SEIZE THE DAY II SEIZURES: TREATMENT PLANS FOR THE ROUTINE AND DIFFICULT-TO-CONTROL EPILEPTIC, CLUSTER SEIZURES AND STATUS EPILEPTICUS

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INTRODUCTION

Deciding on a treatment plan for an animal with seizures depends on a number of factors, including the suspected etiologic cause of the seizures, the frequency and severity of the observed seizures, and the financial constraints or intentions of the owner.

ADDRESS THE UNDERLYING CAUSE

If an underlying cause of the seizures is known or suspected, it should be appropriately addressed, if possible. Thus, animals with hypoglycemia or electrolyte abnormalities may require no therapy other than correction of these deficiencies (or excesses). Likewise, patients with hepatic encephalopathy, hypertriglyceridemia or various intoxications may not require long-term anticonvulsant therapy if the primary disease is appropriately addressed, although they may benefit from shorter-term treatment with these drugs. In some cases, damage to the brain may lead to acquired (probably symptomatic) epilepsy, requiring long-term treatment.

Animals with intracranial diseases also benefit from addressing the underlying condition, although these patients are more likely to require maintenance anticonvulsant therapy. Thus, placement of a ventriculoperitoneal shunt for hydrocephalus, anti-inflammatory and/or antimicrobial medications for meningoencephalitis, surgery or radiation therapy for brain tumors, and other specific therapies address the underlying disease process and may reduce or eliminate the need for anticonvulsant therapy.

MAINTENANCE ANTICONVULSANT THERAPY

Maintenance anticonvulsant therapy is used as an adjunct in symptomatic epilepsy and is the cornerstone of therapy for patients with idiopathic or probably symptomatic (acquired, cryptogenic) epilepsy. The first question to address is: **When to start anticonvulsant therapy?** There are no hard and fast rules on this issue, and each patient much be approached individually. However, some guidelines apply. In general, maintenance therapy should be considered if:

- Seizures are more frequent than once every 6-8 weeks
- Seizures are obviously increasing in frequency
- Status epilepticus or cluster seizures occur

- Seizures last longer than 5 minutes
- Seizures are very severe or involve aggression towards the owner

The second question to address is: **Which anticonvulsant should I choose?** Historically in dogs, the two main initial options for therapy have been phenobarbital and (potassium) bromide. These medications are chosen because of their long history of use, apparent efficacy, ease of dosing, favorable pharmacokinetics and inexpensiveness. There is limited evidence to suggest that phenobarbital may be slightly more efficacious as a first line agent in the dog. Diazepam is not effective as a maintenance anticonvulsant in the dog due to a very short elimination half-life, and the development of tolerance within several weeks.[1] Some of the newer anticonvulsant medications can be effective as initial therapy, and the author uses zonisamide and levetiracetam with some frequency as first-line agents in dogs. Zonisamide is particularly attractive in this setting due to its low incidence of side effects and its relatively long half-life, allowing twice daily administration.[2,3] A generic extended release formulation of levetiracetam is now available, and pharmacokinetic studies suggest that twice daily administration may be effective in canine patients. However, published reports of efficacy in this setting are lacking in veterinary patients. Use of these newer drugs has been limited in the past by their expense when compared with traditional anticonvulsants, although generic versions of most of these newer generation drugs are now available at reduced costs. In the cat, phenobarbital (preferred) and diazepam are the historical maintenance drugs of choice. Bromide is an effective anticonvulsant in the cat, but is associated with a very high incidence of inflammatory lung disease, and is not recommended.[4,5] Diazepam should be used with extreme caution in cats and is generally not recommended, as it has been associated with idiosyncratic hepatic necrosis after oral administration.[6] Levetiracetam may be a reasonable choice in the cat if phenobarbital is not an option, although the drug must be administered three times daily.[7] A recent pharmacokinetic study suggests that extended release levetiracetam may be safe to use once daily in cats.[8] There is limited information available on zonisamide in cats,[9] although side effects seem to occur more frequently in this species.[10]

Initial Maintenance Therapy for Epileptic Animals

- Phenobarbital – 2.5-3 mg/kg q 12 hours (Dogs or cats)
- Potassium bromide – 40-50 mg/kg/day q 24 hours or divided (q 12 hours) (Dogs)
- Zonisamide – 3-5 mg/kg q 12 hours (Dogs and cats)
- Levetiracetam – 20 mg/kg q 8 hours (Dogs and cats)
- Levetiracetam (extended release) – 30 mg/kg q 12 hours (Dogs); 500 mg total q 24 hours (Cats)
- Diazepam – 0.2-1.0 mg/kg q 12 hours (Cats, use with caution and not recommended)

