Antiseizure Medications for Cats

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Background & Pathophysiology

Seizures affect approximately 1% to 2% of cats (author experience). Recurrent seizures (ie, epilepsy) can be classified as structural (ie, caused by an identifiable brain disease such as an infection or tumor) or unknown/idiopathic. Reactive seizures can also be caused by extracranial triggers such as metabolic diseases and toxicities; these seizures are not considered types of epilepsy. In cats, extracranial causes of seizures are not uncommon, and structural epilepsy is more common than idiopathic epilepsy.[1-4] Therefore, blood work, along with a diagnostic investigation to look for a potentially treatable underlying cause, should be performed on any cat presented with seizures. In addition to treating the underlying cause, maintenance antiseizure medications (eg, phenobarbital, zonisamide, levetiracetam; see ***Table***, next page) are warranted in many epileptic cats.

Phenobarbital

Phenobarbital is the most commonly recommended anticonvulsant drug to control epilepsy in cats. It is inexpensive, has an excellent pharmacokinetic profile, and does not appear to cause hepatic enzyme induction or have the same hepatotoxic potential in cats as it does in dogs.[3,5,6] Anticipated adverse effects are usually mild and transient and consist of increased appetite, thirst, sedation, and ataxia. Generalized lymphadenopathy that resolves on withdrawal of the drug has also been reported in a cat receiving phenobarbital.[7] Although q24h dosing

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may be adequate in some cats, q12h dosing is often recommended to ensure a steady serum level.[6,8]

The established therapeutic range of serum phenobarbital levels for dogs (15-45 µg/mL) appears to apply to cats as well.[2] In general, about 40% to 50% of cats become seizure free on phenobarbital, and an additional 30% to 60% are considered well controlled.[3,8]

Because it is difficult for many owners to administer oral medications, an alternative route of administration may be desirable. A recent study provided evidence that therapeutic serum levels of phenobarbital can be achieved via transdermal administration.[9] Two different bases (pluronic lecithin organogel and Lipoderm ActiveMax; pccarx.com) were used, and serum levels between 15 and 26 µg/mL were achieved by administering each at a dose of 9 mg/kg q12h. However, serum levels varied significantly between the different vehicle formulations at the same dosage.[9]

As a general note, transdermal drug absorption depends on the molecule size, chemical nature, and dosage; therefore, not all medications can be absorbed through the skin nor are all medications safe to administer transdermally.[10] Antiseizure medications that have not been shown to be absorbed transdermally should not be prescribed for this route. Serum levels should be monitored at least every 6 months in cats treated with transdermal phenobarbital to ensure safe and effective

TABLE

MEDICATIONS TO TREAT SEIZURES IN CATS

Medication	Oral Starting Dose & Frequency	Time to Steady State	Parenteral Formulation Available?	Adverse Effects	Efficacy in Cats
Phenobarbital[3,5,6,8]	1.5-2.5 mg/kg q12h	2 weeks	Yes	Polyphagia, polydipsia, sedation, ataxia, lymphadenopathy	>70% of cats well controlled or seizure free
Zonisamide[12]	5-10 mg/kg q24h	1 week	No	Vomiting, diarrhea, anorexia, sedation, ataxia	Unknown
Levetiracetam[10,21]	20 mg/kg q8h	1 day	Yes	Inappetence, lethargy, hypersalivation	Improved seizure control in 7/10 cats poorly controlled on phenobarbital alone; improved seizure control in 100% of cats with audiogenic reflex myoclonic seizures
Gabapentin*	5-10 mg/kg q8-12h	Unknown	No	Sedation, ataxia	Unknown
Pregabalin*	1-2 mg/kg q12h	Unknown	No	Sedation, ataxia	Unknown
Diazepam	Not recommended for oral use in cats because of potential for fatal hepatotoxicity[25]				
Potassium bromide	Not recommended for use in cats because of potential for fatal pneumonitis[26]				

*Information is anecdotal.

absorption, and cats should be monitored for dermatologic reactions on the ear pinnae.[9]

Zonisamide

Zonisamide has shown promise as an antiseizure medication in dogs and in cats with experimentally induced seizures; however, no studies have investigated its efficacy in a clinical population of epileptic cats.[11] One major advantage of zonisamide in cats is its long half-life, which allows q24h dosing.[12] In a pharmacokinetic study in normal cats, adverse effects appeared dose related (seen at 20 mg/kg q24h) and consisted primarily of GI signs, depression, and ataxia.[12] Several reports have shown serious adverse effects, including hepatotoxicity, in dogs receiving zonisamide, possibly because zonisamide is a sulfonamide derivative.[13-15] There are no similar reports in cats, although clinicians should be aware of the possibility of sulfonamide-related adverse effects.[16]

