



Modified ketogenic diets in adults with refractory epilepsy: Efficacious improvements in seizure frequency, seizure severity, and quality of life

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ABSTRACT

Objective: This study evaluates the efficacy of a modified ketogenic diet (MKD) on seizure frequency, severity, and quality of life (QOL), as well as potential complications of MKD therapy among adults with drug-resistant epilepsy (DRE).

Methods: Changes in seizure frequency, severity, QOL, and side effects were retrospectively examined among adults, ≥ 17 years of age, with DRE (≥ 2 antiepileptic drugs [AEDs]), after 3 months of MKD therapy. Attention was paid to medication or vagus nerve stimulator (VNS) changes as well to evaluate potential confounders.

Results: A total of 60% ($n = 33$) of the 55 individuals reported $\geq 50\%$ seizure frequency improvement, 42 (76%) reported improvement in seizure severity, and 48 (87%) reported improvement in QOL. More patients following a modified ketogenic diet – 15 g net carbohydrate daily (MKD-15) (95%) compared with a MKD-50 (69%) reported improvement in QOL ($p = 0.02$). Weight among the entire sample declined from 77.5 (20) kg to 73.9 (19.0) kg ($p < 0.0001$), and total cholesterol (TC), low density lipoprotein (LDL), and total cholesterol:high density lipoprotein (TC:HDL) increased significantly ($p = 0.03$, $p = 0.04$, and $p = 0.02$, respectively). Free carnitine values were available for a select number of patients, 26 (47%) at baseline, and 7 (13%) at follow-up, of which 8 (31%) at baseline, and 2 (29%) at follow-up had carnitine deficiency (< 25 nmol/mL). Constipation was noted in 5 patients (9%), and no kidney stones were reported during the study period. There were no statistical differences in number or dose changes for AED or VNS during the study period.

Significance: Modified ketogenic diet therapies reduce seizure frequency and severity and improve QOL among adults with DRE with few side effects outside of weight loss, a desired outcome among many adults with DRE. More restrictive MKDs may offer improved seizure severity and QOL. Modified ketogenic diet therapy increases LDL cholesterol, which may be cardioprotective if related to an increase in LDL particle size with high saturated fat intake; however, more research is needed examining LDL particle size changes among those receiving MKD therapy.

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1. Introduction

Ketogenic diet (KD) therapy aims to reduce glycolysis and shift human metabolism to the use of fatty acid and ketone bodies for energy [1,2]. The use of ketogenic and modified ketogenic diets (MKDs), including the Modified Atkins Diet (MAD) and the low glycemic index treatment (LGIT), has increased over the past several decades. However, the majority of the available evidence supports the efficacy of these diets in improving seizure frequency, with few reports describing

other effects, such as those on seizure severity, quality of life (QOL), or lipid metabolism.

Not surprisingly, QOL is significantly worse in patients with drug-resistant epilepsy (DRE) [3–6]. While reduction in seizure frequency is a primary goal, researchers have reported that seizure frequency may not be correlated with QOL [7,8], and seizure severity has been found to negatively impact QOL [9]. The burden of antiepileptic drugs (AEDs) has been found to be a major determinant of poor QOL [7,8,10,11]. To achieve seizure freedom, high doses of AEDs are often prescribed, though is only successful in approximately 5–10% of patients [3].

Ketogenic diet therapy has demonstrated efficacy in reducing seizure frequency by $\geq 50\%$ by approximately 45% of adults following KD and MKDs [12,13]. Additionally, researchers have reported improvement in seizure severity [14–16] and QOL [15,17,18], despite the perceived restrictiveness of the diet, with the first anecdotal mention of this in the 1930s [19].

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Weight loss is a side effect of KD therapies [15,17,20–22], which among adults, may be beneficial and potentially contribute to improvements in QOL. However, concerns that KD therapies may worsen serum cholesterol concentrations may limit its use among adults because of concerns for increased risk of cardiovascular disease (CVD). Few researchers have reported the effects of KD therapies on serum lipids among adults with DRE [15,17,20,21], generally finding increases in low density lipoprotein (LDL); though this may be an initial response to KD therapies as the effect appears to lessen with prolonged use [22, 23]. Recent reports have highlighted the impact of diet composition on long-term markers of CVD risk and mortality, indicating potential benefit from carbohydrate restriction and a higher proportion of energy from fat [24–26].