Phenobarbital is available in generic tablets (15, 30, 60, 90, 100 mg) or suspension (3 and 4 mg/ml) formulations, as is diazepam (2, 5, 10 mg tabs; 1 and 5 mg/ml suspension). Zonisamide is available as 25, 50 and 100 mg capsules. Levetiracetam is

available as 250, 500, 750 and 1000 mg tablets and a 100 mg/ml suspension. Extended release levetiracetam is available as 500 and 750 mg tablets; these should not be broken, as it interferes with the extended release mechanism. Bromide is typically compounded from the chemical grade salt, and complexed with potassium (KBr) or less frequently with sodium (NaBr). It should be noted that due to molecular weight differences between the cation, equal amounts of KBr and NaBr do not contain the same amounts of bromide, and therefore have different anticonvulsant potencies (250 mg KBr = 211 mg NaBr). KBr is available from a number of compounding pharmacies. Liquid formulations are preferred over capsules, as they facilitate dosage adjustments, and KBr is best administered with food to reduce gastrointestinal irritation. Dietary salt affects serum levels of bromide, and a constant salt level should be maintained in the diet.

Monitoring Maintenance Therapy

A complete blood count (CBC), serum biochemical evaluation and urinalysis should be performed before starting maintenance anticonvulsant therapy, both as part of the diagnostic evaluation (see previous talk) and as a baseline before starting therapy. In addition, the metabolism of these drugs varies between patients. Blood levels are essential to guide therapy for phenobarbital and bromide, and may be indicated for some of the newer drugs, depending on the response to therapy. Steady state of a drug after regular oral dosing depends on its half-life in the body, and varies between medications and species. Monitoring times and desired blood levels are shown below for dogs.

Table 1.

These desired blood levels are a guide only, and must be interpreted in light of the resulting seizure frequency and clinical condition of the patient. When measuring therapeutic blood levels, as with any medications, a serum separator tube (“tiger top”) should be avoided, as the separator device may bind the drug and artificially decrease the serum levels. After the establishment of acceptable therapeutic levels of the medication, it is generally recommended that blood levels along with a CBC, serum chemistry and urinalysis be monitored every 6-12 months or in the event of an acute change in seizure frequency or new onset of sedation, weakness or ataxia. Animals receiving phenobarbital may also benefit from pre-and post-prandial serum bile acid evaluation at these times to detect changes in hepatic function. Therapeutic monitoring is very important for phenobarbital and bromide, but has been utilized less frequently for the newer generation of drugs. As these newer medications are quite safe, they have generally been used to effect, and until fairly recently, routine therapeutic monitoring for these drugs was not available.

Potential Adverse Effects of Maintenance Therapy

Adverse effects of phenobarbital include sedation, polyphagia, polyuria, polydipsia, weight gain, pelvic limb ataxia, weakness, and in rare cases hepatic failure and blood

dyscrasias. Overt hepatic damage is an unusual sequela with this medication, particularly if the serum levels are maintained below 35 μg/ml. It should be noted that increases in liver enzyme levels are common with this medication, and this does not indicate hepatic failure. If this is a concern, serum bile acids should be evaluated. Side effects of bromide are similar for the most part, including sedation, polyphagia, polyuria, polydipsia, and weight gain but in rare cases also includes pancreatitis. Vomiting related to the salt content can be minimized by administration with food. Diazepam may lead to sedation and polyphagia, and rare idiosyncratic reactions causing acute hepatic necrosis have been described in the cat.[6] Zonisamide and levetiracetam may both cause sedation, while the former may also cause vomiting, diarrhea and inappetence. A reversible idiosyncratic hepatic failure has been reported in dogs that received zonisamide, but this appears to be a very rare sequela.