Levetiracetam

Levetiracetam has a novel mechanism of action and may also be neuroprotective.[17,18] In cats, it has a short half-life (≈3 hours), which necessitates q8h administration,[18] which may be a drawback for many owners. An extended-release tablet exists but is not available in a tablet size appropriate for patients that weigh less than 35 pounds and cannot be split.[19]

Recently, the pharmacokinetics of single-dose administration of 500 mg extended release levetiracetam in cats were investigated. The results suggested that q24h dosing of this formulation may be possible in many cats.[20] No adverse effects were observed in any of the 7 cats.

Levetiracetam has an excellent safety profile, and there are no reports of serious adverse effects associated with its use in veterinary patients. Reported adverse effects in cats are mild and can include inappetence, lethargy, and transient hypersalivation.[18,21]

One study evaluated levetiracetam as an add-on therapy in 10 cats with epilepsy that were poorly managed with phenobarbital; 7 cats experienced more than 50% reduction in seizure frequency during the 3-month follow-up period.[21] In a recent randomized clinical trial, levetiracetam was found to be more effective than phenobarbital in controlling a specific type of epilepsy recently described in geriatric cats.[22] These cats suffer from seizures triggered by auditory stimuli that usually start with myoclonic jerks but may progress to generalized tonic-clonic seizures.[23] Of the newer generation of antiseizure medications, levetiracetam has the best side effect profile and is the only drug with documented efficacy in cats.

Other Antiseizure Medications

Gabapentin and pregabalin are similar medications used in dogs to treat neuropathic pain and, less commonly, seizures. Neither the pharmacokinetics nor the antiseizure efficacy of these medications have been investigated in cats, although there are anecdotal reports of their use for seizure management in this species.[24] Use of gabapentin as a sedative in fractious cats and for analgesia in cats with musculoskeletal pain has been reported.[25,26]

Use of potassium bromide and oral diazepam is not recommended in cats, as these drugs have been associated with potentially fatal adverse allergic pneumonitis and hepatitis, respectively.[27,28]

Imepitoin was recently approved in Europe to treat dogs with epilepsy. Its efficacy in dogs was comparable to that of phenobarbital in a large randomized blinded study, and its adverse effects appeared to be more tolerable than those of phenobarbital.[29] This drug is not available in the United States, and there is no information available regarding its safety or efficacy in cats.

See next page for references.

