CAVM in Practice

Use of a Ketogenic Diet in the Successful Management of a Dog With Refractory Epilepsy

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Abstract
Epilepsy is one of the most common neurological conditions seen in dogs. Idiopathic or primary epilepsy is diagnosed whenever an alternate structural, inflammatory, or metabolic cause cannot be confirmed. About 30% of dogs with idiopathic epilepsy will become refractory to standard treatments and still sustain a considerable incidence of seizures. Dietary changes have been investigated as aids in the treatment of seizures; however, using a ketogenic diet as a means of metabolic therapy has been minimally investigated in dogs. This report describes the successful use of a ketogenic diet in the management of epilepsy in a dog.

Case Report
4-year-old, 22 kg, spayed female Lurcher dog presented to an emergency service for a new onset of generalized, tonic-clonic seizures. She had been found at the bottom of stairs with paddling and excessive drooling evident, a glazed appearance to the eyes, and having passed a bowel movement. The estimated duration for this episode was 2 to 4 minutes, after which the patient remained recumbent for another 1 to 2 minutes. She then quickly arose and seemed to be normal. A second, similar episode occurred later that afternoon. Results of a physical examination performed at the initial presentation were normal. No significant abnormalities were noted on a CBC and blood chemistry panel. Thoracic radiographs were within normal limits. Her pertinent medical history included only an idiopathic pneumothorax which had occurred a year prior. The patient’s diet consisted of a commercial dry kibble fed as an isolated meal twice daily. The brand name could not be recalled by the client, so the details of the macronutrient composition were not calculated. Oral phenobarbital was initiated at approximately 2.9 mg/kg (64.8 mg PO q 12 hr) (Figure 1).

Four months after the initial seizure, the patient presented for a neurology consultation. No dietary changes had yet been implemented. She was averaging 2 to 3 seizures per month, and her neurologic examination showed no abnormalities. At the time of the initial seizure, the primary care veterinarian had prescribed potassium bromide at an approximate dose of 34 mg/kg/day (750 mg PO q 24 hr). Phenobarbital and bromide serum levels had been tested recently and found to be 28.7 mg/dL (reference range 15-45 mg/dL), and 1.0 mg/dL (reference range 1-3 mg/dL), respectively. The client complained that the patient was very dull and occasionally aggressive. Levetiracetam extended release was subsequently initiated, in addition to the other medications, at an approximate dose of 34 mg/kg (750 mg PO q 12 hr).

Seven months after the initial seizure the patient presented for a follow up visit. No dietary changes had been made.
Magnetic resonance imaging of the brain and a spinal fluid analysis were performed, and both were within normal limits. The CBC and blood chemistry panels were also within normal limits. The client reported that the patient was still having weekly seizures. Based on the previous potassium bromide plasma level of 1.0 mg/dL, that dose was doubled to 750 mg (68 mg/kg PO q 12 hr). Instructions were given to the client to begin feeding a ketogenic diet. The patient’s weight at this visit was 21.8 kg. Using an online calculator (a), the daily energy requirement for this pet was estimated to be approximately 989 kcal. The formulated homemade diet consisted of a daily portion of 350 grams 80% lean ground beef, 40 grams red cabbage, 1 tablespoon chia seeds, and 1 teaspoon of a calcium supplement (b). This recipe equated to approximately 68% of the calories derived from fats, 28% from protein, and 3% from carbohydrates. While the various styles of ketogenic diets have not been well-described in veterinary medicine, the breakdown of macronutrient percentages would be similar to a modified Atkins or modified ketogenic diet in people (1). The initial recipe was formulated using an online calculator provided by an organization (c) familiar with ketogenic approaches for dogs. In the author’s experience, this is often a good starting place for the diet. Depending on the patient tolerance and the perceived efficacy of the diet, alterations in macronutrient composition can be made if desired. To ensure that the macronutrient ratios remained relatively consistent, the formulated diet was fed raw to the patient, since cooking foods can change the macronutrient composition dramatically (2). Instructions were given to transition from the commercial dry kibble to the homemade ketogenic recipe over the course of 1 week, gradually adding the new food while reducing the old food. The aim was to obtain serum ketone levels of 0.2–1 mmol/L.

About 3 weeks after starting the ketogenic diet, the patient had gone 15 days without an observed seizure, the longest seizure-free interval since the onset of seizures. The client also reported that the ataxia had been more severe since increasing the potassium bromide. A CBC and blood chemistry panel were performed and were within normal limits. The phenobarbital level was 20.3 mg/dL (reference range, 15-45 mg/dL), and the potassium bromide level was 4.0 mg/dL (reference range, 1-3 mg/dL). Serum ketones measured 0.2 mmol/L with a handheld ketone meter (d). The addition of 2 tablespoons of commercial medium-chain triglyceride (MCT) oil (e) was advised to help boost ketone levels. The bromide dose was reduced back to 34 mg/kg (750 mg PO q 24 hr) to help reduce the ataxia.