This study evaluates the efficacy of a MKD on seizure frequency, severity, and QOL, as well as potential complications of MKD therapy among adults with DRE.

2. Methods

This study was approved by the Institutional Review Board of Rush University Medical Center. Data for this retrospective study were obtained from an ongoing quality improvement initiative at the Clinic for Dietary Treatments of Epilepsy at the Rush Epilepsy Center. Adults (≥ 17 years) with DRE (defined as greater than or equal to two AEDs prior to MKD therapy [27]), with baseline and approximately three-month follow-up appointments at the clinic between October 2012 and April 2016, who were deemed compliant with the MKD were included.

Data obtained at baseline and three-month follow-up visits included the following: demographics (gender, race, age at MKD initiation), anthropometrics (height and weight), seizure type, AED type and dose, and changes to either during MKD therapy, history of vagus nerve stimulator (VNS) placement prior to MKD and VNS setting changes made during MKD therapy, seizure frequency, fasting serum lipid panels and carnitine levels, as well as changes in seizure severity and QOL at follow-up. Incidence of constipation and kidney stones were assessed at follow-up. Compliance was determined based on multiple-pass 24 h diet recalls conducted by the Registered Dietitian Nutritionist (RDN) using validated techniques [28], excluding those with daily consumption of ≥ 75 g net carbohydrates. Noncompliance (≥ 75 g net carbohydrate per day) was chosen based on a 25% leeway on the upper end of LGIT therapy allowing for 60 g total carbohydrate daily [29]. Self-reported urinary ketones were documented for many patients; however, neither serum nor urinary ketones were used as an indicator of compliance due to self-reported nature, and because those following MKD-50 many not be expected to achieve positive ketosis [29,30].

At the initial visit, prior to starting a MKD, all patients attended a group education class and received personalized MKD goals from the RDN. They were seen by both the RDN and epileptologist at baseline and three-month follow-up intervals. Modified ketogenic diet education targeted 15 g net carbohydrate (MKD-15) and 50 g net carbohydrate (MKD-50) with personalized protein (1 g/kg dosing weight using either actual or adjusted weight using a 25% adjustment factor), and fat goals. Both protein and fat goals were provided in grams per day, as well as standard household measurement techniques for ease of understanding.

2.1. Outcome measures

Primary treatment outcomes assessed at pre-MKD baseline and after approximately three months of MKD therapy (based on clinic availability) included 1) improvement in seizure frequency based on self-report at clinic visit and/or seizure logs when available (defined as $\geq 50\%$ improvement), 2) improvement in seizure severity (defined as self-reported decrease in duration or intensity), and 3) improvement in QOL

(defined as self-reported improvement in mood, alertness, memory, sleep, and/or attention).

Secondary variables of interest included the following: 4) type of diet, defined as MKD-15 or MKD-50 (determined by compliance with diet-recall at 3-month follow-up), 5) changes in weight (measured using standard techniques), 6) changes in fasting serum total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), and TC:HDL ratio, 7) frequency of free carnitine deficiency (<25 nmol/mL) [31], 8) frequency of constipation, and 9) nephrolithiasis (kidney stones) at follow-up.

2.2. Statistical analysis

Primary outcomes of improvement in seizure frequency, seizure severity, and QOL were reported as frequency and percentage. Diet type, number of AEDs, change in AED number, change in AED dose, and VNS were compared between patients with and without improvement using Mann–Whitney U test (for nonnormal continuous variables) and Chi-square or Fisher's exact test (for categorical variables). Weight loss and lipid profiles were compared between baseline and follow-up with paired t test and McNemar's test, and also between two types of diet MKD-15 and MKD-50 with two-sample t test. All statistical analyses were performed with SAS 9.4 (SAS Institute Inc., Cary NC, USA).

