

Empirical therapy in liver disease

Without a definitive diagnosis, empirical therapy can be useful.



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Medical management of liver disease without a definitive diagnosis can be challenging. There are many cases in which a diagnosis is not reached, due to financial concerns or ambiguous diagnostic test results. In these instances, veterinarians may be called upon to provide empirical medical therapy for their patients. A multimodal approach is often taken, usually combining therapeutic diets, antioxidants, antibiotics, ursodeoxycholic acid and occasionally corticosteroids. While it is not ideal to treat liver disease empirically, these therapies can provide clinical benefits. In this article, a few of the commonly used empirical therapies are discussed.

Dietary modification

In Pets with an identified, specific type of hepatic disease, the goal of feeding is to provide sufficient nutrition while minimizing the harmful effects of protein metabolism, such as seizures. The ideal diet in specific hepatopathies, such as portosystemic shunts, is highly digestible; protein-

restricted while containing high-quality protein; with the majority of calories provided by nonprotein sources.¹ Examples of appropriate diets are ROYAL CANIN™ canine Hepatic LS 14 Formula, ROYAL CANIN feline Renal LP, and Hill's Prescription Diet® l/d.® With nonspecific hepatopathies as discussed in this article, recommend an optimal diet for the individual Pet—without a firm diagnosis, the focus of feeding these patients is to maintain a high-quality protein source, not protein-restricted. In cats with hepatic lipodosis, getting them to eat is more important than following strict guidelines regarding the content of the food.

Antioxidants

S-adenosyl-methionine (SAME) is a naturally occurring substance in most cells of the body. SAME replenishes depleted glutathione stores, scavenges free radicals and protects liver cells from injury caused by toxic bile acids in laboratory studies.² When the liver is damaged and depleted of natural SAME stores, it appears that supplementing SAME restores hepatic glutathione levels and improves hepatic

Table 1: Diagnostic evaluations for a patient with suspected liver disease

- Complete blood count
- Serum chemistry profile
- Electrolyte concentrations
- Urinalysis
- Fecal evaluation
- Bile acids
- Abdominocentesis and fluid analysis
- Coagulation tests
- Survey radiography
- Ultrasonography
- Scintigraphy
- Liver aspiration
- Bile culture
- Liver biopsy

function.² Cats may particularly benefit from supplementation with SAME, given their difficulty in synthesizing glutathione. SAME administration is indicated as an adjunctive treatment for many causes of hepatic disease, and it may improve liver function. It can be potentially beneficial for chronic hepatitis, hepatic lipidosis, triaditis and cholangiohepatitis and is also indicated for acetaminophen toxicity.³ The recommended dose of SAME is approximately 18 mg/kg administered orally per day, rounded to the closest tablet size, for both dogs and cats. The medication should be given on an empty stomach at least one hour before feeding. There are no known adverse effects, and drug interactions are theoretical.⁴ Length of treatment may vary and could be lifelong if the primary disease is never resolved.

Vitamin E has been found in experimental studies to have an antioxidant effect in protecting hepatocytes from toxic injury and cholestatic concentrations of bile acids.⁵

The recommended dose of vitamin E is 100 IU to 400 IU administered orally, once to twice daily for dogs and 30 IU administered orally, once daily for cats. Vitamin E is also potentially beneficial for chronic hepatitis/hepatic cirrhosis and copper-associated hepatopathy.⁵

Other therapies

Ursodiol (ursodeoxycholic acid) is a commercially available, natural bile acid. It has been shown to provide some benefit in liver disease because of its “thinning” effect on biliary secretions, theoretically making it easier for bile sludge to exit the gallbladder and bile ducts. Ursodiol has also been found to have anti-inflammatory, immunomodulatory and antifibrotic effects on the liver.⁶ The dose for Ursodiol is 15 mg/kg orally over 24 hours.⁶ Ursodiol is contraindicated in cases of extrahepatic biliary obstruction, as diagnosed by ultrasonography.⁷ Again, length of treatment may vary depending on the primary disease process, and could be lifelong.

Milk thistle has been used in many species as a hepatoprotectant against toxicosis, chronic and acute liver disease and cirrhosis. Many of its benefits have been extrapolated from human research. The biologically active ingredient in milk thistle is silymarin, and the mechanism of action is not completely understood. Silymarin has been recommended as an adjunctive therapy for nearly every form of chronic inflammatory or necrotizing liver disease in people. It has been shown to increase glutathione levels and to affect hepatocyte receptors for drug uptake.⁸ In dogs and cats, recommended doses of silymarin are 20 to 50 mg/kg/day orally.⁴ No known drug interactions or contraindications exist for silymarin’s use in dogs and cats.

Unfortunately, as with many nutraceutical products, significant quantitative and qualitative differences can exist between products. It is best to recommend products distributed specifically for use in veterinary patients by reputable companies.⁷

Antibiotics are a rational choice in therapy if a bacterial component to existing hepatic disease is suspected. The antibiotic selected should be broad-spectrum and able to achieve therapeutic concentrations within bile. Potentially hepatotoxic drugs should be avoided. Frequently prescribed initial choices for antibiotics include amoxicillin or amoxicillin-clavulanic acid, ampicillin and cephalixin or cefpodoxime. Metronidazole has a good anaerobic spectrum and is often used in conjunction with one of the other aforementioned antibi-

otics.⁹ Metronidazole should be given at a lower dose with severe hepatic disease (7.5 mg/kg orally twice daily)¹⁰ because it is metabolized by the liver.

Corticosteroids

Prednisone may be beneficial in liver disease patients, but should be used with caution when the type of disease is not known. In patients with chronic active hepatitis, it is used to reduce inflammation. Prednisone should not be used in primary copper storage diseases. If significant fibrosis is present, prednisone may be of little to no benefit.⁷

Conclusion

A definitive diagnosis of the cause of liver dysfunction is ideal, and provides the best

opportunity for treatment success. As previously mentioned, it can be difficult to treat Pets with liver disease without a definitive diagnosis. However, the unfortunate reality is that a definitive diagnosis is not always possible. Having empirical therapies in our arsenal that offer clinical improvement in these Pets is helpful and comforting to clients. 

References

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