DEALING WITH THE REFRACTORY EPILEPTIC

Monotherapy with one of the medications above controls an estimated 60-80% of epileptic dogs and the majority of cats. However, a number of animals will have their condition remain unchanged or worsen in the face of this therapy. In this situation, a number of additional steps may be considered:

- Ensure owner is administering drug correctly
- Ask about dietary changes, other medications or herbal preparations, and topical anti-parasite medications that may interfere with seizure control
- Reconsider diagnosis, pursue additional diagnostic testing
- Ensure optimal blood levels of maintenance drug
- Increase dosing frequency (Phenobarbital - from q12 h to q 8 h) if seizures occur at times corresponding to “trough” blood levels (base on therapeutic monitoring)
- Ensure female dogs have been spayed
- Add a second anticonvulsant drug

Regarding these points, many animals require blood levels of phenobarbital above 25 μg/ml for seizure control, although levels exceeding 35 μg/ml should be avoided. Although unusual, some animals receiving phenobarbital metabolize the drug very rapidly, and may benefit from dosing every 8 hours. Having the owner maintain a seizure diary is useful to document these cases, as seizures may occur during the expected “trough” period of drug metabolism and peak and trough serum levels may be beneficial in guiding therapy. Serum levels of bromide above 3000 μg/ml are tolerated in some dogs, especially when used as a monotherapy.

Adding a Second Anticonvulsant Drug

In the cat, diazepam may be added successfully to phenobarbital to control seizures (although as mentioned above, this drug should be used with extreme caution in this species). In the dog, a combination of phenobarbital and KBr (starting dose 20-30 mg/kg daily) is effective in controlling the majority of patients refractory to monotherapy with either drug alone. However, side effects are common with this protocol, and may

be unacceptable to the owner. These include sedation, pelvic limb weakness and ataxia, polyphagia, polyuria and polydipsia. It should be noted that side effects may subside approximately 1-2 weeks after initiating the new drug, and so patience can pay off. Generally, a balance must be achieved between an acceptable seizure frequency and these side effects, although this may be impossible in some dogs. Generally, the best success is achieved by aiming for a serum bromide level between 2000-3000 mg/l and maintaining a lower phenobarbital level (e.g. 10-20 μg/ml).

If seizure control cannot be obtained with this combination of drugs, then other options exist. Many refractory dogs experience cluster seizures at varying time intervals, with relatively good control between cluster episodes. In this case, administration of rectal or nasal diazepam or other benzodiazepines (see "Cluster Seizures" lecture) may help to control the cluster events and avoid an emergency visit to the hospital. A third anticonvulsant medication may be added, and includes the following choices:

- Zonisamide (Zonegran) – 6-10 mg/kg q 12 hours (dogs only [dose doubled when administered with phenobarbital])
- Levetiracetam (Keppra) – 20 mg/kg q 8 hours
- Felbamate (Felbatol) – 15-20 mg/kg q 8 hours (dogs only)
- Gabapentin (Neurontin) – 10-30 mg/kg q 8 hours (dog) or q 8-12 hours (cat)
- Pregabalin (Lyrica) – 2 mg/kg q 8-12 hours, increasing 1 mg/kg/dose each week to a total of 3-4 mg/kg (dogs only)

These drugs have a variety of mechanisms of action, which appear to be different from phenobarbital and bromide, and patients may receive additional benefit from a multimodal antiseizure effect. Another advantage of the newer drugs is their improved side effect profile, as side effects are essentially limited to sedation (which tends to be less severe than that seen with either phenobarbital or bromide) and gastrointestinal side effects (vomiting, diarrhea) for some drugs. Felbamate is an exception, as there is concern with hepatic dysfunction, particularly when used in combination with phenobarbital. Elimination half-lives are relatively short, and drug steady state levels are reached relatively quickly with administration of a regular oral dose. The main disadvantages of these newer drugs are their expense (although most are now available generically, and costs are decreasing) and requirement for administration every 8-12 hours.

Of these newer generation drugs, the author generally prefers to use zonisamide or levetiracetam. Assays to measure blood levels of these drugs are available at a few select laboratories, but these drugs are often administered to effect. In some cases, success with the addition of an anticonvulsant drug may allow the eventual withdrawal of the initial medication, although this must be accomplished gradually and with caution. The author frequently uses these newer anticonvulsant medications (particularly zonisamide and levetiracetam) as the second drug choice (typically instead of bromide). Other potential interventions to consider in select situations include acupuncture and the administration of a hypoallergenic diet.