3. Results

A total of 74 patients were seen at baseline and follow-up visits, 55 of which met inclusion criteria; Fig. 1. The sample was primarily white (74%), female (73%), with a mean age of 38 years (range: 17–70 years). The majority of patients (89%) had focal epilepsy ($n = 49$). Time on the diet at the follow-up period ranged from two to seven months based on clinic availability. A total of 71% ($n = 39$) were following MKD-15 at follow-up, with the remaining 29% ($n = 16$) following MKD-50. Further description of seizure type, surgical interventions and brain imaging prior to starting MKD, and associated outcomes can be found in a companion paper.

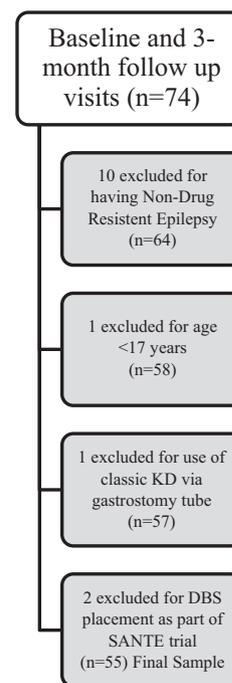


Fig. 1. Exclusion chart among adults with medically intractable epilepsy following modified ketogenic diet (KD) therapy. DBS: deep brain stimulator; SANTE trial: Stimulation of the Anterior Nucleus of the Thalamus.

3.1. Seizure frequency outcomes

A total of 60% (n = 33) of patients reported ≥50% improvement in seizure frequency. There were no significant differences in proportion of patients with ≥50% improvement in seizure frequency based on MKD type (MKD-15 versus MKD-50); [Table 1](#).

3.2. Seizure severity outcomes

A total of 76% (n = 42) reported improvement in seizure severity. Patients on the MKD-15 were more likely to have improvements in seizure severity compared with those on the MKD-50 (p = 0.04); [Table 1](#).

3.3. QOL outcomes

A total of 87% (n = 48) reported improvements in QOL. Those following MKD-15 were more likely to report improvement in QOL (p = 0.02) than those on MKD-50; [Table 1](#). Patients reporting improvement in QOL while on MKD had more AEDs at both time points than those who did not report improvement (3 versus 2 AEDs, respectively; p = 0.04), though number of AEDs did not change between baseline and follow-up.

3.4. Impact of AEDs and VNS on outcomes

Median (interquartile range (IQR)) number of AEDs prescribed at time of MKD initiation and follow-up was 3 (2) at both time points. A total of 85% (n = 47) of patients had no changes to the number of AEDs prescribed, 5% (n = 3) had an AED added, and 10% (n = 5) had a medication discontinued during the study period. A total of 64% (n = 35) had no AED dose changes during the study period, while 27% (n = 15) had a dose increased, and 9% (n = 5) had a dose decreased during the study period. However, they were no statistical differences in number or dose of AEDs based on changes in seizure frequency, severity, or QOL. A total of 35% of patients (n = 19) had a VNS in place prior to MKD therapy, and while 28% had adjustments made during the study period, there were no statistical differences based on changes in seizure frequency, severity, or QOL.

3.5. Weight loss outcomes

A total of 78% (n = 43) of the sample lost weight with a median percent weight loss at follow-up – 5.8% (7.1) (p < 0.0001), which was a median (IQR) loss of – 3.6 (4.9) kg (p < 0.0001); [Table 1](#). Those who experienced improvement in seizure severity lost more weight (p = 0.03) and had a higher percent weight change (p = 0.02) compared with those who did not experience improvement in seizure severity; [Table 1](#). Patients who lost more weight were more likely to have improvement in QOL (p = 0.03); [Table 1](#). There was no difference in percent

weight change based on diet type (MKD-15 versus MKD-50) at follow-up (p = 0.95); [Table 2](#).

3.6. Lipid profile outcomes

Among those with available laboratory values at both baseline and follow-up (n = 22), there was a significant increase in TC (p = 0.03), LDL (p = 0.04), and TC:HDL (p = 0.02) from baseline to follow-up; [Table 2](#). There were no significant differences in lipid values at follow-up based on diet type; [Table 2](#).

