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Dietary intervention for canine epilepsy: Two case reports

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Summary

Epilepsy is a common neurologic disorder in humans and domesticated canines. In both species the etiology is diverse and complex, and even with medication a significant portion of the population does not experience sufficient seizure control and/or has unacceptable side effects. Humans often try alternatives such as dietary therapy or brain surgery, but in dogs, brain surgery is rarely an option and, despite potential benefits, there are no standard recommendations for a dietary approach. Herein we describe 2 retrospective case studies detailing the effects of homemade diets prepared for dogs with uncontrolled epileptic seizures and/or toxic side effects of medication. Basic recipes are provided for each formula—a high-fat “ketogenic” diet and a partial “whole food” diet. Carbohydrate content was reduced or controlled, and in one case this was proven to be essential for seizure control: ingesting carbohydrates would reverse the benefits of the diet and precipitate a seizure. Both dogs experienced fewer seizures and side effects when eating these modified diets compared to when they were administered antiepileptic drugs, including complete cessation of seizures for extended periods. Practical advantages and success of these homemade dietary interventions highlight the potential for diet-based metabolic therapy as a treatment option for seizures not only in humans but also in dogs.

KEYWORDS

dog, ketogenic diet, ketones, metabolic therapy, nutrition, seizures

1 | INTRODUCTION

Epilepsy is characterized by unpredictable recurrent seizures and is a common neurologic disorder in humans¹ and the most common neurologic disorder in dogs.² In both species, the etiology is diverse, complex, and often unknown. Most dogs and humans diagnosed with epilepsy show improvement or cessation of seizures with available antiepileptic drugs (AEDs), yet there remains a significant population that does not show such improvement.^{3,4} These individuals

(about 33% of canines and 30% to 40% of humans) do not respond consistently to medication(s) and/or have severe and unacceptable side effects, rendering them with medication-resistant or refractory epilepsy and a shortened lifespan.^{3,4}

Regarding therapy for refractory seizures, the ketogenic diet—a high-fat, low carbohydrate, and moderate protein protocol—has been used to treat epilepsy for nearly 100 years in both children and adults.⁵ A “classic” formulation is 4:1 (fat : (protein + carbohydrate)); prescribed typically to children). The ketogenic diet forces utilization of primarily

ketone bodies rather than glucose for cell energy, and this metabolic therapy can be a highly effective protocol for stopping seizures, even those that are refractory to all available medications.^{5,6} Some children even remain seizure-free after ceasing the dietary restrictions,^{5,7} and in recent decades less-restrictive formulations that shift the macronutrient ratio and lower the glycemic index (low glycemic index therapy, LGIT) have also been shown to reduce seizures, even if the diet does not produce significant ketosis⁸ (B. Zupec Kania, unpublished data). In some cases, a strict classic ketogenic diet is most effective; a menu of less-strict alternatives includes the modified Atkins (1:1 ratio), LGIT, and various ketogenic formulas, including one high in medium-chain triglycerides (MCTs).^{3,5,7,9} The range of options with proven clinical success, increased palatability, and improved compliance and practicality has facilitated expanded use of these diets to additional ages and disease populations.⁶

For health and for therapeutic insights, the importance of dietary treatments in dogs with seizures should not be overlooked. Canines are carnivores primarily, and although they will eat a variety of foods, they evolved to eat raw meat as a main food source.¹⁰ Therefore, a diet consisting mainly of raw meats has had anecdotal success based on the theory that dietary deficiencies and grains in commercial product can cause or trigger epileptic seizures.¹¹ However, relatively few modern dogs subsist primarily on raw meat or even any raw meat, and no scientific data has yet to confirm its benefits in controlling epilepsy in canines. Furthermore, although most neuroscience research in mammals is conducted in rodents, canines provide different opportunities due to the natural occurrence of epilepsy.² Clearly, laboratory-based rats and mice have significant advantages (ie, limited variability, environmental control, opportunities for genetic modification, rapid growth and reproduction, and relatively low cost). However, valid and ethical research studies are possible using community-based animals such as dogs (ie, housed primarily or exclusively in their home and not in a laboratory setting).^{1,12}

