Managing hepatic encephalopathy

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SCOTT KILPATRICK and ANDREW J BROWN look at the lab tests that can help diagnosis of this condition before considering the role of nursing care

HEPATIC encephalopathy (HE) is a neurological condition that affects small animals and frequently requires intensive nurse management.

It is a complex neurophysiologic syndrome of the CNS that follows a critical loss of functional hepatic mass (65 per cent to 70 per cent) or extensive hepatofugal circulation (portosystemic shunt, including canine congenital portosystemic shunt; cPPS). Clinical signs vary between species. Dogs can exhibit depression, stupor, coma, blindness and seizures while cats will display aggression, seizures, blindness, ataxia, hypersalivation and discolouration of the iris (copper-coloured).

Other clinical signs include gastrointestinal (GI) signs, poor growth (in cPSS), polyuria/ polydipsia, lower urinary tract signs due to formation of urate calculi, renomegaly and, occasionally, coagulopathy.

The pathogenesis of HE in dogs is not fully understood. Hyperammonaemia is considered the most important mediator since ammonia has been demonstrated to be neurotoxic and plasma concentrations are frequently increased in dogs with cPSS. However, the importance of ammonia in dogs is unclear since few studies have examined whether ammonia concentrations correlate to the presence and/or severity of HE in dogs. In addition, hyperammonaemia alone, which can occur in dogs with urea cycle enzyme deficiencies, does not typically result in HE.

Increased plasma concentrations of endogenous benzodiazepines have been demonstrated in dogs with cPSS that have been postulated to be important in causing HE. Other studies have indicated a role for hypercortisolism, and altered tryptophan metabolism in development of HE. Altered manganese metabolism has also been implicated as dogs with a cPSS have increased whole blood manganese concentrations.

Diagnosis

Diagnosis is based on history and physical examination, but is greatly assisted by laboratory analysis. Elevated fasting bile acids suggest hepatic dysfunction. Measurement of a postprandial sample significantly increases sensitivity for the detection of the disease.

Bile acid stimulation test

After a fatty meal the gallbladder contracts, releasing bile acids into the duodenum to allow the emulsification and absorption of fats. In normal animals, hepatic clearance of the bile acids is very efficient, with only low postprandial levels in blood. Significant hepatocellular dysfunction or shunting of blood away from the liver reduces hepatic functional mass giving rise to high levels of bile acid.

• Fast animal for 12 hours.

• Take 1ml to 2ml of blood in plain/gel tube.

• Administer fatty meal or vegetable oil.

• Take a second blood sample two hours after eating.

• Label tubes with name of patient and time of sample before submitting for analysis.

Fasting ammonia

Fasted blood ammonia concentration is a relatively insensitive measure of hepatic function, and only meaningful if increased. Plasma should be harvested on ice and ammonia assayed within 30 minutes, as storage increases the ammonia content of the blood.

Serum biochemistry and haematology

Haematology and biochemistry may show other changes consistent with hepatic dysfunction. These include microcytosis, anaemia, hypoalbuminaemia, low urea, hypocholesterolaemia, hypoglycaemia and possibly low liver enzymes.

Assessment of haemostasis

Because coagulation factors are synthesized in the liver, severe hepatic dysfunction can result in prolonged clotting times. Whole blood should be collected in sodium citrate tubes (filling with the precise volume of blood) and clotting times measured before any invasive procedures.

Diagnostic imaging

Abdominal ultrasound can be useful in the investigation of HE as it can give a more useful indication of the internal structure of the liver and can identify focal or diffuse lesions. Patients with portosystemic shunts may have microhepatica. Occasionally, large shunts or arteriovenous fistulae may be detected with ultrasonography. Computed tomography angiography is the best way of identifying a PSS and determining the anatomical location of the shunt.

Nursing care

Patients with severe HE frequently require intensive monitoring and nursing care. Neurologic signs, systemic blood pressure and routine laboratory parameters including blood glucose must be monitored frequently and closely. Urine output and bladder size should be evaluated since these animals are prone to ammonium urate stone formation in the urinary tract. Patients with stable HE can often be managed at home, but require repeated recheck examinations and laboratory tests.

