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HOW I TREAT CHRONIC HEPATIC DISORDERS IN DOGS

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Chronic hepatic disorders in dogs

Etiology, clinical signs and diagnostic work-up of chronic hepatic disorders in dogs are reviewed in the lecture on canine chronic hepatic disorders.

Treatment of chronic hepatic disorders in the dog

Antibiotic treatment

Antibiotics are indicated in the treatment of hepatic encephalopathy, septic disease and prevention of bacteremia (1-4). In general, first choice antibiotic treatment is directed against most commonly encountered bacteria (*E.coli*) until results of bacterial culture are available.

<p>Septic disease</p> <ul style="list-style-type: none"> ▪ Antibiotic treatment (4-6 weeks): <ul style="list-style-type: none"> ○ <u>Leptospirosis: ampicillin or amoxicillin 22 mg/kg BID for 2 weeks, then doxycyclin 5 mg/kg BID for 2 weeks</u> ○ <u>Amoxicillin-clavulanate 20 mg/kg BID</u> ○ <u>Cephalexin 20-30 mg/kg BID</u> ○ <u>Enrofloxacin 5-10 mg/kg SID</u> <p>Hepatic encephalopathy</p> <ul style="list-style-type: none"> ▪ Reduction of intestinal bacterial ammonia production <ul style="list-style-type: none"> ○ <u>Metronidazole 7,5 mg/kg BID or TID</u> ○ <u>Neomycin 20 mg/kg TID</u> <p>Prevention of bacteremia</p> <ul style="list-style-type: none"> ▪ Reduction of bacterial translocation <ul style="list-style-type: none"> ○ <u>Cephalexin and metronidazole 10-15 mg/kg BID or TID</u>

Choleretic treatment

Choleretics may be used in non obstructive cholestatic disease in dogs, such as cholangitis and cholecystitis (2-4). Ursodeoxycholic acid enhances bile flow and efflux of toxic bile acids, has immunomodulatory and cytoprotective effects. In human medicine it is used for its anti-inflammatory and antioxidant properties, which may justify its use in the treatment of chronic canine hepatitis. It is contraindicated in extrahepatic bile duct obstruction. The recommended dosage is 10-15 mg/kg/day.

Immunomodulatory treatment

Corticosteroids are essential for the treatment of inflammatory non suppurative, non infectious and non septic chronic hepatitis (1-4). They have anti-inflammatory, but also anti-fibrotic and choleretic effects. Prednisolone is administered at an initial dosage of 0,5-2 mg/kg/day for 2 to 4 weeks, then slowly tapered down. Minimal treatment duration is about 3 to 6 months. In dogs corticosteroid-induced induction of hepatic enzymes makes a follow-up by measuring these enzymes difficult, even impossible. Only hepatic function tests (albumine, urea, bile acids, etc) are reliable tests during follow-up. Control liver biopsies 4 to 6 months after treatment initiation are the ideal mean of follow-up in chronic hepatitis. Alternative immunomodulators are azathioprine or cyclosporine, no studies have reported their effects in canine liver disease.

Nutrition

Hepatic diets should contain high quality protein poor in aromatic amino acids in moderately restricted quantities and rely on non-protein sources for energy (2,3). Protein should only be restricted as needed to control neurological signs.

Anticopper medication

D-penicillamine is indicated in chronic active hepatitis with copper overload identified on hepatic biopsies (2-4). The drug also has anti-inflammatory effects. Recommended dosage is 10-15 mg/kg BID with food. Infrequent side effects include mainly anorexia and vomiting. D-penicillamine also chelates zinc, combination of the two medications should be avoided. Once hepatic biopsies prove recovery from hepatitis, renewed copper accumulation may be prevented by administration of zinc salts.

Zinc salts are used for prevention or maintenance therapy after copper chelating treatment to avoid any renewed hepatic copper accumulation (2-4). Zinc induces production of metallothionein in the enterocytes. The protein binds copper and the complex sequestered within senescent enterocytes is eliminated in the feces. The dosage of elemental zinc administered one hour before each meal is 10 mg/kg BID with a maximum total dose of 100 mg/day. Zinc acetate is preferred over zinc gluconate. A follow-up of serum zinc concentrations is indicated (toxic serum concentration > 1000 µg/dL).

Antioxidants

Oxidative stress and cellular damage by free oxygen radicals happen in all forms of chronic hepatitis (2,4,5). Use of antioxidants reduces oxidative stress markers and cellular injury. .

S-adenyl-L-methionine is a glutathione precursor, potent hepatic antioxidant and its use has been proven in some forms of toxic liver disease (acetaminophen, etc). Recommended dosage is 18 mg/kg/day.

Silibinin (milk thistle) has been proven useful for prevention/recovery of certain toxics (amanita mushroom, etc). Therapeutic dosage is unknown, suggested doses range from 50-200 mg/day.

Vitamin E may also be used as antioxidant. The liposoluble vitamin is potentially malabsorbed when fat digestion is compromised in animals with hepatic disease. Recommended dosages range from 100-400 UI SID or BID..

Vitamines

Liposoluble vitamin absorption may be compromised and result in hypovitaminosis K potentially contributing to coagulopathy (2-4). Recommended dosage ranges from 0,5-1 mg/kg SC SID or BID.

Lactulose

Lactulose has multiple beneficial effects in the treatment of hepatic encephalopathy (2-4). Lactulose acidifies intestinal content. Ammonia is then present under its ionic form that is not absorbed and eliminated with the feces. Lactulose also acts as osmotic laxative, increasing thereby loss of ammonia and bacteria with the feces. Being a non protein energy source, it also reduces bacterial ammonia production. In acute hepatic encephalopathy, lactulose may be administered as enema: 3 parts of lactulose for 7 parts of warm water (20 ml/kg) into the colon, leave in place for 15-20 minutes, then remove. Initial oral doses range from 2,5-15 ml/dog BID or TID and should be adjusted according to feces consistency. The aim is softer, but still formed feces.

Diuretic treatment

In case that treatment of the underlying cause is not sufficient and the animal is uncomfortable with the ascites, diuretic treatment is indicated (2-4). Spironolactone is the diuretic of choice. Recommended dosage ranges from 0,5-2 mg/kg BID. Furosemide may be added in case of treatment resistance at an initial dose of 1 mg/kg. Follow-up of hydration status and potassium levels are important.

Antifibrotic treatment

Colchicine may be used in cases where fibrosis is detected on hepatic biopsies (2-4). No study has proven its clinical effect. Side effects are mainly gastro-intestinal. Recommended dosage is 0,03 mg/kg/day.

References

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