The signs of atrophy that have been noted include decreased villus height, decreased absorption and a reduction in brush border enzymes. These changes ultimately compromise the intestinal barrier. Enteral feeding has been shown to be a powerful mechanism to prevent gastrointestinal atrophy in piglets.

A recent randomized controlled clinical trial investigated the effect of enteral nutrition on intestinal permeability, intestinal protein loss and outcome in dogs with parvo-viral enteritis, compared to nil per os (Mohr et al, 2003). Enteral nutrition was associated with a shorter time to recovery, increased body weight gain, and improved gut barrier function. This study suggests that feeding, rather than dietary rest, should be considered for some patients with gastrointestinal disease.

DIET DIGESTIBILITY

Highly digestible diets typically have digestibility values that exceed 90%. A highly digestible diet requires less gastric, pancreatic, biliary and intestinal secretions for digestion. This results in almost complete digestion and absorption in the upper small intestine so that minimal residue is presented to the lower bowel. Minimal residue reduces bacterial byproducts that may contribute to inflammation and osmotic diarrhea. In addition, less residue is available to trigger an abnormal immune response. A variety of commercial highly digestible low residue diets are available. These diets will differ in the protein and carbohydrate sources, fat levels and other gastrointestinal nutrients. There have not been any studies published to date to compare the effect of one diet over another. Nevertheless, these diets enjoy widespread anecdotal evidence of success for the management of a variety of gastrointestinal diseases.

PROTEIN AND AMINO ACIDS

Dietary sensitivity, an adverse reaction to food, is a term used to describe a clinically abnormal response to the ingestion of a particular food. Food allergy or hypersensitivity is an immunological response to the food. Most basic food ingredients, including proteins, lipoproteins, glycoproteins, and lipopolysaccharides, have the potential to induce an allergic response. The predominant allergenic glycoproteins are water-soluble, largely heat resistant, acid stable, and commonly in the range of 10 to 60 kDa. The reason an immunological response against a specific protein (or food allergen) is mounted in certain individuals is not fully understood. Genetics, age, poor digestibility of proteins, a defective mucosal barrier, defective oral tolerance, and increased mucosal permeability are all predisposing factors for food allergy.

The true prevalence of food sensitivity is not fully known. Elimination diets and subsequent re-challenge with the original diet are the only way to confirm a diagnosis of food allergy in pets. The aim is to feed a complete and balanced diet while strictly feeding a protein and carbohydrate source to which the pet has never been previously exposed. Therefore, a detailed diet history is necessary to identify foods not previously fed to the pet. This information is used to create an elimination diet that is hypoallergenic for that particular pet. Gluten sensitivity is a specific example of food hypersensitivity that has been documented in Irish Setters. Treatment requires a gluten (gliadin) free diet, therefore carbohydrates such as wheat, oats, barley, rye or buckwheat should be avoided. Gluten free carbohydrate sources include corn, potato, rice and soy flour.

Guilford et al. (2001) evaluated 55 cats with chronic idiopathic gastrointestinal disease. Twenty-nine percent of the cats were diagnosed with food hypersensitivity on the basis of dietary elimination-challenge studies using commercial selected protein diets as the elimination diet. Clinical signs of an additional 20% of cats resolved on the elimination diet, but did not recur after challenge with the previous diet. Fifty percent of cats were sensitive to more than one food ingredient.

The debate continues on what is the ideal approach for an elimination diet, i.e. a homemade diet versus a commercial product, an intact protein diet versus a hydrolyzed protein diet. It is clear that it is in the best interests of the owner and the pet to feed a complete and balanced diet. This is often difficult to achieve with homemade diets, particularly when owners begin to drift from the formula originally provided for the pet.
Proteins that are incompletely digested have more potential to incite an immune response to the residual antigenic proteins and large polypeptides. Conversely, highly digestible proteins are completely digested to free amino acids and small peptides, which have less potential to elicit an allergic response. Therefore highly digestible protein should be selected for the elimination diet.

The antigenicity of dietary proteins can be minimized by enzymatic hydrolysis to produce low molecular weight protein hydrolysates. Decreasing the size of the proteins that are ingested reduces the chances of immunoglobulin cross-linking and subsequent mast cell degranulation. Hypoallergenic diets have been recommended for both the diagnosis and management of food hypersensitivity in dogs and cats.