Hypokalaemia, hypoglycaemia, azotaemia, constipation, alkalaemia, hyponatraemia and GI bleeding should all be avoided as these conditions are precipitating factors for HE. Avoid using drugs (if possible) that are metabolised by the liver (such as cimetidine, chloramphenicol, barbiturates, ketoconazole) and use highly protein-bound drugs cautiously. Fluids containing lactate should be used with caution as lactate is metabolised in the liver. Consideration should be given to choice of anaesthetic and sedative as the impaired hepatic function may result in a long duration of action. Stored red blood cells also have increased levels of ammonia and should be used cautiously. Fresh blood products may be preferable in animals that require transfusion therapy.

A number of concurrent factors may precipitate the clinical signs of HE, including excessive protein intake, infection, medications, metabolic derangements, renal failure and dehydration. Management of HE should be aimed at reducing these exacerbating factors.

Decrease protein intake

Protein intake is restricted to decrease dietary sources of ammonia, amines, aromatic amino acids, and short-chain fatty acids. Stable animals with HE should begin a diet that is moderately restricted in protein (14 per cent to 17 per cent protein dry matter basis). The diet should consist of highly digestible products. The protein source should high quality, with high levels of branched-chain

amino acids compared to aromatic amino acids. Soy-based protein may be a better source than meatbased protein. A highly digestible carbohydrate source is the main caloric source in the diet. The diet should also have sufficient levels of vitamins and minerals for maintenance. Many veterinary prescription diets are specifically formulated for liver disease.

Decrease ureaseproducing colonic bacteria

Enemas can be used to decrease the number of urease-producing bacteria in the colon and can remove toxic by-products of bacterial metabolism. Warm water enemas may be used. Enemas are most commonly used during an HE crisis and are repeated until no faecal material is present in the evacuated fluid. Lactulose (1,4-betagalactosidofructose) can also be added to the enema solution to lower the blood ammonia levels. Lactulose is hydrolysed by colonic bacteria to lactic, acetic, and formic acids, which cause a marked reduction in colonic pH. This leads to ionic trapping, where ammonia (NH3) accepts a proton to form ammonium (NH4+), which is a much less diffusible molecule. Therefore, the ammonium ions are trapped in the colon and are excreted with the faeces. The large numbers of unabsorbed solute following metabolism also induce osmotic diarrhoea.

In addition, lactulose inhibits ammonia production by colonic bacteria. Only 20 per cent of people with HE show improvement following a warm water enema, but 80 per cent to 90 per cent show benefit from a lactulose enema. The lactulose should be diluted with warm water (three parts lactulose to seven parts warm water), dosed at 1ml/kg to 10 ml/kg, and retained in the colon for 20 to 30 minutes. Neurologic improvement may be seen within a two hour period.

Oral administration of lactulose can also lower colonic pH and is recommended when the patient is more stable. Dosage varies from 2.5ml to 25ml PO q 8 hours. The dosage should result in the passage of two or three soft stools daily.

Decrease ureaseproducing GI bacteria via oral antibiotics

Oral antibiotics can be administered (as long as the patient is not comatose) to decrease the numbers of urease-producing bacteria in the GI tract. Antibiotics also can decrease bacterial deamination of amino acid and reduce the production of aromatic amino acids, mercaptans, and false neurotransmitters by bacteria. Metronidazole, amoxicillin and neomycin have all been used successfully.

• Metronidazole:

7.5mg/kg PO q 12 hours.

• Amoxicillin: 12.5mg/kg to 25mg/kg PO q 8-12 hours.

• Neomycin: 10mg/kg to 22mg/kg PO q 12 hours.