To date, a compelling body of controlled studies regarding diet-based therapies for dogs with seizures remains limited. One study of 21 dogs found that seizures were reduced significantly in dogs fed a proprietary ketogenic MCT (KMCT) diet for 3 months^{13,14} whereas no improvement was seen in dogs fed a standard diet for the same duration. For 3 subjects, seizures appeared to stop entirely, demonstrating a 100% reduction in seizure frequency. In 7 dogs, seizures decreased by at least 50%, and another 5 dogs experienced a lower seizure frequency overall.¹³ This KMCT diet also reduced a subset of attention-deficit/hyperactivity disorder–like features noted in the dogs with epilepsy, including chasing and stranger-directed fear.¹⁵ The benefits of a dietary change were also reported in a separate canine case study wherein phenobarbital alone was ineffective but the addition of omega-3 fatty acids

reduced seizures by 85%.¹⁶ In addition, an investigative study found that 67.7% of owners whose dogs were diagnosed with intractable epilepsy reported changing their dogs diet after receiving their diagnosis.¹⁷ Their justifications for the diet change included reported decrease of seizure frequency (88.2%), seizure severity (61.8%), and protection against the potential side effects of AEDs (62.5%).¹⁷

Herein we describe 2 cases of male (neutered) adult dogs with documented seizures who received homemade, nonproprietary diets to reduce their seizures. The 2 diets included a high-fat “ketogenic” diet and a partial “whole food” diet. The dogs were under the care of a licensed veterinarian, and the cases and dietary protocols are provided based on qualitative and quantitative information collected retrospectively. These retrospective case reports are exempt from ethics approval because there was no experimental intervention and the authors provided no dietary advice. The dogs were treated with best practice veterinary care and owners provided written permission for their dog's inclusion (and use of real names) in this report.

2 | CASE PRESENTATION: CASE 1

The first case, Bo, is a 12-year-old neutered male mixed-breed dog (Figure 1). His medical history included refractory seizures with no known cause consistently for several years—approximately 60 seizures between 4 and 9 years of age despite a daily dose of 40 mg of phenobarbital. Because the medication failed to significantly reduce seizure activity, potassium bromide was added for about 6 months and a low-fat, liver-cleansing diet comprising primarily fish and potato was also attempted. Notably, neither the low-fat diet nor the potassium bromide reduced seizure activity and these were discontinued.

In contrast, a remarkable improvement in seizures and behavior was seen when a dietary approach with a high-fat : (carbohydrate + protein) ratio was established. Case 1 received (per meal) 17 g of a commercially available air-dried fatty lamb diet, one tablespoon of canned pumpkin, and one teaspoon of a 6-oz. virgin coconut oil and 8-oz. MCT oil mixture (approximately 15% of the diet was MCTs). A sprinkle of probiotic milk thistle from human capsules and one senior dog vitamin daily were also included (Figure 1). Case 1 increased his body weight by about 20%, a desired outcome. He continued on phenobarbital initially and was reported to be seizure-free for 33 weeks following the switch to this dietary treatment. The ratio of this diet was calculated to be 1.07:1 (fat: (carbohydrate + protein); Figure 1A), approximating the ratio of the typical modified Atkins diet (1:1) prescribed to adult humans (15). Although this diet may have produced significant ketosis (changes in urine or blood ketones are not available), significant ketosis may not be necessary in all

| A | Case 1 | Protein (gm) | Fat (gm) | Net Carb (gm) | Fiber (gm) | Calories |
|---|--|-----------------|-------------|------------------|---------------|----------|
| | Homemade ketogenic dogfood diet | 24.19 | 19.73 | 2.85 | 1.31 | 310 |

| B | Quantity | Component |
|---|------------|--|
| | 17 grams | fatty lamb |
| | 1 | canned pumpkin |
| | tablespoon | blend of medium chain triglyceride (MCT) oil and virgin coconut oil |
| | 1 teaspoon | probiotic milk thistle |
| | 1 capsule | 1 senior dog vitamin |

C




FIGURE 1 Dietary intervention for Case 1. A, Macronutrient content of dietary therapy in a standard meal administered to Case 1 (Bo). Approximately 15% of the fat was MCT. Note that the ratio of fat: (protein + carbohydrate) is approximately 1:1, similar to that for a modified Atkins diet (MAD) prescribed to adult humans. All calculations based on KetoDietCalculator (www.ketodietcalculator.org). B, Measurements of components of the main homemade ketogenic recipe (~1:1 ratio) that was administered to Case 1. Portion sizes would need to be adjusted for an individual dog's daily requirements. C, Case 1, "Bo," an adult neutered mixed-breed dog with refractory epilepsy

cases (see Cases 2 and 8). Comprehensive daily records detailed food intake and medical/behavioral issues.