Monomeric or elemental diets have been recommended for human patients with severe gastrointestinal disease. M arks et al. (1997) evaluated the effects of a purified diet on intestinal structure and function in cats with methotrexate-induced enteritis. The purified diet was associated with marked villus blunting and increased bacterial translocation compared with a diet containing intact protein. The results of this study suggest that a purified diet containing free amino acids cannot be recommended for cats with methotrexate induced enteritis. In addition, there are no commercially available monomeric diets for pets. Therefore, a human formula would need to be selected, but these are typically not complete or balanced for dogs or cats. In this situation, the diet would need to be modified to ensure that factors such as protein requirement, taurine and arachidonic acid requirements are met.

Novel protein, hydrolyzed protein, and monomeric diets have been recommended by various authors for pets with inflammatory bowel disease, even though the role of dietary sensitivity in inflammatory bowel disease has not been elucidated. Given that the chosen diet is complete and balanced for the pet, there appears to be minimal risk associated with this decision. However, Guilford et al. (2001) has suggested that the initial protein selected for the IBD patient may indeed be a “sacrificial protein” as the IBD patient is at risk of developing sensitivity to the undigested food proteins entering the lamina propria from increased mucosal permeability. A second novel protein diet may be required after 4 weeks of therapy. M arks et al. (2002) evaluated the effect of a hydrolyzed protein diet in six dogs with inflammatory bowel disease. Dietary therapy alone improved clinical signs in four dogs, concurrent medical therapy was required in two dogs. Histopathological improvements were also noted in duodenal biopsies after therapy.

Long considered a non-essential amino acid, it has been suggested that glutamine is particularly beneficial for intestinal health. Glutamine preserves the intestinal barrier function, increases brush border enzyme activity, promotes protein synthesis and aids recovery from intestinal injury. Glutamine is the preferred fuel source for enterocytes. It is also used as a substrate for denovo synthesis of purine and pyrimidine nucleotides for DNA and RNA synthesis. GLUT epithelial have very a high turnover rate, therefore glutamine now appears to be a conditionally essential nutrient for optimal GIT function in starvation and stress. Glutamine supplementation has been reported to improve nitrogen balance, decrease mucosal atrophy, decrease bacterial translocation, and stimulate the immune system in humans and laboratory species.

A few clinical studies have supported the use of novel, highly digestible protein sources for the management of gastrointestinal disease in dogs and cats. N elson et al. (1988) reported that clinical signs resolved in 13 dogs with lymphocytic, plasmocytic idiopathic chronic colitis when they were fed a cottage cheese and rice diet. In 11 dogs, two commercial diets not previously fed to these dogs were successfully substituted for the initial test diet, without causing recurrence of signs. Only two of these 11 dogs subsequently tolerated a switch to diets that had been fed at the time of onset of signs of colitis. Resolution of clinical signs has also been reported in 6 cats with lymphocytic-plasmocytic colitis fed a diet of lamb and rice or horsemeat, or a prescription diet. Likewise, Paterson (1995) reported that 20 dogs that exhibited both a non-seasonal puritus and gastrointestinal signs had either improvement or complete resolution when fed either a homemade fish and potato or commercial fish and soy based diet. In two of the dogs were subsequently maintained successfully on the commercial food. Simpson et al. (1994a) evaluated the effect of a selected protein chicken and rice diet for the management of idiopathic chronic colitis. Within one month, clinical signs of straining, fecal blood, fecal mucus and fecal consistency were significantly improved. Within two months of dietary therapy, 90% of 11 dogs were stabilized and did not require drug therapy to control clinical signs of disease.