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Table 1. Monitoring Anticonvulsant Therapy in Dogs

Medication	Time to Steady State	Desired Blood Levels
Phenobarbital	10-14 days	15-35 μg/ml
Bromide	3-4 months	1000-3000 μg/ml (or 1-3 mg/ml or 100-300 mg/dl)
Diazepam	5-10 days	Monitoring not typically performed
Zonisamide	3-5 days	10-40 μg/ml (extrapolated from humans)
Levetiracetam	1-2 days	5-45 μg/ml (extrapolated from humans)

TREATMENT OF CLUSTER SEIZURES AND STATUS EPILEPTICUS

DEFINITIONS

- **Cluster seizures** – two or more seizures occurring within a 24-hour period.
- **Status epilepticus** – continuous seizure activity lasting longer than 5 minutes, or the occurrence of multiple seizures without recovery of baseline neurologic function between episodes.[1,2] Status epilepticus can be generalized or focal in nature, or in rare cases, can be nonconvulsive.[3]

PATHOPHYSIOLOGY AND GOALS OF TREATMENT

The vast majority of seizures are self-limiting events, with eventual spontaneous return to resting or baseline neurologic function. However, during status epilepticus, a variety of changes occur within cells and networks of cells that result in a situation where the seizure activity becomes self-sustaining. These changes may be independent of the initiating cause of the seizure, and involves a variety of molecular mechanisms. Repetitive seizures cause inhibitory $GABA_A$ receptors to move from the synaptic membrane to the cell interior, while excitatory N-methyl-D-aspartate (NMDA) receptors may be recruited to the cell surface.[1] Stores of inhibitory neurotransmitters may become depleted and increased expression of drug efflux transporters such as P-glycoprotein may occur.[4] After a period of time, these cellular alterations may lead to pharmacoresistance to first-line agents that would normally be effective in seizure termination at earlier phases, such as the benzodiazepines.

Generalized status epilepticus can cause profound acidosis, hyperthermia, cardiac arrhythmias, hypoxia, neurogenic pulmonary edema, rhabdomyolysis, myoglobinuria, renal failure, cerebral edema, elevated intracranial pressure and neuronal necrosis, and therefore constitutes a medical emergency.[5] The goals of treatment are to stop the seizures, support systemic organ functions, and protect brain function. Finally, ongoing seizure activity/seizure control should be closely monitored. These goals are described in greater detail below.

1) Stop the Seizures

The most critical and pressing goal of therapy is to stop the seizures, by any means necessary. The initial drug chosen is usually a benzodiazepine (diazepam or midazolam), but depends on the suspected underlying cause.

- If hypoglycemia is suspected (juvenile toy breed dog, hunting dog or insulin overdose), administer 1-2 ml/kg of 50% dextrose intravenously (IV) diluted 1:1 in saline. Oral dextrose may be used in animals able to swallow when intravenous access is not readily achieved.
- In small or toy breed dogs that have recently whelped and are nursing puppies, the administration of calcium gluconate may be considered to address potential hypocalcemia.

Animals with known idiopathic, symptomatic or probably symptomatic (acquired/cryptogenic) epilepsy and those with unknown etiologies typically receive a benzodiazepine as the first-line drug.