Disruption in the routine of Case 1 triggered a short relapse and loss of seizure control. Specifically, he was boarded for several days, returned with very loose bowel movements, and then refused to eat for 2 days while his owner was in the hospital. After administering his medication and oil supplement, Case 1 regurgitated, had a seizure 2 hours later, and two more episodes later that day. His diet was reverted successfully to the initial diet (Figure 1). However, daily phenobarbital was reduced gradually to 8 mg because of compromised liver function. This combination of diet and greatly reduced medication effectively controlled his bowel movements and seizures; no seizures occurred for the next 15 weeks. A different medical condition (urinary infection) and procedure (12 teeth removed) triggered another relapse (nine seizures in 8 weeks), an extended medical journey, and additional medications that were unsuccessful. Overall, the experience of Case 1 experience aligned with that of the human experience: illness, stress, and disruption of the diet affected seizure control and well-being significantly.

In terms of long-term follow-up, Case 1 continues to eat a 1:1 ratio "ketogenic" diet (Figure 1) and remains seizure-free for several months at a time; seizure-free periods are interrupted by a few days of (typically) 3 to 6 short tonic-clonic

seizures. Valium (diazepam), 10 mg, is administered after each seizure and the combination of diet and postseizure diazepam has reduced or eliminated visits to the emergency room. Although Case 1 continues to be prescribed an 8-mg maintenance dose of phenobarbital, switching to the diet greatly reduced his ongoing dose (by 80%), and his owners hope to eventually eliminate antiepileptic medications altogether. He is reported to be in excellent spirits and health between episodes.

3 | CASE PRESENTATION: CASE 2

The second case, Dante (Figure 2), was a neutered male husky who started having regular seizures with no known cause at 8 years of age. His past medical history is that he manifested with 5 tonic-clonic seizures prior to his diagnosis of epilepsy and also had frequent small myoclonic jerks. Once diagnosed, Case 2 was treated initially with 3 mg/kg of phenobarbital every 12 hours. Even this relatively low dose had significant intolerable side effects on behavior and physiology: he became lethargic, incontinent, and had no appetite. After 2 weeks the owners stopped the phenobarbital treatment and instituted a dietary change (Figure 2) that reduced commercial food consumption, added whole food

| A | Case2 | Protein (gm) | Fat (gm) | NetCarb (gm) | Fiber (gm) | Calories |
|---|--|--------------|----------|--------------|------------|----------|
| | Homemade dogfood recipe | 57 | 13 | 104 | 15 | 760 |
| | Overweight management commercial food (3 cups) | 54 | 13 | 107 | 33 | 760 |

| B | Quantity | Component |
|---|----------|---|
| | 1 cup | overweight management commercial food |
| | 1 cup | boiled rice (brown or white) |
| | 1 cup | protein (e.g. chicken, beef, turkey, tuna, salmon) |
| | 1 cup | organic low-sodium stock (chicken, beef or vegetable) |
| | ½cup | cooked/steamed vegetables (e.g. carrots, beans, broccoli, squash) |

FIGURE 2 Dietary intervention for Case 2. A, Macronutrient content of dietary therapy administered to Case 2 (Dante) as compared on an equal caloric basis with an overweight management commercial dog food. Macronutrient content was calculated using a mix of potential components (ie, 25% of each of the 4 potential vegetables) and, unlike Case 1, there was no significant portion of MCTs. Note that the homemade recipe was not higher in fat than the commercial recipe, and that the 2 diets have similar macronutrient content. All calculations based on KetoDietCalculator (www.ketodietcalculator.org). B, Measurements of components of the homemade recipe administered to Case 2. The diet controlled seizures and allowed flexibility in the whole food components. Note that this recipe was provided by the dog's owner, and portions would need to be adjusted for an individual dog's daily requirements. C, Case 2, "Dante," an adult male neutered husky who had severe side effects when administered seizure medication and experienced complete seizure control when adhering to the diet

components, and eliminated any additional carbohydrates and treats. His behavior improved immediately and his tonic-clonic seizures resolved. Within 1 month of starting the new dietary protocol, the frequent myoclonic jerks also resolved completely. Case 2's appetite and behavior were reported as excellent upon switching to the new diet. Unlike Case 1, Case 2 did not gain weight after changing to the new diet.

