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FELINE HEPATIC LIPIDOSIS: PREVENTION AND TREATMENT

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INTRODUCTION

Feline hepatic lipidosis (FHL) is characterized by an excessive accumulation of lipids in the liver and is one of the most common hepatobiliary disorders of cats. The clinical and laboratory findings commonly associated with FHL include: prolonged anorexia, weight loss, muscle wasting, hepatomegaly, icterus, and elevated liver enzymes activities. The diagnosis of FHL is confirmed by histologic examination of a liver biopsy or the cytologic evaluation of a fine needle aspirate of the liver. In most cats with FHL, hepatic lipidosis is the only detectable underlying abnormality, for that reason the syndrome is qualified as idiopathic FHL. When FHL is associated with another pathologic condition (i.e.: inflammatory bowel disease, cholangiohepatitis, renal disease, diabetes mellitus, hyperthyroidism, cardiomyopathy, ...) the syndrome is qualify as secondary.

The prognosis of Feline Hepatic Lipidosis (FHL) has dramatically improved over the last 15 years through the recognition that long-term (3-8wks) and aggressive tube feeding reverses the condition in more than 80 % of the cases. Despite the recognition that anorexia, protein malnutrition and excessive mobilization of peripheral fat stores play a major role in the pathophysiology of FHL, the underlying molecular mechanisms responsible for triglyceride accumulation in the hepatocytes have still to be established.

PREVENTION

A syndrome of hepatic lipidosis indistinguishable from FHL has been induced by changing obese cats from highly palatable commercial diets to a poorly palatable, but complete and balance, purified diet. Most of the cats fasted rather than ate the purified diet. Cats were allowed to fast until their serum became icteric, reached a predetermined minimum bodyweight similar to that of a healthy lean cat of the same length and body type (range 8.0 to 9.3 lbs -3.6 to 4.2 kg) or a maximum of 7 weeks. Four to 7 weeks of voluntary fasting resulted in histologic signs of hepatic lipidosis in all cases. 87% of the cats also showed increased liver enzymes activities and icterus. When commercial diets were re-introduced at the end of the fast, 84% of the cats became anorectic either immediately or within several days.

Based on this observation, fasting should be avoided in overweight cats. Food intake should always be monitored following stressful events such as moving to a new house, arrival of another pet or a stranger in his/her territory, when owners leave for a long vacation, or if the diet is changed, especially to a less palatable one (obesity diets for example). In healthy obese cats, a fast of several weeks is necessary to induce the clinical disease and a fasting episode of a few days should not be life threatening.

Food monitoring can be complicated when several cats have access to the same food bowl. A weight loss of > 10 % over a week following a dietary change and/or a stressful event is indicative of complete fasting. Monitoring of Serum Alkaline Phosphatase (SAP) is also a useful way to assess liver lipid accumulation. In the above model, SAP was consistently above normal limit 3 weeks before the clinical disease. Obesity is not associated with significant accumulation of lipids but fasting will result in a rapid and severe accumulation of membrane bound lipid vacuoles in the hepatocytes. Increased serum liver enzyme activities and total bilirubin occur only when lipid accumulation becomes extremely severe and the cytoplasm is barely visible on histology. Hepatocytes appear to be able to accumulate very large amounts of triglycerides before losing their ability to function properly. Therefore accidental findings of liver lipid accumulation not associated with an elevation of liver enzyme activities are rather an indicator of poor food intake than diagnostic for FHL. Similarly, any disease process associated with poor intake will induce liver lipid accumulation, which, if very severe, can complicate the primary disease. Obese cats are more likely to suffer from hepatic lipidosis as they have more peripheral lipids that they can mobilize to induce severe triglyceride storage in their liver.

Why do cats accumulate lipid in their liver when fasting has yet to be resolved. Long term fasting in obese humans and dogs is not associated with hepatic lipidosis. Fasting will result in severe and acute hepatic lipid accumulation within a few days in guinea pigs, pregnant ewes, ponies and post-partum cows. Those observations are suggestive of species differences in catabolic metabolism related to fasting. Small amounts of protein (22 g/day or 25 % of the calories for maintenance) given to cats as sole source of nutrients reduced the accumulation of liver lipids over a 4 weeks period compared to complete fast or isocaloric amounts of lipids and carbohydrates. None of the cats receiving 6g protein/kg of lean body weight/day showed an increase of SAP over a 6 weeks weight loss, when all the control fasted cats developed clinical hepatic lipidosis over the same period. These observations suggest that protein by providing limiting amino acids and/or modifying hormonal balances successfully prevent the accumulation of lipids induced by severe energy restriction. Nitrogen balance during fasting, also indicates that cats would not be as efficient in sparing their protein than other species. Therefore low calorie high protein regimens could be a safer alternative to induce rapid weight loss in obese cats. The underlying molecular mechanisms linking amino acid deficiencies and triglyceride accumulation in the hepatocytes remain, however, to be established.

TREATMENT

Nutritional support is the first consideration in the treatment of FHL. The prognosis is directly related to the ability of the clinician to aggressively meet the energy and nutrient requirements via enteral feeding. In surviving cats, tube-feeding will completely reverse the condition with a return to normal liver histology within a few weeks of nutritional management. The first week of treatment is critical as many cats appear sicker initially, probably due to severe nutrient, electrolyte and fluid shifts associated with re-feeding. Within a couple of weeks, a significant reduction in serum liver enzyme activities and total bilirubin should be observed.