3.7. Incidence of carnitine deficiency, constipation, and kidney stones

Free carnitine values were only available for a select number of patients, 26 (47%) at baseline, and 7 (13%) at follow-up, of which 8 (31%) at baseline, and 2 (29%) at follow-up had carnitine deficiency (free carnitine <25 nmol/mL [31]). Although not assessed at baseline, constipation was noted in 5 patients (9%) at follow-up, and no kidney stones were reported during the study period.

4. Discussion

In addition to further demonstrating the efficacy for MKD to improve seizure frequency, this study is one of the first to report changes in seizure severity and QOL outcomes, while also reporting seizure type and number and adjustments to AEDs and VNS during MKD therapy among adults with DRE following MKD therapy. Our retrospective review demonstrates that MKDs are effective in improving seizure frequency, severity, and QOL among patients with DRE, while also aiding in weight management.

The results of this small, retrospective study are similar to those reported in recent meta-analyses [12,13] in that we noted an improvement in seizure frequency among adults on MKD therapy; however, in the current study, a large proportion of the sample (60%) with DRE reported ≥50% improvement in seizure frequency after the first three months of MKD therapy, with previous reports between 30% and 60% [12,13]. Our high percentage may be because noncompliance was an exclusion criterion in the current study. Compliance was determined based on 24 h diet recalls by the RDN, excluding those with daily consumption of ≥75 g net carbohydrates; this value was chosen based on a 25% leeway on the upper end of LGIT therapy allowing for 60 g total carbohydrate daily [32]. Individuals following a diet <75 g net carbohydrate per day would be expected to have lower blood glucose and an elevation in serum ketones; however, prior researchers have noted that some individuals fail to produce serum and/or urinary ketones despite diet compliance to the LGIT, which is similar to the MKD-50 [29, 30]. Neither the LGIT or MAD are specifically used at our institution; instead, MKD-15 and MKD-50 (with net carbohydrate intake of approximately

Table 1

Changes in seizure frequency, seizure severity, and quality of life after 3 months of modified ketogenic diet therapy among adults with intractable epilepsy based on diet type and weight changes.

	Total	p	Improvement in seizure frequency			Improvement in seizure severity			Improvement in quality of life		
			<50%	≥50%	p	No	Yes	p	No	Yes	p
Total sample n (%)	55 (100%)	–	30 (40%)	33 (60%)	–	13 (24%)	42 (76%)	–	7 (13%)	48 (87%)	–
Diet prescribed n (%)											
MKD-15	39 (71%)	–	14 (36%)	25 (64%)	0.33	6 (15%)	33 (85%)	0.04	2 (5%)	37 (95%)	0.02
MKD-50	16 (29%)		8 (50%)	8 (50%)		7 (44%)	9 (56%)		5 (31%)	11 (69%)	
Weight loss n (%)											
Yes	43 (78%)	–	18 (82%)	25 (76%)	0.77	8 (62%)	35 (83%)	0.13	3 (43%)	40 (83%)	0.03
No	12 (22%)		4 (18%)	8 (24%)		6 (38%)	7 (17%)		4 (57%)	8 (83%)	
Weight kg	73.9 (19.0)	<0.0001	70.6 (27.5)	71.0 (21.1)	0.87	70.3 (23.1)	71.8 (26.6)	0.49	65.3 (16.5)	72.1 (26.2)	0.36
Change kg	– 3.6 (4.9)	<0.0001	– 3.9 (5.9)	– 4.6 (5.2)	0.89	– 1.8 (4.2)	– 5.8 (4.3)	0.03	0 (7.3)	– 4.3 (4.6)	0.26
Weight change %	– 5.8 (7.1)	<0.0001	– 5.5 (7.0)	– 6.0 (6.7)	0.84	– 1.9 (4.7)	– 6.6 (4.6)	0.02	0 (9.0)	– 6.1 (5.5)	0.22

MKD-15: modified ketogenic diet – 15 g net carbohydrate; MKD-50: modified ketogenic diet – 50 g net carbohydrate; median (interquartile range (IQR)).

Table 2
Changes in weight and lipid profiles after 3 months of modified ketogenic diet (MKD) therapy among adults with intractable epilepsy.