- Diazepam (0.5 mg/kg) can be administered IV, intranasally or rectally to control seizures. The dose can be repeated twice, if necessary. Anticonvulsant action only lasts about 15-30 minutes, and therefore some form of longer acting therapy is required if the seizures stop. Midazolam can be substituted for diazepam in this scenario, and lorazepam (0.2 mg/kg) may also be considered. These drugs may also be administered IV or intranasally, but are not likely to be effective with rectal administration. In addition, unlike the others, midazolam can be successfully administered intramuscularly (IM).
- If the animal responds to a benzodiazepine bolus, phenobarbital may be considered for longer-term control. Naïve animals not previously receiving anticonvulsants can be loaded with 16-20 mg/kg divided into 4 doses and administered every 30-120 minutes (i.e., 4-5 mg/kg q 30-120 minutes). Epileptics already receiving phenobarbital may benefit from an additional "mini-loading dose" (5-10 mg/kg) depending on their serum levels of the drug. Phenobarbital should be continued at regular maintenance intervals (2-3 mg/kg IV, IM or PO q 12 hours or at the animals regular dose) after this.
- Animals with severe cluster seizures or status epilepticus with some inter-ictal time (i.e., non-continuous) usually respond to a constant rate infusion (CRI) of diazepam (0.1-2.0 mg/kg/hour IV). The CRI can be started at the low end of the range (0.1-0.25 mg/kg) and gradually increased as necessary to control seizure activity. Once controlled, a seizure-free state is maintained for 12 hours, after which the infusion is gradually tapered (usually reduce dose by half every 4-6 hours) and stopped. The CRI can be administered with a syringe pump, if available, or by mixing with 0.9% saline in a small IV bag or Buretrol system. Diazepam is degraded by light and binds to plastic, and the syringe and tubing should be covered with brown plastic or aluminum foil, if possible. Midazolam can again be substituted in this scenario, and is less likely to cause thrombophlebitis.
- Animals with continuous, prolonged seizure activity or those refractory to benzodiazepines may receive pentobarbital (3-15 mg/kg IV to effect), if available. This drug induces general anesthesia, and is extremely effective in stopping the outward manifestation of the seizure. However, respiratory and cardiovascular function may be depressed, and these systems must be monitored very closely. Although intermittent bolus doses can be used, a CRI (2 mg/kg/hr adjusted to effect) may be more effective. Similar to benzodiazepine CRIs, animals may be kept seizure free for approximately 12 hours, and then weaned from the drug. It can be difficult to distinguish recovery from pentobarbital anesthesia from overt seizure activity. However, paddling movements of the limbs typically indicate the former, while seizure activity is usually characterized by overt tonic or clonic muscle contractions. Electroencephalography, if available, can help to differentiate these two scenarios. This medication also reduces the metabolic requirements of the brain, and is considered to have neuroprotective effects.

- Propofol may be used as a substitute for pentobarbital if general anesthesia is required to control seizure activity. Due to its short duration of action, this drug must be given as a CRI (6 mg/kg initial bolus followed by 0.1-0.6 mg/kg/min). Substantial respiratory depression is common with this medication, and anesthesia must be closely monitored. In addition, propofol can have pro-convulsant effects in some patients. Some consider this to be the treatment of choice for patients in status epilepticus secondary to hepatic encephalopathy (typically after surgical repair of a portosystemic shunting vessel).
- If pentobarbital and propofol are not available, the use of an inhalant anesthetic (e.g., isoflurane or sevoflurane) to maintain general anesthesia should be considered as a last resort. Both require close monitoring of respiratory and cardiovascular parameters.
- A parenteral formulation of levetiracetam is also available. Although its use in animals with status epilepticus or cluster seizures has been limited to date, it may prove useful in this role, based on reports in humans and preliminary experience in canine patients.[1,6] Pharmacokinetic studies in dogs suggest that a dose of 20-60 mg/kg IV results in blood concentrations within the range considered to be effective in humans (5-45 μg/ml) for greater than 8 hours.[7,8] Levetiracetam is approximately 100% bioavailable after IM administration and results in similar blood levels, although peak concentrations are not reached until about 40 minutes after the drug is given.[8]
- Reports of other medications for refractory status epilepticus are infrequent in veterinary medicine. There is a report of a dog with granulomatous meningoencephalitis and status epilepticus responding to intravenous ketamine infusion after failure to respond to diazepam and propofol.[9] This report follows several human case reports reporting similar efficacy for ketamine in the scenario of refractory status epilepticus, the rationale being blocking of NMDA receptors which may be responsible for the self-sustaining nature of this condition.[1,6,10] Additional therapies reported in refractory human cases include valproic acid, lidocaine, and topiramate.[6,11,12]

2) Support and Monitor Systemic Functions

As described above, status epilepticus can have profound effects on many body systems, and systemic functions must be closely monitored. These include:

- Mental status and level of consciousness
- Respiration, oxygen saturation and blood gases (if available)
- Cardiac rate and rhythm, blood pressure
- Body temperature
- Serum electrolytes, glucose, BUN and creatinine
- Fluid status and hydration
- Muscle damage and evidence of myoglobinuria (which may cause renal failure)

Intravenous fluid therapy is often indicated in order to maintain hydration, and may help prevent renal damage if myoglobinuria is a concern. As severe seizure activity may

lead to non-cardiogenic pulmonary edema, thoracic radiographs, pulse oximetry, and blood gas analysis should be considered in animals with compromised respiration. Aspiration pneumonia is also a concern, particularly in large recumbent dogs. Oxygen therapy may be administered in some of these patients. Active cooling should be considered in animals that are severely hyperthermic. Basic supportive nursing care must be performed in recumbent and stuporous animals, including applying artificial tears/lubrication to the eyes, providing adequate bedding/padding, periodically changing body position, turning from side to side, and passive range of motion of the limbs.