Of the energy-providing nutrients, fat is the most difficult to digest. It requires an interplay between the intestine, liver and pancreas. A deficiency of pancreatic enzymes (as occurs with exocrine pancreatic insufficiency and pancreatitis) impairs digestion and results in malabsorption of dietary nutrients. Although the digestion of protein and carbohydrate will be affected, the digestion of fat is most severely impaired since lipases are absent from the normal array of intestinal brush border enzymes. Bacteria in the intestinal tract can metabolize undigested fat to hydroxy-fatty acids, which can lead to secretory diarrhea in the large intestine. Bacteria also deconjugate bile acids, further impairing fat digestion and absorption. For this reason, fat restriction is beneficial in conditions where fat may become available for microbial metabolism, for example in malabsorption syndrome, small intestinal bacterial overgrowth, bile acid deficiency, and/or gastroenteritis. U nlike amino acids and monosaccharides, which are absorbed directly into the blood stream, fat is discharged from enterocytes into lacteals and transported to the systemic circulation via mesenteric lymph vessels and the thoracic duct. Lymphangectasia, a disorder characterized by congestion and/or dilatation of lymphatic vessels, will impair fat transport. Restriction of dietary fat is clearly indicated for the management of several gastrointestinal disorders. However, what constitutes...
Nutritionists consider a restricted fat diet to be one that contains less than 18% of the energy from fat. Using this recommendation, it is clear that many diets formulated for the management of gastrointestinal disease are not actually low fat diets.

Simpson et al. (1994b) evaluated the effect of a low fat diet in the management of 20 dogs with exocrine pancreatic insufficiency. Clinical signs resolved in all 20 dogs, and there was an average 24% increase in body weight.

Polynsaturated fatty acids are essential for the maintenance of membrane integrity as constituents of membrane phospholipids and the provision of substrates for eicosanoid synthesis, e.g., prostaglandins (PG), thromboxanes, and leukotrienes (LT). Long chain ω-3 fatty acids such as eicosapentaenoic acid and docosahexaenoic acid, directly compete with arachidonic acid for the lipooxygenase and cyclooxygenase enzymes. Subsequent metabolism of eicosapentaenoic acid generates less inflammatory mediators such as LT B₂ and PG E₂ compared to the metabolism of arachidonic acid. In addition, the metabolism of eicosapentaenoic acid produces hydroxy-fatty acids that block the production of LT B₂, a potent chemotactic factor, from arachidonic acid. Therefore, in general, ω-3 fatty acids are anti-inflammatory compared with the derivatives of ω-6 fatty acids. Fish oils have been suggested to improve the clinical status of human patients with ulcerative colitis and Crohn's disease. Indeed, many diets formulated for the management of gastrointestinal disease in pets have been enhanced with ω-3 fatty acids. However, there have not been any published studies to evaluate the effect of ω-3 fatty acid supplementation on gastrointestinal disease in dogs and cats. The ideal dose of the long chain fatty acids is not yet known and there is certainly no evidence to support an ideal ratio of ω-6 to ω-3.

Medium chain triglycerides (MCT's) which contain 8-12 carbon chains, have been recommended for some gastrointestinal diseases. It has been suggested that they are less dependent on micelle formation and the lymphatic vasculature for digestion and absorption. It has been suggested that MCT's reduce the palatability of the diet. In addition, MCT's have been associated with the development of hepatic lipidosis in cats.

**DIETARY FIBER**

Fiber, which is the non-digestible carbohydrate of plants, can be classified according to solubility or fermentability. Soluble fibers form a gel in water which delays gastric emptying and inhibits absorption in the small intestine. Insoluble fibers such as cellulose and oat fiber increase bulk and fecal water content, absorb toxins and normalize both segmental and propulsive motility. Both insoluble and soluble dietary fiber may be beneficial in the symptomatic treatment of certain large bowel diarrhea since fiber helps to normalize transit time and increase fecal water content. A diet containing intestinal transit time, insoluble fibers are often recommended for patients with constipation.

Fermentable fibers such as beet pulp, pectin, guar gum, gum arabic, and fructo-oligosaccharides may have a positive effect on the mucosal barrier by stimulating the growth of intestinal bacteria such as lactobacilli and bifidobacter. These bacterial species have been shown to be beneficial to gastrointestinal health by decreasing the growth of pathogens such as Clostridia and E. coli. In addition, they produce the short chain fatty acids butyrate, acetate and propionate, which provide fuel for the colonocytes. Short chain fatty acids enhance sodium and water absorption, increase mucosal blood flow and increase gastrointestinal hormone release. These mechanisms contribute to the trophic role that short chain fatty acids have on the intestinal mucosa, stimulating enterocyte and colonocyte proliferation.