Based on calculated macronutrient composition (Figure 2A) this diet was not high in fat, not a ketogenic ratio, and not significantly lower in carbohydrates. It was, however, a more controlled diet with a high proportion of whole food components. Components were adjusted according to availability, and the owners indicated that gravy was added occasionally. Despite no marked shift in macronutrient

composition, the change in diet was highly beneficial and there was a clear relationship between the diet change and cessation of seizures.

Case 2 also provides an unexpected positive control of the relationship between diet and seizures: rare seizures occurred exclusively after well-intentioned family members fed him a carbohydrate-laden treat with a high glycemic index, for example, pizza crust. This reversal of seizure control parallels the clinical experience whereby a person on the ketogenic diet who inadvertently or purposefully ingests additional carbohydrates risks having an acute seizure.¹⁶ Loss of seizure control can happen within an hour of exposure to carbohydrates (including even small amounts ingested or absorbed in toothpaste and lotion; B.

Zupec Kania, unpublished results). In Case 2, additional carbohydrate had a clear cause and effect: when there were no lapses in diet, seizures did not occur.

Unfortunately, at age 10, Case 2 developed a spinal tumor, which resulted in the loss of hind limb function and ultimately took his life. Nevertheless, maintaining seizure control and optimal health with a homemade dietary protocol greatly increased his quality of life in his final years. His owners reported that it was easy to maintain, effective, and affordable.

4 | DISCUSSION

Herein we describe 2 case reports of canine epilepsy with reduced seizure frequency when transitioned to nonprescription, nonproprietary homemade diets. The diets differed in macronutrient ratio but both cases achieved a complete cessation of seizures for extended periods and greatly reduced or eliminated their daily dose(s) of medication. This contrasts with their experience (and that of other dog owners) reporting minimal seizure control and sometimes severe side effects—including permanent liver damage—with antiepileptic medications commonly prescribed to treat canine seizures. It is important to note that the cases presented were different/mixed breeds with different lifestyles and different characteristics of their seizure disorder, further suggesting that a dietary approach may be widely applicable. Neither case was supplemented with carnitine, and the MCT content was negligible for Case 2.

The medical journey of the first case is highly complex and variable, and thus it parallels the experience of some patients with epilepsy: multiple medications, side effects, tests, and medical visits.¹⁸ The experience of the dog's owners parallels the experience of parents whose child is treated successfully with a ketogenic diet after multiple failed medications and is a major positive aspect of his case, along with greatly reduced health costs. It is notable that for Case 1 a nonfat, liver-cleansing diet with fish and potato did not offer improved seizure control but a ketogenic diet did, suggesting that the high-fat ratio is important, and reducing (but not eliminating) the chance that the reported reduction in seizures was inaccurate, was a placebo effect (an important consideration in canine epilepsy studies¹⁹), or was due to the natural progression of the disease. However, this result may not be due to similar mechanisms as in humans given the difference in the metabolism of canines.¹¹ Inducing ketosis in dogs has been found to be much more difficult than in humans; however, this may elucidate other beneficial mechanisms of the diet in canines that have not been researched so far.¹¹ Case 1's history emphasizes the need for strict adherence to a therapeutic diet and, like in humans, highlights the ongoing risk of losing seizure control due to poor appetite, stress, illness, and disruption in routine.