Many highly digestible, complete and balanced feline diets have been used successfully in cats with hepatic lipidosis. Cats with hepatic lipidosis will usually tolerate 35 to 45 % of their calories as protein, a level that is found in most commercial cat foods. As mentioned above protein deficiency...
appears to be important in the etiology of the syndrome. Protein restriction (20 to 25 % of the calories, i.e.: feline renal diets) should only be considered if the patient shows signs of encephalopathy, an uncommon presentation in this syndrome.

During fasting, the animal metabolism is geared towards using lipids as the main source of energy and to spare glucose and protein. This explains that as long as their amino acid requirements are fulfilled, FHL cats will tolerate high levels of fat (30-60 % of the calories as fat) in their diets. Glucose intolerance was a common presentation in FHL cats before clinicians realized that prolonged fasting depresses pancreas responsiveness to carbohydrates. Cats should not be fed more than 25 to 35% of their calories as carbohydrates. Diets high in glucose or simple sugars, such as most human liquid diets should be avoided.

Cats with hepatic lipidosis are usually anorectic and tube feeding is required. Forced feeding (i.e.: spoon or syringe feeding cats) will not allow sufficient energy intake, stress the animal and contribute to food aversion. Nasogastric (5-8 French size), esophageal (10-12 French) feeding and gastrostomy (20 French) tubes have been used successfully. Small bore nasogastric tubes can be placed with local anesthesia but require the use of liquid formulas such as feline liquid diets. Some canned diets mixed with the same volume of water and blended will be liquid enough to pass through nasogastric tubes. Most blenderized cat food (can mixed with 1 volume of water and dry mixed with 3 volume of warm water) will pass through larger bore gastrostomy and oesophageal feeding tubes. After 1 or 2 weeks of stabilization at the hospital, tube feeding can be managed by most owners at home. In the author’s experience, although oesophageal and gastrostomy tubes are better tolerated, nasogastric tubes are well accepted, easy to place and to replace, and associated with minor complications, but they will require an Elizabethan collar. Oesophageal and gastrostomy tube placement do require full anesthesia.

Appetite stimulants (i.e.: diazepam, oxazepam, cyproheptadine) have not been found useful in the management of FHL cats. Moreover, liver dysfunction might compromise the metabolism of those agents.

Food should be introduced progressively over a 4 to 7 day period, the goal being to feed 60 to 80 kcal/kg/d (30 to 40 Kcal/lb/d). Common complications include epiphora (watery eyes with naso-gastric tubes), vomiting/diarrhea, tube removal, hypokalemia and hyperglycemia. Less common complications include hypophosphatemia, aspiration pneumonia and peritonitis. Cats should be carefully monitored for signs of infection (fever, tachycardia, abnormal breathing, abnormal auscultation). The epiphora will resolve after removal of the naso gastric tube. Vomiting can usually be controlled by giving metoclopamide parenterally (0.1-0.2 mg/lb or 0.2 - 0.4 mg/kg SQ) 10 to 15 min before the meal. Diarrhea often occurs with high carbohydrate human liquid diets or when the food is introduced too rapidly.

Elizabethan collars are highly recommended to minimize the risk of tube removal. Regular blood work is advised initially to monitor serum electrolytes, glucose and phosphorus. Hyperglycemia is common with high carbohydrate human liquid diet (> 40 % of calories from glucose see above). In case of hypokalemia and/or hypophosphatemia (serum P < 2.0 mg/dl, P < 0.65 mmol/L), potassium (5-10 mEq per os/cat/day with the meal) and/or phosphate (0.01-0.03 mmol potassium phosphate /kg/hr in fluids, monitor q 3-6 hrs and stop infusion when P > 2 mg/dl ) should be supplemented in the diet or given with the fluids. Vitamin K1 (1.5 mg /kg IM, 3 treatments at 12 hour intervals) might be helpful in cats with bleeding problems. Increased bleeding time linked to Vitamin K deficiency has been observed in 50 % of FHL cats.

L-carnitine (250-500 mg/cat) supplementation has been recommended in the management of FHL, especially in more severe cases but diets devoid of carnitine have been used successfully to control the disease.

B-vitamins (2 x the normal daily dosage given by the manufacturer), vitamin C (30 mg/kg), vitamin E (100-400 mg/cat), taurine (250 mg), zinc (7-8 mg elemental) supplementations have also been recommended on an empirical basis in cats with hepatic lipidosis. Controlled studies to substantiate the benefits of such supplementation above what is already in commercial cat food are not available.

Food aversion may be a complicating factor in cats with hepatic lipidosis. Cats that refuse to eat a diet that they associated with nausea may continue to avoid that diet even after full recovery. Exposing cats with hepatic lipidosis to different commercial diets before tube-feeding, might predispose them to develop an aversion to all those diets. This could explain why some lipidotic cats take much longer than others before resuming voluntary intake even though all laboratory parameters appear within normal limits. It is this author’s opinion that anorexia should be demonstrated with a minimum of diets and tube-feeding started immediately in cats with hepatic lipidosis. No food should be offered per mouth for the first 10 days of nutritional support. Cats expressing an interest to eat can then be presented small amounts of novel food until normal appetite resume.

Cats often look worse during the first few days of treatment than when first presented. Clinicians should not get discouraged too early. Tube feeding is the only treatment that will reverse hepatic lipidosis and those cats must be fed. Increasing the number of meals, continuous tube feeding using a peristaltic pump or total parental nutrition should be considered if the animal cannot keep the food down. A majority of cats with idiopathic hepatic lipidosis will show clinical and laboratory signs of improvement within a week. In the experience of the author, nearly all cats that survive the first week of treatment do recover completely. FHL complicated by other disease (renal disease, IBD, …) have a more guarded prognosis and require to also manage the primary disease.

REFERENCES available from author upon request