

## **The Use of Potassium Bromide In Treating Canine Epilepsy**

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Potassium bromide is emerging as one of the most frequently compounded veterinary prescriptions. It is important to note that bromide is the therapeutic component of this salt when used for epilepsy. Potassium chloride is not a substitute for this agent and will actually worsen canine epilepsy.

The drug of choice for treating canine epilepsy is phenobarbital. It is preferred due to its relatively long half-life (compared to other antiepileptic drugs), its low cost, and its relative lack of toxicity. Higher doses or chronic use of phenobarbital, however, may result in hepatotoxicity and other therapies must be initiated.

Potassium bromide is typically used when adverse effects occur from phenobarbital, or when maximum doses of phenobarbital are no longer effective in controlling seizures. Potassium bromide has no hepatic toxicity. Several studies have been published regarding the use of potassium bromide in canine epilepsy. One study showed an 83 percent decrease in seizure frequency in dogs compared to their pre-bromide status. Nearly 78 percent of owners in this study reported an increased quality of life and a decreased severity of seizures in their dogs.

Potassium bromide has a depressant effect on neuronal excitatory activity. It competes with chloride for active transport across cell membranes. The result is hyperpolarization of the neuronal cell membrane and an increase in seizure threshold. The membrane becomes hyperpolarized as bromide replaces chloride in all body fluids preventing chloride from crossing neuronal membranes, depolarizing, and allowing an action potential to occur. Bromide enhances the inhibitory effect of GABA by hyperpolarizing neuronal membranes. Phenobarbital and bromide successfully treat canine epilepsy when used in combination as they work synergistically to enhance the activity of GABA and simultaneously raise the seizure threshold.

The pharmacokinetics of potassium bromide have been studied in dogs. The half-life is approximately 24 days. Due to this extremely long half-life, it should take about 4 months to achieve steady state plasma concentrations without loading doses. The therapeutic serum level of potassium bromide is generally 1000-2000mg/L. Potassium bromide is well absorbed orally with peak absorption in about 1.5 hours. Bromide is reabsorbed by the renal tubules and this contributes to the long half-life in dogs. Bromide is not cleared by the liver, so it is useful in dogs with hepatic compromise. While potassium bromide may be used as monotherapy in animals with hepatic disease, its greatest use is in combination with phenobarbital allowing for lower doses of both agents.

The most common side effect seen with potassium bromide is sedation which is, however, usually self-limiting and disappears after 3 weeks of therapy. Due to the gastric irritant properties of potassium, potassium bromide may also cause gastrointestinal upset. As the combination of sedation and gastrointestinal irritation may result in aspiration from vomiting, patients receiving initial loading doses of potassium bromide should be fed from elevated food bowls to reduce the possibility of aspirations from vomiting. Renal function should be carefully monitored in patients receiving potassium bromide. Age related renal changes can lead to bromide accumulation and toxicity. Bromism is characterized by lethargy, ataxia, gastrointestinal upset and even death. Diuresis with 0.9 percent sodium chloride can reverse bromide toxicity. As chloride ions replace bromide ions, bromide will be excreted in the urine. Similarly, dogs maintained on potassium bromide should be very carefully monitored when receiving saline or other forms of sodium chloride. Dietary changes in sodium chloride intake can result in seizure breakthrough from increased sodium chloride intake or bromism from decreased sodium chloride intake. Owners should be instructed to avoid changes in diet without consulting a veterinarian. Other adverse reactions include polydipsia, polyphagia, and erythematous dermatitis (bromide rash).

Signs of toxicity include ataxia, sedation or stupor, and muscle pain. Toxicity is more likely from chronic administration or during the loading dose administration and may be more likely to occur in animals with renal insufficiency. For chronic toxicity, dosage reduction of 10 percent to 25 percent is usually adequate to resolve clinical signs. Acute toxicity rarely results in death due to vomiting from intense gastrointestinal upset.

Standard gut emptying protocols should be employed after a known overdose. Administration of oral or parenteral sodium chloride, parenteral glucose and furosemide is helpful in eliminating toxic bromide levels.

Diuretics decrease bromide levels through increased urinary elimination. High salt diets decrease bromide levels through displacement resulting in increased urinary elimination of bromide. Abrupt reduction of sodium chloride intake increases bromide levels potentially to toxic levels. CNS depressants may cause synergistic sedation, especially during the initial few weeks of therapy. Potassium sparing drugs may result in potential hyperkalemia, especially during the loading phase.

Potassium bromide is not available as an FDA approved drug in the United States due to the toxicity profile in humans. Pharmacists can, however, compound it. Depending on patient size and dosage form preference, potassium bromide can be compounded into capsules or an oral solution to be added directly to the food. The solubility of potassium bromide is about 1 gram in 1.5ml water. Due to the bitter taste and gastrointestinal irritant properties of this drug, veterinary pharmacists are sensitive to the need to work with veterinarians and pet owners to develop a palatable dosage form. Due to the long half-life of potassium bromide, loading of the initial doses is a frequently utilized option.

Serum bromide levels should be measured within the first few days of completion of loading. Serum levels should be monitored for the first 2-3 months of therapy and should be checked every 6 months to maintain target levels of 1-3mg/ml or the level required for control of the individual animal.

Use of potassium bromide during gestation suckling is not recommended. Potassium bromide crosses the placenta and is excreted in milk. Human infants have been reported to suffer bromism and growth retardation after maternal treatment with bromides during pregnancy as well as nursing.

Oral solutions containing potassium bromide should be refrigerated and discarded after 6 months to avoid contamination. Owners should be advised to handle medications with gloves or wash hands after administration as potassium bromide has been reported to cause skin rash and mental deterioration in humans who are chronically exposed.