3) Protect Brain Function

Prolonged, severe seizure activity can lead to cerebral edema, increases in intracranial pressure and neuronal necrosis. Select cases may benefit from oxygen therapy, mannitol (0.25-1.0 g/kg IV over 10-20 minutes) and furosemide (0.7 mg/kg IV, 15 minutes after mannitol) in order to address these effects. Compression of the jugular veins, coughing and sneezing all increase intracranial pressure, and should be avoided in animals where this is suspected to be increased. Therefore, jugular catheters, collection of blood from the jugular vein, neck bandages, nasogastric tubes, and nasal oxygen catheters should all be avoided. Intravenous lidocaine should be considered to reduce the coughing reflex if intubation is required. Elevation of the head approximately 30 degrees from the horizontal is a simple way to promote venous return from the brain and potentially reduce intracranial pressure. Pentobarbital administration, in addition to stopping seizure activity, also has the advantage of reducing cerebral metabolism, which can have neuroprotective effects in patients with status epilepticus.

4) Monitor ongoing seizure activity

Patients should be closely monitored to ensure the cessation of seizures and for the recurrence of seizure activity after initial therapy. This is typically done by visual observation and examination of animals for motor activity consistent with seizures. Whenever possible, cessation of seizure activity should be confirmed electrophysiologically with the aid of electroencephalography (EEG). This may detect animals whose outward motor manifestations of the seizure activity have stopped, but who continue to have abnormal electrical brain activity, known as nonconvulsive status epilepticus (NSE). Although NSE has rarely been reported in veterinary patients,[9] this is likely a reflection of the infrequency with which veterinary clinicians perform EEG in this setting. The author has documented a number of canine patients with apparent NSE after prolonged convulsive status epilepticus or presenting with a primary complaint of altered mentation (Mariani, unpublished observations). An EEG is part of the routine diagnostic evaluation of human patients presenting with stupor or coma, and in the author's opinion, the same should be offered to veterinary patients wherever possible.

AT-HOME THERAPY FOR CLUSTER SEIZURES

Some owners can be taught to administer benzodiazepines in the home environment in order to reduce the number of seizures in dogs (or cats) prone to cluster seizure events. The goal is usually to prevent further seizures, reduce the number and severity of subsequent seizures, and avoid an emergency visit to the veterinary hospital. Diazepam has been used most often via the rectal route; a standard dose (0.5 mg/kg) can be administered, although in some animals on chronic phenobarbital therapy, a higher dose (1-2 mg/kg) may be required due to increased metabolism of the drug.[13,14] Drugs administered rectally in the dog undergo a substantial first-pass effect and hepatic metabolism as the majority of absorbed drug enters the portal circulation.[15] As a result, the bioavailability of diazepam after rectal administration is only about 2.7-7.4% at doses of 0.5 and 2.0 mg/kg respectively in dogs not receiving phenobarbital.[16] However, some anticonvulsant effect is achieved as the main metabolites of diazepam (desmethyldiazepam and oxazepam) posses 20-50% of the activity of the parent drug.[17-19] Lorazepam is unsuitable for rectal administration, as its primary metabolite (lorazepam glucuronide) does not have anticonvulsant activity.[15] Midazolam does have a metabolite with reported pharmacologic activity (1-hydroxymidazolam), although the contribution of this reported activity is controversial.[20]

Intranasal (IN) administration of benzodiazepines avoids several of the shortcomings of the rectal route. The IN route avoids substantial first pass metabolism, and drug is directly absorbed into the systemic circulation thorough the dense vascular plexus present in the nasal passages.[21] In addition, there is evidence for direct movement of drug through the cribriform plate and into the central nervous system.[22-24] Several studies suggest that the bioavailability of diazepam is much higher after IN administration than after rectal.[25,26] and this route has been used successfully by the author in several emergent clinical cases (0.5 mg/kg). Preliminary experience suggests that intranasal lorazepam (0.2 mg/kg) may also be useful as an alternative to rectal diazepam for at-home use by owners.[27] Intranasal or IM midazolam (0.5 mg/kg) is another option available for these scenarios.

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