Drug monitoring for patients receiving anticonvulsants

Phenobarbitone

Regular monitoring of patients receiving phenobarbitone is advised, typically starting two weeks after initiating treatment, which is when steady state concentrations in the serum are likely to be achieved. Repeat monitoring at 6 weeks, at which stage enhanced clearance due to auto-induction of microsomal enzymes may have impacted serum concentrations , and then ongoing 6 monthly is recommended. Any dosage alteration should be accompanied by measurement of blood phenobarbitone concentrations after 2 weeks.
There is usually little difference between peak and trough levels, however, trough levels (before the next dose) are usually best to assess the lowest concentration during the day. Measurement of both peak (4-6 hours after dosing) and trough samples may be useful in patients with breakthrough seizures, and peak samples are preferred in patients with signs of toxicity. As a general rule, consistency in sample timing is advantageous for the purpose of comparison.

Adverse effects associated with phenobarbitone are more commonly seen with higher serum concentrations. Increases in ALP and ALT are relatively common in the dog. This may occur as soon as two weeks after initiating treatment and is usually not associated with clinical disease. Hepatotoxicity resulting in decreased albumin and increases in bilirubin and bile acids is less commonly encountered, but is potentially life-threatening. If routine monitoring profiles document changes in serum bilirubin and albumin, or there is clinical suspicion of hepatic disease, serum bile acid determination is strongly advised.

Haematological abnormalities develop in small numbers of patients (approximately 4% in one study). This may include immune mediated haemolytic anaemia, thrombocytopaenia, neutropaenia or a combination. Typically this occurs in the first 6 months of treatment and is reversible with appropriate treatment and withdrawal of phenobarbitone.

Low Free and Total T4 are common in dogs receiving phenobarbitone, but are not associated with clinical hypothyroidism.

Potassium bromide

Bromide has a half life of approximately 21 days in dogs and 14 days in cats, although there is variability between individuals, linked to both bioavailability and renal clearance of the drug. High chloride intake may affect renal excretion and lower serum concentrations. Renal disease may also impact clearance of the drug.

Steady state concentrations are expected to be reached after approximately 6-12 weeks, and monitoring is advised at this stage, and then annually unless there is a change in dosage rate

or clinical signs. Bromide is not subject to hepatic metabolism and may be prescribed in patients with hepatic disease.

Patients receiving bromide have an increased risk of pancreatitis. Annual monitoring of bromide concentration may be accompanied by assessment of renal and pancreatic parameters.

Levitracetum

Levitracetum has a relatively short half-life in dogs and cats compared to other anti-convulsants, and minimal accumulation occurs. Monitoring may occur within days of initiating treatment of altering the dosage regimen. Recommendations regarding monitoring of levitracetum are currently vague. Where there is poor control of seizures, both peak (2 hours after dosing) and trough (approximately 8 hours post dose) is recommended.

Side effects of levitracetum are directly related to its pharmacological action and idiosyncratic or cumulative effects are not documented.

In vitro metabolism by plasma enzymes may occur which will affect the measured concentration and serum samples are thus essential.

References:

2015 ACVIM Small animal consensus statement om seizure management in dogs. JVIM 2016 Mar-Apr; 30(2);477-490
Monitoring recommendations Clinical Pharmacology Laboratory Auburn University