	Total sample			MKD-15 (n = 14)			MKD-50 (n = 8)			p
	Baseline	Follow-up	p	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
Weight (kg) ^{ab}	77.5 ± 20	73.9 ± 19	<0.0001	76.3 ± 20.4	72.7 ± 19.5	−3.7 ± 5.3	80.6 ± 19.5	77 ± 17.9	−3.6 ± 3.8	0.95
TC (mg/dL) ^a	208.2 ± 54	228.1 ± 60.4	0.03	229.1 ± 54.2	256.6 ± 55.1	27.4 ± 45.2	171.5 ± 29.3	178.1 ± 28.9	6.6 ± 28.2	0.25
TG (mg/dL) ^c	75 (50)	73 (79)	0.21	72 (50)	65 (84)	1 (27)	82.5 (51.5)	80.5 (67.5)	3.5 (34.5)	1
HDL (mg/dL) ^a	60 ± 20.9	59.1 ± 23.2	0.74	66 ± 21.9	65.9 ± 25.8	−0.1 ± 14.1	49.4 ± 14.8	47 ± 10.7	−2.4 ± 10.0	0.69
LDL (mg/dL) ^a	130.9 ± 45.5	148.4 ± 58.7	0.04	144.6 ± 48.0	169.4 ± 61.3	24.8 ± 42.5	106.9 ± 29.8	111.6 ± 30.8	4.8 ± 25.0	0.24
TC:HDL ^c	3.8 ± 1.4	4.4 ± 2.2	0.02	3.5 (2.8)	4.0 (3.5)	0.4 (0.94)	3.1 (2.2)	3.6 (1.2)	0.3 (0.6)	0.44

^aMean ± standard deviation; ^bMKD-15 n = 39; MKD-50 n = 16; ^cMedian (IQR); TC: total cholesterol; TG: triglycerides; HDL: high density lipoprotein; LDL: low density lipoprotein.

15 or 50 g per day) with individualized protein and fat goals to offer more guidance were used.

Our approach to MKD is to focus on whole foods rich in fiber, vitamins, minerals, antioxidants, and prescribe personalized carbohydrate, fat, and protein goals to prevent over- and underconsumption of specific nutrients, including protein. Individualized MKD therapy may have also enhanced compliance by preventing excess protein and inadequate fat intake, both of which may reduce efficacy of KD therapies by reducing ketosis. Additionally, we feel our approach to providing specific protein recommendations, using a slight protein restriction (while still within the recommended daily allowance for protein intake in adults), may prevent excess protein intake, and be anti-ketogenic if consumed in excess of individual needs for normal health by way of gluconeogenesis. Additionally, it encourages focus on eating more nutrient-dense carbohydrates that provide phytochemicals and fiber (i.e., vegetables, nuts, and seeds). Excess protein intake has been associated with increased risk for long-term heart failure among men [33]. Although replacing carbohydrate with protein [32,34] and intake of sufficient protein (>0.7 g/kg/day) have been found to play a beneficial role in the prevention of cardiovascular and all-cause mortality among a population without epilepsy [35], the authors of this study found that among overweight men (body mass index (BMI): 26.3 ± 3.3 kg/m²), higher total protein intake trended toward increased risk of heart failure (p = 0.05), with a mean follow-up of 22.2 years, indicating that consuming a high protein version of ketogenic-type diets may increase cardiovascular risks long term. Median protein intake for those in the lowest quartile was 78.4 g/day versus the highest at 109.1 g/day. If extrapolated to the current population, an appropriate comparison as median BMI at baseline and follow-up for the current study would be 27.1 ± 6.5 and 26.1 ± 5.8 kg/m², this would be equivalent to a protein intake of approximately 1.0–1.4 g/kg/day. Classic KDs typically employ a protein restriction to approximately 0.8 g/kg/day [36], whereas the MAD and LGID do not typically restrict protein. We did not use dietary protein intake as an indicator of diet compliance in the current study, thus, it is possible that participants in the current study consumed higher than recommended amounts of protein. More research is needed to evaluate the impact of higher protein consumption on cardiovascular risk factors in the setting of low-carbohydrate, high-fat, ketogenic-style diets.

