Therapeutics

DIGOXIN MONITORING

Species: Dog, Cat

Specimen: Serum

Container: Plain (red top) or gel tube

Collection protocol: 8 hours post dosing; fasted sample.

Special handling/shipping requirements: Standard

General information:

Indications for digoxin therapy include the treatment of heart failure, atrial fibrillation and supraventricular tachycardia. In recent years, the first line use of digoxin for the treatment of heart failure in dogs and cats has reduced significantly, due to the use of alternative drugs such as pimobendin and ACE inhibitors. It also has a narrow therapeutic window, particularly in cats who are sensitive to toxic concentrations.

Currently, the principal use of digoxin is for the management of dogs that have atrial fibrillation and concurrent heart failure due to mitral valve disease (MMVD) and dilated cardiomyopathy. In dogs with Stage C MMVD, on digoxin at 0.0025-0.005 mg/kg PO q12 to control atrial fibrillation, a steady state post-pill plasma concentration at 8 hours of 1.03-1.92 nmol/L (0.8-1.5 ng/mL) is recommended.

Not indicated in patients with pericardial disease, hypertrophic cardiomyopathy with outflow tract obstruction, or restrictive myocardial disease, unless accompanied by myocardial failure or supraventricular tachycardia.

Monitoring:

At least 6 days after initiation of therapy to allow development of a steady state.

Ongoing monitoring of therapy includes assessment of renal function, electrolytes and calcium every 2 to 3 months, after any changes in therapy or changes in animal's clinical condition.

Reference(s):

Keene BW et al; ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *Journal of Veterinary Internal Medicine* 33:1-14, 2019.

Plumb DC. In *Veterinary Drug Handbook*. 8th edtn (pocket). Pp439. Wiley-Blackwell, Ames, Iowa, USA, 2015.

Tilley LP et al. In *Manual of Canine and Feline Cardiology*, 4th edition. Pp305. Saunders Elsevier, St. Louis Missouri, USA. 2008

PHENOBARBITAL / PHENOBARBITONE THERAPY MONITORING

Species: Dog, cat

Specimen: Serum

Container: Plain (red top) tube (gel tube can interfere with result)

Collection protocol: Fasted overnight. Trough sample preferred, within 1 hour of next scheduled dose. Peak is 4-8 hours post dosing.

Special handling/shipping requirements: Standard

General information: Commonly used and well-tolerated anti-epileptic drug used for initial and long-term management of seizures in dogs and cats.

Monitoring:

1. At the first steady state concentration point of 2 weeks, then at the steady state clearance time point of 6 weeks after initiating therapy and six-monthly after that.
2. Fasted trough samples taken first thing in the morning just prior to dosing are recommended to optimise consistency when comparing to published information, to avoid diurnal variation and dietary induced fluctuations in absorption.
3. Assess any time there are two or more seizures between scheduled monitoring.
4. Assess 2 weeks after any dosage adjustment.
5. Six-monthly monitoring should include routine haematology, hepatic enzymes, and albumin, as phenobarbital usage may be associated with hepatotoxicity and blood dyscrasias.

Interpretation:

Dogs: effective therapeutic range of 65-150 µmol/L

Cats: effective therapeutic range of 65-194 µmol/L

Two idiosyncratic reactions to be aware of are an acute hepatotoxicity, resulting in a rapid and severe increase in ALT compared to ALP; and an idiosyncratic immune-mediated anaemia, neutropenia, thrombocytopenia or a combination of these, usually within the first 6 months of treatment.

Long term treatment can result in development of PU/PD, elevated ALP concentrations and more seriously, development of drug-induced hepatotoxicity. Hepatotoxicity is considered more to occur when phenobarbital concentrations are >150 µmol/L. A bile acid stimulation test may be useful to detect altered liver function.

If ALP elevations are high and Cushing's needs to be ruled out, then ACTH stimulation testing and low dose dexamethasone suppression testing can be done as these tests are not affected by phenobarbital dosing.

T4 concentrations may be suppressed in dogs on phenobarbital, so interpret low T4 concentrations with caution.

Reference:

Podell M et al. 2015 ACVIM Small animal consensus statement on seizure management in dogs. *Journal of Veterinary Internal Medicine* 30:477-490, 2016.

Finnerty KE et al. Evaluation of therapeutic phenobarbital concentrations and application of a classification system for seizures in cats: 30 cases (2004-2013). *Journal of American Veterinary Medical Association* 244:195-199, 2014.

POTASSIUM BROMIDE (KBR) MONITORING

Species: Dog

Specimen: Serum

Container: Plain (red top) or gel tube

Collection protocol: Due to long elimination half-life, samples can be collected at any time >2 hours after dosing to avoid any peak effect variability.

Special handling/shipping requirements: Standard

General information about the disease:

Used as an anti-epileptic drug commonly in conjunction with phenobarbitone (PB) or as monotherapy in dogs with hepatic dysfunction, in large-breed dogs and working dogs in which side effects from PB are unacceptable.

Signs of bromide toxicity include: stupor or coma, blindness, ataxia, tetraparesis, dysphagia, and megaoesophagus. When being used with phenobarbital, sedation and weakness may become evident. Clearance may be decreased in dogs with impaired renal function.

Monitoring:

1. At 1 and 3 months after therapy has been initiated then yearly after that.
2. A month after a change of dose.
3. If there are more than 3 seizures before the next scheduled assessment or if signs of toxicity are suspected.
4. If the dog is on PB therapy when KBr is added to the therapeutic regime then serum PB concentration should also be measured 4-6 weeks after KBr introduction. KBr seems to enhance the excretion or metabolism of PB and frequently the serum PB concentration drops after KBr is introduced.

Interpretation:

Monotherapy**:** 100-300 mg/dL

Combination with phenobarbital: 80-250 mg/dL

Reference(s):

Podell M et al. 2015 ACVIM Small animal consensus statement on seizure management in dogs. *Journal of Veterinary Internal Medicine* 30:477-490, 2016

Taylor SM. Neuromuscular Disorders. In Nelson RW and Couto CG, (Eds). *Small Animal Internal Medicine* 5th edition. Pp1024. Elsevier Mosby, St. Louis Missouri, USA, 2014