Nutritional Impact of Hepatic Dysfunction
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Dietary management plays an important role in patients with liver disease. Maintaining appropriate nutrition helps support hepatic regeneration and aids symptomatic relief for clinical signs. Correction of malnutrition can improve liver function and enhance the liver’s functional reserve.

Protein Metabolism
Restriction of protein intake has become a standard part of the management of hepatic encephalopathy (HE). However, protein restriction may be inappropriate for most patients with liver disease. There is evidence that the rate of protein catabolism is increased in hepatic failure, and that maintenance of positive nitrogen balance is beneficial in the face of hepatic failure.

Excess protein restriction leads to catabolism of endogenous proteins and increased ammonia production, loss of skeletal mass with decreased capacity for detoxification of ammonia, and increased potential for HE. Many serum proteins, including albumin, transport proteins, and proteins normally produced by the liver are decreased in hepatic failure. These may be further decreased by inadequate protein intake, which may occur if protein is unrestricted to control HE.

Protein restriction should only be restricted as needed. If protein restriction is necessary, a minimum intake of 2 g protein/kg body weight/day is recommended for dogs and 4 g/kg for cats. However, it is important that protein adequacy (e.g., serum albumin) be monitored to assure that protein depletion does not occur.

Dietary meat and blood, including endogenous blood from gastrointestinal bleeding, are poorly tolerated, perhaps because of high ammonia and potential from homocysteine and myoglobin. On the other hand, protein from soybeans and milk are well-tolerated by patients with liver failure.

For example, dogs with liver failure may suffer acute induced portosystemic shunts (PSS) that were fed a diet containing 18% isolated soy protein gained weight and remained neurologically normal for the duration of a 16-week study.

An amino acid imbalance is reported to occur in HE, with a relative increase in aromatic amino acids and a decrease in branched-chain amino acids (BCAA) in blood and cerebrospinal fluid. This led to the theory that correcting the plasma amino acid profile should reverse or prevent HE.

However, BCAA-supplemented diets did not reduce the incidence nor severity of HE in dogs with liver failure secondary to PSS. Thus, priority should be placed on providing adequate amounts of high-quality, highly digestible milk or vegetable protein.

Carbohydrate Metabolism
Glucose storage and glucose synthesis often decrease in advanced hepatic disease, contributing to fasting hypoglycemia. Depleted glycogen stores result in premature protein catabolism to supply amino acids for gluconeogenesis. The longer a patient with hepatic failure spends in the fasting state, the greater the loss of muscle tissue and protein depletion. Nitrogen balance and nutritional status can be improved by the consumption of several small meals, including a bedtime snack.

Fat Metabolism
In some patients, hepatic dysfunction can interfere with the digestion and absorption of dietary fats and fat soluble compounds. Bile acids from the liver are important for the normal digestion and absorption of long-chain triglycerides (LCTs), the normal lipids found in most diets. Even when fat malabsorption is not clinically apparent, fat digestion may be somewhat reduced. Colonic microflora can ferment these undigested fats, producing hydroxy fatty acids that can cause diarrhea and enhance problems with deficiencies of fat-soluble vitamins and essential fatty acids.

In patients with fat malabsorption, restriction of LCTs is recommended. However, patients have been observed to consume more fat in the diet or in supplements in cases of poorly controlled HE.

Branched-chain amino acid (BCAA)-supplemented diets did not reduce hepatic encephalopathy.
adequate essential fatty acids must be provided (i.e., dietary LCTs between 5 to 10% of diet dry mater)- Medium-chain triglycerides (MCT) may be useful as an alternate energy source for these patients. These fats can be readily absorbed despite a lack of bile acids and are readily oxidized as an energy source. Both dietary and parenteral MCTs have been successfully used to enhance the nutritional status in patients with liver disease.

Vitamins and Minerals

Vitamin deficiencies are recognized in veterinary patients with hepatic disease, with the exception of Vitamin K. Coagulopathies second to Vitamin K deficiency should be treated with injectable vitamin K1. Vitamin C, thought not usually recognized as an essential vitamin for dogs or cats due to endogenous synthesis, may be deficient in some patients with liver failure. Oral supplementation with 1.5 mg vitamin C/kg body weight/day is recommended for vitamin C-dependent species, such as cats, and may be appropriate for dogs or cats with liver disease.

Zinc (Zn) deficiency is common in patients with hepatic disease, and can contribute to HE via altered amino nitrogen metabolism. Correction of zinc deficiency enhanced hepatic nitrogen clearance and psychomotor scores, and reduced lipopolysaccharide production in human cirrhotic HE patients. Zinc deficiency can lead to increased iron and copper (Cu) accumulation in the liver, while supplementation may help reduce hepatic fibrosis. Dietary zinc should provide at least 3.5 mg zinc/100 kcal metabolizable energy. Copper storage disease is well-known causes of hepatic failure in genetically predisposed dogs. Liver Cu often reaches 10,000 ppm with primary Cu storage disease, compared to normal levels of less than 400 ppm. Copper may also accumulate in liver secondary to other hepatic diseases, especially cholestatic disorders; however, secondary Cu accumulation rarely exceeds 2,000 ppm. Hepatic copper can be enhanced by Cu-chelating agents or zinc acetate. Dietary restriction of copper probably plays a minor role in reducing hepatic copper concentrations in diseased dogs.