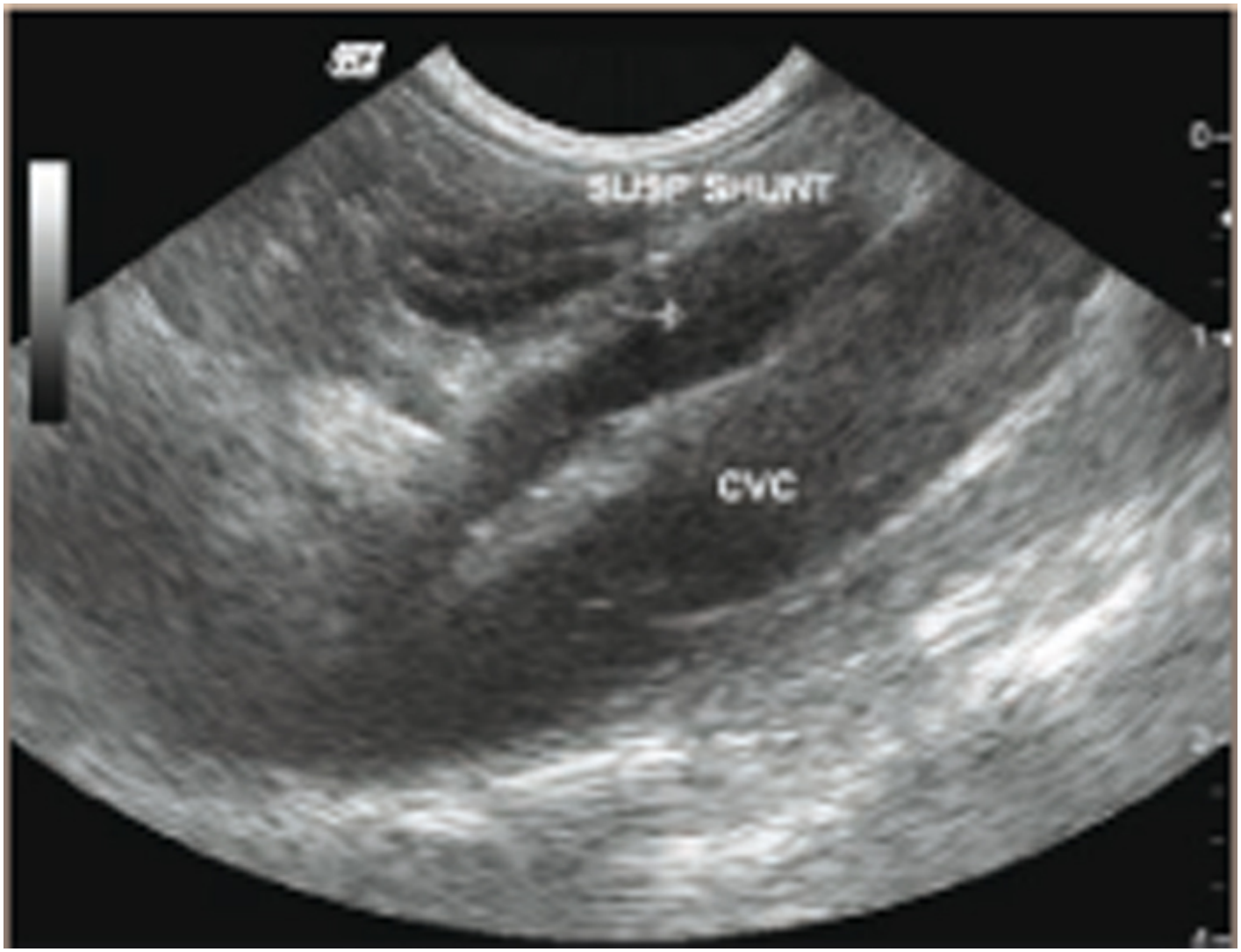
Seizure control

Patients with severe HE may develop seizures. Potassium bromide at a dose of 40mg/ kg to 60mg/kg PO, once daily, or gabapentin 20mg/kg to 60mg/kg/day, divided tid, may aid in controlling seizures. Sodium bromide intravenously can rapidly increase serum levels. Phenobarbital should be used with caution since it is protein bound and metabolised by the liver. However, 3mg/kg to 5mg/kg bid may effectively control seizures.

The apparent role of GABA/ benzodiazepine receptors/ chloride ionophore complex in the pathogenesis of HE has led to experimental studies with flumazenil, a benzodiazepine antagonist. Results are conflicting and this therapy is not routinely recommended at this time.

Prognosis

Prognosis for patients with HE is fair to good with mild HE, but guarded to poor with more severe clinical signs. Prognosis improves if the underlying cause of HE can be successfully treated. Poor prognostic indicators include a prothrombin time value more than 100 seconds, certain underlying causes (viral infection, idiosyncratic drug reaction, aflatoxin toxicosis), a very young age and a very old age.



Ultrasound can be useful in the diagnosis of portosystemic shunts, which can be one of the causes of hepatic encephalopathy. The arrow in the image is highlighting the abnormal vessel. CVC indicates the caudal vena cava.