References

1. Schriefl S, Steinberg TA, Matiasek K, Ossig A, Fenske N, Fischer A. Etiologic classification of seizures, signalment, clinical signs, and outcome in cats with seizure disorders: 91 cases (2000-2004). *J Am Vet Med Assoc*. 2008;233(10):1591-1597.
2. Moore SA. Seizures and epilepsy in cats. *Vet Med Res Rep*. 2014;5:41-47.
3. Finnerty KE, Barnes-Heller HB, Mercier MN, Giovanella CJ, Lau VW, Rylander H. Evaluation of therapeutic phenobarbital concentrations and applications of a classification system for seizures in cats: 30 cases (2004-2013). *J Am Vet Med Assoc*. 2014;244(2):195-199.
4. Bailey KS, Dewey CW. The seizuring cat: diagnostic work-up and therapy. *J Feline Med Surg*. 2009;11(5):385-394.
5. Cochrane SM, Black WD, Parent JM, Allen DG, Lumsden JH. Pharmacokinetics of phenobarbital in the cat following intravenous and oral administration. *Can J Vet Res*. 1990;54(1):132-138.
6. Cochrane, SM, Parent JM, Black WD, Allen DG, Lumsden JH. Pharmacokinetics of phenobarbital in the cat following multiple oral administration. *Can J Vet Res*. 1990;54(3):309-312.
7. Baho MJ, Hostutler R, Fenner W, Corn S. Suspected phenobarbital-induced pseudolymphoma in a cat. *J Am Vet Med Assoc*. 2011;238(3):353-355.
8. Pakozdy, A, Sarchahi AA, Leschnik M, Tichy AG, Halasz P, Thalhammer JG. Treatment and long-term follow-up of cats with suspected primary epilepsy. *J Feline Med Surg*. 2013;15(4):267-273.
9. Delamaide Gasper JA, Barnes Heller HL, Robertson M, Trepanier LA. Therapeutic serum phenobarbital concentrations obtained using chronic transdermal administration of phenobarbital in healthy cats. *J Feline Med Surg*. 2015;17(4):359-363.
10. Eichstadt LR, Davidson GS. To compound or not to compound: a veterinary transdermal discussion. *Int J Pharm Compd*. 2014;18(5):366-369.
11. Chung JY, Hwang CY, Chae JS, et al. Zonisamide monotherapy for idiopathic epilepsy in dogs. *N Z Vet J*. 2012;60(6):357-359.
12. Hasegawa D, Kobayashi M, Kuwabara T, Ohmura T, Fujita M, Orima H. Pharmacokinetics and toxicity of zonisamide in cats. *J Feline Med Surg*. 2008;10(4):418-421.
13. Miller ML, Center SA, Randolph JF, Lepherd ML, Cautela MA, Dewey CW. Apparent acute idiosyncratic hepatic necrosis associated with zonisamide administration in a dog. *J Vet Intern Med*. 2011;25(5):1156-1160.
14. Schwartz M, Muñana KR, Olby NJ. Possible drug-induced hepatopathy in a dog receiving zonisamide monotherapy for treatment of cryptogenic epilepsy. *J Vet Med Sci*. 2011;73(11):1505-1508.
15. Cook AK, Allen AK, Espinosa D, Barr J. Renal tubular acidosis associated with zonisamide therapy in a dog. *J Vet Intern Med*. 2011;25(6):1454-1457.
16. Noli C, Koeman JP, Willemse T. A retrospective evaluation of adverse reactions to trimethoprim-sulphonamide combinations in dogs and cats. *Vet Q*. 1995;17(4):123-128.
17. Lyseng-Williamson KA. Spotlight on levetiracetam in epilepsy. *CNS Drugs*. 2011;25(10):901-905.
18. Carnes MB, Axlund TW, Boothe DM. Pharmacokinetics of levetiracetam after oral and intravenous administration of a single dose to clinically normal cats. *Am J Vet Res*. 2011;72(9):1247-1252.
19. Beasley MJ, Boothe DM. Disposition of extended release levetiracetam in normal healthy dogs after single oral dosing. *J Vet Intern Med*. 2015;29(5):1348-1353.
20. Barnard LR, Barnes Heller HL, Boothe DM. Pharmacokinetic analysis of single dose extended release levetiracetam per os in healthy cats. *J Vet Intern Med*. 2017;31(4):1225-1361.
21. Bailey KS, Dewey CW, Boothe DM, Barone G, Kortz GD. Levetiracetam as an adjunct to phenobarbital treatment in cats with suspected idiopathic epilepsy. *J Am Vet Med Assoc*. 2008;232(6):867-872.
22. Lowrie M, Thomson S, Bessant C, Sparkes A, Harvey RJ, Garosi L. Levetiracetam in the management of feline audiogenic reflex seizures: a randomised, controlled, open-label study. *J Feline Med Surg*. 2017;19(2):200-206.
23. Lowrie M, Bessant C, Harvey RJ, Sparkes A, Garosi L. Audiogenic reflex seizures in cats. *J Feline Med Surg*. 2016;18(4):328-336.
24. Muñana KR. Update: seizure management in small animal practice. *Vet Clin North Am Small Anim Pract*. 2013;43(5):1127-1147.
25. Pankratz KE, Ferris KK, Griffith EH, Sherman BL. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined community cats: a double-blind, placebo-controlled field trial. *J Feline Med Surg*. 2017. doi: 10.1177/1098612X17719399
26. Lorenz ND, Comerford EJ, Iff I. Long-term use of gabapentin for musculoskeletal disease and trauma in three cats. *J Feline Med Surg*. 2013; 15(6):507-512.
27. Center SA, Elston TH, Rowland PH, et al. Fulminant hepatic failure associated with oral administration of diazepam in 11 cats. *J Am Vet Med Assoc*. 1996;209(3):618-625.
28. Boothe DM, George KL, Couch P. Disposition and clinical use of bromide in cats. *J Am Vet Med Assoc*. 2002;221(8):1131-1135.
29. Tipold A, Keefe TJ, Löscher W, Rundfeldt C, de Vries F. Clinical efficacy and safety of imepitoin in comparison with phenobarbital for the control of idiopathic epilepsy in dogs. *J Vet Pharmacol Ther*. 2015;38(2):160-168.