High amounts of fermentable fiber may lead to excessive gas production (flatulence) and, by increasing fecal water, may lead to unacceptably loose stools. Thus, when selecting a high fiber diet, it is important to know the quantity and type of fiber present, as the response seen in an individual animal will vary depending on the diet used. Leib et al. (2000) reviewed the medical records of 37 dogs diagnosed with chronic idiopathic large-bowel diarrhea. Twenty-three of 27 dogs were classified as having a very good to excellent response to a soluble fiber (Metamucil) supplementation. Diarrhea returned in 6 of 11 dogs when fiber supplementation was withdrawn.

**PREBIOTICS/PROBIOTICS**

The gastrointestinal tract provides a home to a diverse population of bacteria. Recent research is focusing on methods to manipulate the gastrointestinal bacterial population to improve health (Sparkes et al., 1998a, 1998b, Zentek et al., 2002). Prebiotics are dietary substances, such as fructooligosaccharides (FOS), mannanoligosaccharides (MOS), inulin, resistant starch, or arabinogalactans (AG) that promote the health of beneficial bacteria in the gut and deter the growth of pathogenic bacteria, such as E. coli, Salmonella and Campylobacter. Human studies support a beneficial effect of added FOS or MOS in diets for prevention or control of infectious diarrhea. Willard et al. (1994) evaluated the effect of 1% fructooligosaccharides in 16 IgA-deficient German Shepherd dogs with small intestinal bacterial overgrowth. FOS supplementation resulted in significantly lower aerobic/facultative anaerobic bacterial colony-forming.
units in the small intestine. The results of this study indicated that FOS could affect the population of bacteria in the small intestine in dogs with small intestinal bacterial overgrowth. Swanson et al. (2002a and b) reported that supplemental fructooligosaccharides (FOS) and (or) mannanoligosaccharides (MOS) have beneficial effects on colonic health and immune status of dogs.

Probiotics are live microbial feed supplements that are administered to improve the microbiological balance in the intestine. To be effective, a probiotic must survive the acidic environment of the upper gastrointestinal tract, and must be capable of proliferating and colonizing the large intestine. In humans, there is increasing evidence that intestinal bacteria are important in the pathogenesis of IBD. Studies in mice indicate that probiotics can inhibit inflammation and prevent the development of colonic adenocarcinoma.

The ability of a probiotic strain to survive transit through the feline (Marshall-Jones et al., 2004) and canine (Baillon et al., 2006) gastrointestinal tracts has been reported. In addition, several markers of intestinal health and systemic health were evaluated. Potential health promoting effects of the probiotic noted included increased phagocytic capability of neutrophils, a substantial reduction in serum endotoxin levels, and a lowering of erythrocyte fragility indices. Furthermore there was a significant decrease in the number of Clostridia reflecting a change in the colonic microflora towards a healthier balance. These changes are indicative of beneficial changes in immune function and gastrointestinal barrier integrity, suggesting the possibility that probiotics could play an important role in protecting from disease. Indeed, probiotics have been demonstrated to significantly decrease the shedding of Campylobacter bacteria from infected cats (Baillon et al., 2003), and probiotic supplementation was associated with a lower rate of reinfection, suggesting that it could strengthen the resistance of healthy cats to infection with Campylobacter species.

**ANTIOXIDANTS**

In humans, supplementation with antioxidants, especially vitamin E, has been utilized in the management, and perhaps prevention, of various gastrointestinal diseases. Antioxidants such as vitamin E, vitamin C, carotoids and taurine appear to be safe in pets, but the clinical use of these antioxidants in gastrointestinal disease has not been evaluated.

**COBALAMIN**

Recent studies have clearly shown that cats and dogs with severe or chronic GI disease may become deficient in cobalamin (Simpson et al. 2001). The deficiency is documented by serum analysis of cobalamin levels, usually along with measurement of serum folate. This deficiency must be corrected with parenteral supplementation as the vitamin is important in a number of cellular processes, including GI epithelial cell turnover and repair.

**ZEOLITE**

Zeolite, or sodium silico aluminate, a tetrahedral clay, is capable of absorbing bacterial toxins, bile acids, and gases. By forming a protective film on the intestinal mucosa, zeolite helps to enhance the intestinal mucosal barrier. Zeolite has been used in piglets and calves in the management of weaning diarrheas. Grandjean & Crépin (1992) reported that the addition of clays to food decreased the duration and the severity of diarrhea in sled dogs. Clays have also been shown by Fioramonti & Droz-Lefaiz (1987) to reduce diarrhea induced by cholera toxin in dogs.


