Newer Anti-epileptic Drugs in the Veterinary Patient

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There are several anti-epiletic drugs (AED) that are being used with more frequency in our veterinary patients with recurrent seizures. Many of these drugs have been used in human epilepsy for many years and were developed for alternative mechanisms of action as well as a higher safety profile. These newer anticonvulsants can be used both as add on drugs as well as monotherapy. Generally, it is not recommended to add a second AED until a first line drug is given at an adequate dose and frequency with an appropriate blood level and fails to control the severity and frequency of seizures to an acceptable level. Despite using these new AEDs with more frequency, there is still very limited information on the efficacy of these drugs in the treatment of epilepsy in the veterinary patient.

Levetiracetam (Keppra) is a novel AED and the mechanism of action is not completely understood. Pharmacologic testing has been performed on dogs with very little side effects appreciated, with sedation being the most common side effect at high dosages. This drug has a short half-life of approximately 3-4 hours in the dog and therefore should be given three times daily in most cases.[1] Metabolism is almost entirely renal, however a recent pharmacokinetic study suggests that metabolism of levetiracetam is significantly altered with concurrent phenobarbital administration and therefore dosage adjustments (increased) may be necessary.[2]

The initial dosage is 20 mg/kg orally three times daily. Levetiracetam can be used in cats at the same dosage. There is also an extended release formulation (Keppra XR) that has recently been approved by the FDA in humans and is administered only once daily. There is currently no veterinary literature on the extended release formulation however this may show promise for use in the future.

Zonisamide is a sulfonamide-based AED and also has an incompletely understood mechanism of action. Suspected mechanisms of action include enhancement of GABA by chloride channel binding as well as blockage of T-type calcium and voltage gated sodium channels. It is metabolized primarily by the liver and has a half-life of approximately 15 hours in the dog. Zonisamide is generally well tolerated in dogs but does have several possible side effects including sedation, ataxia and vomiting. In addition, because zonisamide is a sulfa drug, hypothyroidism and KCS are possible side effects. There is also a recent case report of idiosyncratic hepatic necrosis in a dog receiving zonisamide.

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[1] Moore SA, et al. Levetiracetam pharmacokinetics in healthy dogs following oral administration of single and multiple doses. Am J Vet Res. 2010 Mar;71(3):337-41.
[2] Moore SA, et al. The pharmocokinetics of levetiracetam in healthy dogs concurrently receiving phenobarbital. J Vet Pharmacol Ther. 2011 Feb; 34(1):31-4.

If zonisamide is given as monotherapy, then the initial dosage is 5 mg/kg orally twice daily. If it is used in addition to phenobarbital, the dosage is higher, at 10 mg/kg orally twice daily, as phenobarbital increases hepatic metabolism. Zonisamide has been used to a smaller degree in cats but seems to have more side effects than in dogs.

Gabapentin is a drug that is used extensively for neuropathic pain, but also has anticonvulsant properties with the main mechanism of action likely through inhibition of voltage-gated calcium channels. It is well tolerated in the dog with sedation being the main side effect. Gabapentin is mostly excreted by the kidneys, but does undergo some hepatic metabolism (30-40%) in the dog.[3] The short elimination half-life, about 3-4 hours in the dog, necessitates three-time daily dosing. The initial dosage is 10 mg/kg every 8 hours in the dog. Gabapentin can also be used in the cats but likely needs to be given at a lower starting dose of 5-10 mg/kg every 8 to 12 hours.

Pregabalin is essentially the "next generation" of gabapentin. It has a greater affinity for the voltage-gated calcium channels than gabapentin and apparently is more effective in people than gabapentin. It appears to be fairly well tolerated in the dog with sedation and ataxia being the most common side effects. Expense of this drug may limit the use, especially in large dogs. Current suggestion for dosage is 2-4 mg/kg every 8-12 hours.[4,5] Currently there is no information available about its use in cats.

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[3] Dewey, CW. A Practical Guide to Canine and Feline Neurology 2nd ed. Ames: Wiley-Blackwell, 2008: 247.

[4] Dewey CW, et al. Pregabalin as an adjunct to Phenobarbital, potassium bromide, or a combination of phenobarbital and potassium bromide for treatment of dogs with suspected idiopathic epilepsy. J Am Vet Med Assoc. 2009 Dec 15;235(12):1442-9

[5] Salazar V, et al. Pharmacokinetics of single-dose oral pregabalin administration in normal dogs. Vet Anaesth Analg. 2009 Nov;36(6):574-80.