The second case was treated with a homemade recipe that is more practical for most owners in terms of logistics and cost. It was not a “ketogenic” diet, and thus may be less effective for some dogs than it was for Case 2. The strength of this case, in addition to its practicality, and the dog becoming seizure-free without medication, is the clear relationship between the diet and seizure control, specifically the clear loss of seizure control with a lapse in the diet (ie, carbohydrate-containing treats). Anecdotally, Case 1's owners also reported that while in the process of researching his condition and customizing his diet, ingestion of a nonketogenic treat seemed to trigger a seizure event. Despite the difference in these 2 dietary therapies, collective evidence along with these cases suggests that there is a strong link between diet and epilepsy, but more research is needed to elucidate these mechanisms in canines.¹¹

Like in humans, canine epilepsy has been increasing in incidence.²⁰ Although the increase could be due partially to genetic predisposition and selective breeding—for example, shepherds, retrievers, and terriers have high rates of epilepsy^{21–23}—epilepsy in dogs is often idiopathic and is not a condition limited to purebred dogs. Lifestyle factors that influence seizures in dogs are similar to those that influence human epilepsy—diet, sleep, exercise, environmental toxins, and in utero environment, among others,^{20,23}—and therefore it is important to consider modifiable environmental factors in dogs. The diet-related improvements noted here are consistent with previous reports—including a randomized study—showing that changes in diet can reduce seizures and improve behavior.^{13–15}

The need for alternatives to current AEDs in dogs is underscored by their lack of efficacy in some cases and harmful side effects in others,⁴ including—as detailed in Case 1's report—liver damage from prolonged use of phenobarbital. In addition, AEDs can have adverse behavioral effects, as observed prominently in Case 2. The dietary approach did not produce either of these negative outcomes; dogs experienced good health and mood, a near or complete cessation of previously uncontrolled seizures, and relief from debilitating side effects caused by anti-seizure medication. Owners reported that making and administering the diet was manageable logistically, found it to be supportive of mental and physical health, and noted it was much less expensive than bills for veterinary services and seizure medications, all factors that owners consider important when caring for an animal.²⁴ This dietary approach also reduced or eliminated emergency room visits—a cost, health risk, and quality of life issue that is a concern common among dog owners, individuals with epilepsy, and human caregivers.²⁵ By preparing homemade meals, dog owners can personalize each treatment to form the most practical and effective diet for each dog.²⁶ Caution and medical supervision are advised to monitor physiologic responses such

as gastrointestinal or allergic reactions, metabolic changes, or vitamin deficiencies.^{7,26,27} These consequences can, in turn, impair everyday function and manifest in behavior. Dietary transition should be gradual, and the medical history and progression should be monitored closely.

5 | LIMITATIONS

Detailed urinalysis or blood work is not available due to the retrospective and noninterventional nature of these cases. Thus, the level of ketosis is unknown, and, as noted, ketosis is not always well correlated with antiseizure efficacy in humans, and ketosis levels in dogs do not appear to change considerably despite the beneficial effects.^{8,11} Based on this evidence and these initial reports, this may also be the case in dogs. Owners noted and described seizure events carefully over extended periods but did not use a standard tracking program. We note that the cases presented here are of male dogs, and we have no a priori information that dietary therapy would be ineffective in female dogs. We have found some sex differences in the behavioral (not seizure-reducing) effects of ketogenic diets in rodents,²⁸ but the efficacy of a diet-based approach in treating seizures is similar in male and female children and adults.^{6,29} Despite inherent limitations these cases reports add to the very limited literature on dietary therapy for canine seizures and provide healthy recipes that can be made at home. Reducing costs and emergency room visits is a common goal for patients and caretakers.

6 | FUTURE DIRECTIONS

Together these case reports highlight the potential of dietary therapy as a treatment option for epilepsy in dogs. Moreover, the close social relationships between humans and dogs have mutual benefits in supporting changes that improve health and seizure control, and studying lifestyle-related changes in dogs housed in the community presents the unusual opportunity of a research model with a window into a “real-world” context, with lifestyle factors that mirror and share those of humans. A previous preclinical research study administered a ketone supplement to nonepileptic dogs,³⁰ and dogs with epilepsy may be a good model to test emerging nondiet ketone-enhancing strategies. Future standardized and placebo-controlled prospective work is needed to best develop canine-specific formulas for wider applications and to understand the key mechanism(s) whereby metabolic therapy works in dogs. Ultimately, canine studies using homemade diets and metabolic strategies could facilitate comparative and translational data and thereby improve epilepsy treatment and awareness.

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DISCLOSURE OF CONFLICTS OF INTEREST

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