



## Case Report

## Is there a role for diet monotherapy in adult epilepsy?

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## ABSTRACT

Ten adults were treated with ketogenic diet monotherapy for epilepsy. Four patients were naïve to antiseizure drugs (ASDs), and six previously tried and stopped ASDs. Of four treatment-naïve participants, two (50%) were free from disabling seizures on Modified Atkins Diet (MAD) monotherapy for >1 year. Two (50%) stopped. Four of six patients (67%) who had previously tried ASDs became seizure-free on diet monotherapy, and two experienced >50% seizure reduction. Side effects included amenorrhea, weight loss, osteoporosis, and hyperlipidemia. Diet monotherapy may be feasible, well-tolerated, and effective for adults with epilepsy who refuse pharmacotherapy and those for whom lifelong diet therapy is recommended.

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## 1. Introduction

Initial antiseizure drug monotherapy controls seizures in approximately half of patients with newly diagnosed epilepsy. Remission rates range from 63 to 84% in patients with focal epilepsy on monotherapy with 5 of the most common antiseizure drugs [1]. However, long-term retention is low because of side effects, ranging from 32 to 58% after 3 years [1]. Ketogenic diets are effective in approximately half of patients with antiseizure drug-resistant epilepsy [2–4]. The Classic Ketogenic Diet (KD; composed of a 4:1 ratio of grams of fat:carbohydrates and protein combined) is used in unique circumstances first-line or as monotherapy, for instance in patients with infantile spasms, Glucose Transporter Type 1 (GLUT1) deficiency syndrome, and children on ketogenic diets alone after seizures are controlled and antiseizure drugs have been successfully weaned [5,6].

The use of KD in adults is limited by restrictiveness [7]. Studies have shown successful compliance with a Modified Atkins Diet (MAD) [8,9], which also produces urine and serum ketones but without hospital admission, weighing foods, or calorie calculation [7]. As a result, epilepsy centers are beginning to offer MAD to adults [10].

Demand for access to ketogenic diets is increasing in adults with newly diagnosed epilepsy wishing to avoid antiseizure drugs, patients who have experienced adverse effects from antiseizure drugs and stopped, and patients that require lifelong antiseizure treatment. The

purpose of this study was to identify circumstances in which ketogenic diets are used first-line or as monotherapy to control seizures in adults.

## 2. Materials and methods

Adults (age ≥ 18 years) evaluated in the Johns Hopkins Adult Epilepsy Diet Center (AEDC) [10] from August 2010 to August 2016 were followed with written informed consent obtained from the patient or a legally authorized representative. Individuals with newly diagnosed epilepsy (two or more unprovoked seizures or one seizure and an EEG that captured epileptiform activity) who chose to avoid pharmacotherapy and adults with a history of uncontrolled epilepsy who tried and stopped all antiseizure drugs prior to the initial visit were assessed. Patients who were seizure-free for 1 year or more on no antiseizure drugs before starting diet therapy were excluded. Seizure classification was made using the current International League Against Epilepsy classification system and review of EEG and clinical data [11]. Baseline prediet seizure frequency was determined based on review of records in patients already on a ketogenic diet prior to the initial visit and by reviewing seizure calendars for 1 or more months prior to diet initiation for patients beginning a ketogenic diet de novo.

One participant on a 3:1 ratio ketogenic diet prior to the initial visit remained on the same ratio for the duration of the study. All other participants were prescribed a 20-gram per day net carbohydrate limit MAD. All participants recorded urine ketone body production (goal acetoacetate ≥ 40 mg/dL) biweekly, seizure frequency daily, and weights weekly [10]. Seizure frequency, diet compliance, side effects, and routine laboratory studies were assessed at 3- to 6-month intervals during routine outpatient visits.

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Descriptive statistics were used to represent patient characteristics and treatment outcomes. Proportions were based on all categorical variables. Means, medians, ranges, and standard deviations were calculated for continuous variables as appropriate.

### 3. Results

Of 201 consented participants, 10 were on no antiseizure drugs at the time of the initial visit and met inclusion criteria (Table 1). Four participants were naïve to antiseizure drugs (all female, ages 19–86 years at the time of the initial visit; median: 38 years). Six participants had previously tried one or more antiseizure drugs and stopped prior to the initial visit (3 female, ages 18–52 years at the initial visit). Of the four treatment-naïve participants (Table 2; Participants 1–4), three were diagnosed with focal epilepsy and one with juvenile absence epilepsy based on EEG findings and/or clinical history. Participant 3 was on a low-carbohydrate diet, and Participant 4 was already on a MAD prior to the initial visit, and the other 2 were diet-naïve. All participants were offered antiseizure medication by their outpatient neurologist but elected MAD as an alternative citing concern for potential side effects as their reason.

Two participants (1 and 2) began MAD but could not comply despite unlimited access to dietary counseling, did not achieve urinary ketosis (40 mg/dL), and did not have cessation of seizures. Participant 1 was lost to follow-up after 2 months. Participant 2 subsequently tried a Low Glycemic Index Treatment (LGIT) but could not tolerate the carbohydrate restriction of either the MAD or LGIT. Levetiracetam then lamotrigine at maximum therapeutic doses did not control seizures.