The patient was rechecked about 5 weeks after starting the ketogenic diet. Her neurological examination remained normal other than a mild spinal ataxia, evidenced by long-striding and occasional scuffling in the pelvic limbs, which was attributed to side effects of medications. Her most recent seizure, the second one noted since beginning the ketogenic diet, had occurred 11 days prior. Serum ketones were measured and were 0.4 mmol/L. The potassium bromide was discontinued at this time due to excessive sedation and ataxia seen by the client at home. Zonisamide was started in place of the bromide at approximately 13 mg/kg (300 mg PO q 12 hr).

A follow-up visit took place about 3 months after starting the ketogenic diet. Thirty-seven days had passed since her last noted seizure, despite the potassium bromide being discontinued. Additionally, the client had reduced the phenobarbital to 30 mg (1.3 mg/kg PO q 48 hr). The zonisamide and levetiracetam doses were unchanged. The MCT oil had

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**Figure 1**

Ketogenic diet — ketotimeline

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been discontinued due to decreased appetite, but otherwise the diet was unchanged. It was also reported that the patient was no longer ataxic at home, and this was reflected on the current neurological examination. Serum ketones at this visit measured 0.3 mmol/L. Blood glucose was 71 mg/dL (reference range, 70-138 mg/dL).

The patient was rechecked again about 4.5 months after the transition to the ketogenic diet. A seizure was occurring on average about every 60 days, and these were reported to be milder (shorter and less violent) in nature. Her neurological examination was normal. The zonisamide and levetiracetam doses were unchanged. Serum ketones measured 0.4 mmol/L, and blood glucose was 75 mg/dL (reference range, 70-138 mg/dL).

Eight months after starting the ketogenic diet (which remained consistent throughout), the patient was averaging an isolated seizure about every 80 days, despite no longer receiving phenobarbital or potassium bromide. The zonisamide and the levetiracetam were continued at the same dosages. Serum ketones measured 0.3 mmol/L and blood glucose was 74 mg/dL. A comprehensive plasma electrolyte and trace mineral panel, in addition to a vitamin profile, was submitted to a university laboratory to screen for severe nutritional deficiencies. All values reported were within normal limits. No changes were made to the medications or diet.

About 4 years after initiation of the ketogenic diet, 2 years had elapsed since the last noted seizure. The zonisamide and the levetiracetam extended release were continued at the same dosages, 13.6 mg/kg and 34 mg/kg every 12 hours, respectively.

At the last follow up, approximately 1 year later, the patient was now 3 years from her last seizure. The zonisamide and the levetiracetam extended release were continued with no dosage changes.

Discussion

Idiopathic epilepsy is one of the most common neurological disorders diagnosed in dogs (3). Epilepsy is defined as chronic, recurring seizures. The epilepsy is termed idiopathic if no underlying structural brain disease is found on advanced brain imaging (ie, MRI and CT), no metabolic cause is determined with routine biochemical analysis, and the patient is clinically normal during the interictal period (3-5). Most dogs with idiopathic epilepsy suffer their first seizure between the ages of 1 and 5 years, although some exceptions occur.

Phenobarbital or potassium bromide are the recommended initial drugs of choice for monotherapy when treating seizures (6-7). Sadly, it is estimated that up to 30% of dogs with idiopathic epilepsy will be refractory to conventional therapy (8). Uncontrolled seizures are a common reason many clients ultimately choose to euthanize their dogs (9). Several alternative therapies including vagal nerve stimulation, supplements (omega-3 fatty acids, vitamin E), and the ketogenic diet have been minimally investigated for use in dogs with refractory epilepsy (8). A small study in dogs looking at the efficacy of the ketogenic diet in the management of epilepsy was not promising (10). However, this study had a low number of participants, and the average level of ketosis reached was relatively minimal (~0.1 mmol/L). In contrast, there are numerous reports in humans that suggest positive benefits for seizure control with the adoption of a ketogenic diet (11).

A ketogenic diet consists of a much higher fat content (70% to 90% of total calories) along with severe carbohydrate restriction (3% to 5% of total calories) (12). This creates a hormonal shift which enhances lipolysis of triglycerides in the body’s fat stores, freeing fatty acids which can then be used to create energy through beta-oxidation in the mitochondria. In the liver this produces ketone bodies, primarily acetone, acetoacetic acid, and beta-hydroxybutyrate. Ketones can cross the blood-brain barrier for use in the CNS and can be an effective fuel source for many tissues in the body (13, 14). The exact mechanism by which a ketogenic state aids in seizure control is unknown, although several mechanisms have been proposed. These include reduced cellular stress, increased fuel supply to neurons, reduced glutamate activity, enhanced gamma aminobutyric acid (GABA) synthesis, and enhanced mitochondrial efficiency (15).