Hypokalemia is a common preexisting cause of HE in human patients with hepatic disease. It is also linked to glucose intolerance, which is common in hepatohepatic disease. Hypokalemia can result from profuse vomiting or diarrhea, poor intake or from excessive use of loop diuretics in the management of ascites. Patients should be monitored for evidence of hypokalemia or acid-base imbalances.

Clinical Indications for Dietary Therapy

No single diet or product can meet the nutritional and clinical needs of all patients with liver disease. Selection of an appropriate product depends on the specific clinical signs observed. A number of pharmaceutical agents used in the management of hepatohepatic disorders are associated with side effects that may impact dietary needs. Glucocorticoids used in the management of chronic progressive hepatitis may cause or aggravate ascites, HE, glucose intolerance and gastrointestinal ulceration. Colecystokinin used to inhibit bile flow, has been associated with nausea, vomiting and hemorrhagic diarrhea.

Anorexia and vomiting may also accompany therapy with D- penicillamine or other Cu chelators. Diarrhea may result from excessive lactose administration. These effects should be taken into consideration when planning total patient management. Introduction of a new diet while a patient is nauseated may lead to a learned aversion to that food. Patients should be stabilized before introducing a food intended for long-term feeding.

Hepatic Encephalopathy

It is important to correct acid-base and electrolyte disorders and to maintain body weight in patients with liver failure in order to reduce the risk of HE. In the absence of a functional liver, the skeletal muscle serves a primary role in detoxifying ammonia. To help maintain muscle mass, protein should be restricted only as needed to prevent HE. Use of lactulose and supplementation with highly digestible, nonmotile proteins may allow an increase in protein intake in encephalopathic patients.

Vegetable proteins such as soybeans, and milk proteins such as casein are important sources of protein for patients susceptible to HE. Minimal protein requirements for many dogs have been determined to be 2.5 – 3.0 g/kg body weight, and most of the cases we have seen have required about 3.5 g/kg body weight.

Clotting Disorder or Reference Value Disorder?

Liver failure can lead to disturbed blood clotting. The activated coagulation time (ACT) test has long been used to assess coagulation of whole blood in cats. According to many veterinary references, the ACT values for normal cats should be no more than 45 seconds. However, most of these recommendations appear to be based on a single study of 22 cats from which samples were collected from jugular catheter in dogs, but only 11% of the individuals had evidence of hepatic encephalopathy. The authors concluded that the increases in ALT, GGT and SAP often observed with phenobarbital were due to enzyme induction. However, abnormalities in coagulation time (whole blood [AST]), albumin, total bilirubin or prothrombin time, are not considered to be important indicators of hepatic function.

Phenobarbital is the drug of choice for treatment of idiopathic epilepsy in dogs; however, this drug has been reported to induce hepatic injury. A recent study evaluated changes in hepatic parameters in normal dogs treated for 6 months with phenobarbital at levels appropriate for management of epilepsy. Treatment-induced hepatic enlargement was detected by physical examination, radiology and ultrasonography, yet no consistent evidence of hepatic toxicity was found on histopathological examination.

Serum alkaline phosphatase (SAP), alanine transaminase (ALT) and gamma-glutamyltransferase (GGT), all liver enzymes known to be induced by phenobarbital, increased during treatment, while other indicators of liver function remained normal. The authors concluded that the increases in ALT, GGT and SAP observed with phenobarbital were due to enzyme induction, not hepatic injury. However, abnormalities in coagulation time (whole blood [AST]), albumin, total bilirubin or prothrombin time, are not considered to be important indicators of hepatic function.

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Benefits of Selective Breeding in Bedlington Terriers

A cohort of 1- to 2-year-old Bedlington terriers evaluated between 1987 and 1996 showed that 94% of the tested were affected with copper toxicosis, based on liver copper content. None of the affected dogs was bred. A second cohort evaluated between 1990 and 1997 showed 45% were heterozygote carriers and 46% were homozygote healthy carriers, but only 11% of the individuals had detectable hepatic copper. However, phenotypic reduction in the incidence of copper toxicosis, from 40% to 11%, was achieved through effective screening and cooperation by dog breeders and veterinary professionals.

Oxidative Damage in Liver Disease

There is a considerable evidence that the severity of hepatic damage in individuals with chronic liver disease is associated with oxidative damage. Increased plasma concentrations of reactive oxygen species, which are also called free radicals — and degradative products of lipid peroxidation, such as malondialdehyde and hydroxyl radicals (measured as TBARS) are found with chronic and cholestatic liver disease.

New evidence has shown that the potential oxidative damage extends well beyond the diseased liver. As shown in the graph (at right), cholestatic liver disease induced by chronic bile duct ligation significantly increases the number of antioxidants whereas the opposite was observed, as well as increased lipids peroxidation in kidney and heart tissue: This study suggests that oxidative damage secondary to liver disease may affect many tissues and organs, even those separated by the blood-brain barrier.