Rectal Administration of Zonisamide for Seizures Is Not Effective

Mark T. Troxel, DVM, DACVIM (Neurology)
Massachusetts Veterinary Referral Hospital
Woburn, Massachusetts

In the Literature

Michaels JR, Hodshon AJ, Thomas WB, Boothe DM, Williams L. Pharmacokinetics of zonisamide following rectal administration to healthy dogs. *Am J Vet Res*. 2016;77(12):1374-1380.

FROM THE PAGE ...

Maintaining anticonvulsant serum concentrations in hospitalized epileptic patients is important, but it can be challenging in patients too sedate for oral medications or that need food withheld. There are few commercially available IV versions of the common oral maintenance anticonvulsants. Rectal anticonvulsant administration may provide an alternate route of administration to patients that must be fasted.

A previous study investigated the pharmacokinetics of single-dose (10 mg/kg) rectal zonisamide and found that therapeutic concentrations were not reached.[1] This study examined whether therapeutic plasma concentrations of rectal zonisamide could be reached at higher doses. In a randomized crossover study of 8 healthy dogs, each dog was given a total of 4 zonisamide doses rectally (20 or 30 mg/kg) in each of 2 diluents (sterile water or polyethylene glycol) with a 7-day washout period between doses. Plasma was collected for zonisamide concentration analysis immediately before and at predetermined points up to 48 hours postadministration.

Rectal zonisamide failed to reach plasma concentrations in the recommended therapeutic target range of of 10 to 40 µg/mL at both doses and in both diluents. It is possible that higher doses (eg, 40 mg/kg, 60 mg/kg) might reach therapeutic concentration. However, the authors also found that zonisamide formulations >100 mg/mL could not be maintained in suspension. Doses >30 mg/kg of a 100 mg/mL concentration would require large volumes of medication that may not be tolerated by the patient. It was concluded that rectal zonisamide delivery does not appear to be a viable alternative to oral zonisamide at doses of 20 mg/kg or 30 mg/kg.

Because rectal zonisamide does not reach therapeutic plasma concentrations, it is not a viable route of delivery.

This study did not specifically address use of rectal zonisamide in emergent patients (eg, patients with status epilepticus, cluster seizures), as therapeutic concentrations were not achieved and peak plasma concentration did not occur until 6 hours post-administration—far too late for use in emergent settings. However, this would likewise be an unviable option for these patients.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. In-hospital treatment can be challenging for epileptic patients unable to take long-term maintenance anticonvulsants.

2. To date, phenobarbital and levetiracetam are the only commercially available injectable versions of standard maintenance oral anticonvulsants. Sodium bromide (NaBr) can be made into a sterile solution for IV administration to replace oral KBr but requires specialty compounding and sterilization in advance of its use.

3. As rectal zonisamide does not reach therapeutic plasma concentrations, it is not a viable route of delivery.

Reference

1. Brewer DM, Cerda-Gonzalez S, Dewey CW, Boothe D, Van Horne K. Pharmacokinetics of single-dose rectal zonisamide administration in normal dogs. *J Vet Intern Med*. 2015;29(2):603-606.