This report highlights the utility of a ketogenic diet in the treatment of idiopathic epilepsy in dogs. This patient was still having weekly seizures despite receiving 3 anti-convulsants at appropriate dosages. Additionally, she was experiencing significant medication side effects including dullness and ataxia. After the ketogenic diet was initiated, the frequency of the seizures began to decrease. At the time of publication, the patient has gone over 3 years without a seizure, a remarkable contrast to the previous weekly episodes. Furthermore, the dog was completely weaned off the phenobarbital and potassium bromide, resulting in resolution of the dullness and ataxia. Zonisamide and
levetiracetam were continued because no appreciable side effects were observed and no serious long-term consequences are known with either of these medications. The combination of the levetiracetam and zonisamide was assumed to be aiding the patient’s seizure control in a multi-modal manner, but most of the anti-seizure effect is thought to be attributable to the ketogenic diet. While zonisamide and levetiracetam have fewer side effects, their anti-seizure effectiveness is not considered as robust as that of phenobarbital and potassium bromide (6). This patient’s seizures were more frequent when she was given the combination of phenobarbital and potassium bromide. While the zonisamide was initiated in the same time frame as the ketogenic diet, it is the author’s opinion from prior experience that this medication would not reduce the frequency of seizures from weekly to 0 within 3 years.

The success of a ketogenic diet in this dog underscores the potential of metabolic therapy in the management of idiopathic epilepsy. To address the potential problems with adherence that feeding a ketogenic diet can encounter, periodic measurements of serum ketones and blood glucose were made in this patient to ensure proper compliance. A point-of-care handheld measuring device (c) has been validated for use in dogs (16). The ketones measured in this patient were 200% to 300% higher than the average ketone measurement in the previous small study evaluating a ketogenic diet in dogs (8). This is possibly due to the higher percentages of calories from fat fed to the current patient (69%) compared to that in the previous study (57%) or may just represent individual variation. The addition of a MCT oil supplement (d) was added in an attempt to boost ketone levels. Adding MCTs to the diet has been shown to elevate plasma beta-hydroxybutyrate levels in dogs and humans (17–19). Unfortunately, in this patient the MCT supplement was thought to cause decreased appetite and was discontinued by the client. Despite this, the patient’s serum ketones were consistently measured to be 0.3–0.4 mmol/L. While this level is higher as compared to previous veterinary studies, it is still much lower than the average (about 4 mmol/L) measured in humans when on a ketogenic diet (1). This difference is not because dogs do not produce ketones well, but rather because they are efficient in utilizing ketones for energy; therefore, very high levels do not accumulate in the plasma (20).

Given the very limited ingredients in the formulated diet, a plasma trace mineral test and a vitamin panel were performed about 8 months after starting the diet. No abnormalities were noted on these panels, and routine lab work (CBC and blood chemistry panel) was also normal. These biochemical measurements, along with normal physical examinations, gave reasonable confidence that immediate nutritional needs were being met. Furthermore, the client reported that the patient was not only free from seizures, but thriving in her day-to-day life. This observation is in line with anecdotal reports in people in which recommended daily requirements of vitamins and minerals may differ while on a long term ketogenic diet. Given the severe restriction of ingredients in this patient’s ketogenic diet, there is a concern that long-term nutritional deficiencies may arise in the future. Adverse consequences from nutritional deficiencies can take time to develop, and it is advisable that if a long-term ketogenic diet is to be administered, a consultation with a board-certified veterinary nutritionist is appropriate in order to minimize any long-term complications.

This case report shows the successful management of epilepsy in a dog that was once refractory to 3 common seizure medications. Examples such as this can provide motivation for veterinarians to consider metabolic therapy in their canine patients with refractory epilepsy.

Endnotes

a. https://petnutritionalliance.org/dog.php
b. Animal Essentials Seaweed Calcium, Animal Essentials, Phoenix, AZ, 85085
c. KetoPet Sanctuary, KetoPet, Georgetown, TX, website: https://www.ketopetsanctuary.com
d. Precision Xtra Blood Glucose and Ketone Monitoring System, Abbott Laboratories, Abbott Park, IL
e. Bulletproof™ Brain Octane C8 MCT Oil, Seattle, WA, 98104
f. Michigan State University Veterinary Diagnostic Laboratory, Lansing, MI, 48910

References