Two participants (3 and 4) became free of disabling seizures on MAD monotherapy. Participant 3 had late-onset focal epilepsy of unknown etiology (MRI and EEG unrevealing). She had 5 seizures in 3 years on a low-carbohydrate diet before being seen in the AEDC to initiate the MAD and complete seizure cessation after starting MAD, now seizure-free for 18 months (the longest seizure-free interval since seizure onset). Participant 4 began MAD independently following seizure onset because of a grade II right frontoparietal oligodendroglioma. Prior to starting MAD, she had focal sensorimotor seizures involving the left arm with or without altered awareness (mean: 4 per day) and had complete resolution of seizures with altered awareness and less frequent (mean: 1 per day) sensory changes that did not affect her daily activities after beginning the MAD (diet duration: 23 months).

Six participants previously tried one or more antiseizure drugs and stopped prior to the initial visit to AEDC (Participants 5–10). Three were naïve to diet therapy, and 3 were already on ketogenic diet monotherapy. Four (67%) became seizure-free on MAD monotherapy, one participant (6) had an 88% reduction in seizure frequency on MAD, and one (9) had a 99% seizure reduction on a 3:1 ratio ketogenic diet, compared with historical prediet baseline. Overall, mean diet duration

was 53 months (SD ± 64 months; range: 18–183 months). Of note, this included one participant (8) with a diagnosis of juvenile myoclonic epilepsy, whose seizures were previously well-controlled on valproic acid monotherapy with a breakthrough seizure 16 years prior in the setting of attempting to taper valproic acid. The patient elected to begin MAD and self-taper valproic acid prior to the initial clinic visit and remained seizure-free on MAD monotherapy at the time of study completion (diet duration: 22 months). Two patients with GLUT1 deficiency syndrome (Participants 9 and 10) were placed on ketogenic diet therapy, and antiseizure drugs were tapered prior to the initial visit.

Two women (Participants 1 and 4) on MAD developed amenorrhea, and one man (Participant 9) with GLUT1 deficiency on a classic ketogenic diet was diagnosed with osteoporosis and hyperlipidemia. Osteoporosis was diagnosed with Bone Densitometry (DXA) on transition to AEDC at age 19 years (after being on KD for 14 years), and he was referred to an endocrinologist and started on vitamin D supplementation, which he had not been on during the first 14 years of diet therapy, in addition to calcium and a multivitamin. Hyperlipidemia was present 2 years prior to transition to AEDC and improved (LDL decreased from 190 to 169 mg/dL, and total cholesterol decreased from 267 to 239 mg/dL) with reduction in the ketogenic ratio from 4:1 to 3:1 before transition to AEDC and switching from heavy cream to olive oil as a fat source after transition to AEDC. No patients reported chronic constipation, and one man (Participant 8) experienced intentional weight loss of 15 kg, while no significant weight changes were noted in other participants. Four participants were granted driving privileges by their state's Motor Vehicle Association.

### 4. Discussion

Approximately half of patients with newly diagnosed epilepsy respond to the first antiseizure drug tried [12]. Long-term retention rates are low, likely because of adverse effects [1]. As a result, a subset seeks alternatives to antiseizure drugs, of which ketogenic diets such as the Classic Ketogenic Diet or the Modified Atkins Diet may be a reasonable option. Two patient populations were studied, adults treated with MAD first-line, and those that had tried one or more antiseizure drugs previously but stopped, using diet therapy as an alternative. Both populations showed surprisingly good outcomes. Half of patients that tried MAD first-line remained free from disabling seizures following a year or more of diet monotherapy, and half stopped because of difficulty complying with the carbohydrate restriction and increased fat requirements. Two-thirds of patients that used ketogenic diet therapy as an alternative to additional antiseizure drug trials became seizure-free, and two had an 88% or greater seizure reduction. Average diet duration was over 4 years. Four patients have been granted driving privileges.

Two patients that became seizure-free on MAD carry the diagnosis of genetic generalized epilepsy (juvenile absence epilepsy or juvenile myoclonic epilepsy). Prior studies have demonstrated efficacy of the MAD in this patient population [13,14]. Three patients in these prior publications were on MAD monotherapy, and none achieved seizure freedom (two stopped MAD because of lack of motivation, and one experienced a 90% reduction in seizure frequency), so these new findings are encouraging. To our knowledge, this is the first study to report control of focal-onset epilepsy in adults on MAD monotherapy, which was achieved in half of participants with focal epilepsy who were compliant on MAD. One participant had an underlying primary brain tumor, and preliminary studies show that MAD may be beneficial in this population [15].

Side effects included amenorrhea, hyperlipidemia, osteoporosis, and intentional weight loss. The complex interactions between hormones and ketone production are not well-understood and warrant further investigation. Hyperlipidemia may be reduced by limiting or eliminating heavy cream and decreasing the fat ratio of the ketogenic diet. Early vitamin D and calcium supplementation may reduce the risk of osteoporosis.

**Table 1**  
Participant demographics.

	Diet first-line treatment	Diet after antiseizure drugs
N	4	6
Female, N (%)	4 (100%)	3 (50%)
Age at diet (years), median (range)	38 (19–86 years)	27 (6–52 years)
Age at seizure onset (years), median (range)	38 (10–83 years)	31 (2 months–51 years)
Seizure type, N (%)		
Focal or multifocal	3 (75%)	2 (33%)
Generalized	1 (25%)	2 (33%)
GLUT1 Deficiency Syndrome	0 (0%)	2 (33%)
Number of antiseizure drugs tried, mean, standard deviation (range)	0	4 ± 3 (1–9)
On diet at initial visit to AEDC, n (%)	2 (50%)	3 (50%)

GLUT1 = Glucose Transporter Type 1.  
AEDC = Adult Epilepsy Diet Center.

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