Seizure severity and QOL were clearly improved for the entire population, regardless of MKD type. A higher percentage (95%) of those following MKD-15 reported improvements in QOL versus 69% following MKD-50. This is the opposite of what may be expected as MKD-15 is more restrictive. More individuals following MKD-15 (64% vs 50% in MKD-50) reported ≥50% improvement in seizure frequency and seizure severity (85% vs 56%, respectively). Although neither outcome achieved statistical significance, these discrepancies are clinically relevant. It is possible that a higher proportion of individuals reported improvement in QOL when following the more restrictive MKD-15 because they experienced greater seizure frequency and severity improvements. We are not the first to report this improvement in seizure severity [14–16], which is generally described as improvement in seizure intensity or length, and is a factor that likely also impacts epilepsy-related QOL.

While the better response may be due to higher levels of ketosis that would be expected with a more restrictive version of the diet (MKD-15),

ketones were not routinely documented in the electronic medical record. It is also possible that those following the MKD-15 had a better response because of synergistic effects [1,2] with more restrictive KD therapies, or possibly a higher perceived benefit by the KD treatment team, thereby resulting in implementation of MKD-15 among patients with more frequent or bothersome seizures. The use of MKD-15 over MKD-50 for those with higher seizure frequency or severity may have increased the likelihood of observed benefit compared with those with milder epilepsy started on MKD-50. Additionally, in our study, compliance may have been overall better among those started on MKD-15 compared with MKD-50. The MKD-50 (similar to the LGIT but with more fat and protein guidance) may be viewed as the most liberal of the MKD therapies utilized for epilepsy, which may have resulted in higher rates of use of MKD-50 among those less able to adhere to more restrictive diets, such as MAD or MKD-15 in the current study. At our institution, MKD-50 is often utilized for those with limited baseline nutrition knowledge or ability to implement a restrictive diet, thus potentially leading to higher chance of errors in implementing the diet. Regardless, all patients included in this analysis were deemed compliant with either the MKD-15 or MKD-50.

Perhaps the multiple improvements found in the current study are due to the multiple, parallel synergistic mechanisms by which KDs cause an antiseizure effect, as KDs have also been found to exert an antiepileptogenic effect [1,2]. Thus, waiting to initiate MKD until after the individual has developed DRE (as has typically been done with KDs) may not only potentially increase the likelihood that the seizures may worsen, but also become more refractory to the effects of the diet similar to medications.

The side effects reported in the current study are similar to other reports with KD therapies among adults with epilepsy. Among those with epilepsy, MKDs are known to result in weight loss [17,19,22,23,29] and changes in lipid profiles [15,17,20,21], specifically, increases in LDL and reductions in TG, which is concerning as rises in LDL have long been linked to increased CVD risk [37–44]. Given the short duration and small sample sizes, it is helpful to compare with longer-term research examining CVD risk factors among the general public. Several large studies were published, generally reporting that compared with low-fat diets, low carbohydrate, higher fat (ketogenic-style) diets result in significantly greater weight loss, more favorable glycemic control and lipid profiles, and reduction in CVD risk factors [24–26]. Furthermore, high carbohydrate intake has been found to be associated with higher total mortality, whereas total and individual fat types were related to lower total mortality and not associated with myocardial infarction (MI), CVD or CVD mortality, and an inverse association with saturated fat intake and stroke [26].

Researchers have demonstrated that consumption of saturated fat decreases LDL receptor activity, protein, and mRNA abundance [45], which may explain the rises in LDL seen with high-fat, ketogenic-style diets. Interestingly, consumption of diets high in saturated fat has been found to result in higher total LDL concentration due to an increase in LDL particle size when compared with a low-fat diet [46]. This rise in large LDL particles may be cardioprotective as having high levels of small LDL particles has been associated with a twofold greater risk of developing coronary artery disease [37,38], MI [39], stroke [40] as well as

overall CVD [41], with small LDL particles being more strongly associated with risk than total LDL or large LDL particle size [41–44]. While rises in LDL are found with short-term use of KD therapies, there is insufficient evidence to conclude that the use of KD therapies increases CVD risks without further research on the impact on LDL particle size or long-term studies evaluating incidence of CVD with long-term KD therapy among patients with epilepsy.

Constipation was substantially less in the current study (9%) than that reported by prior researches among adults receiving MKD therapy at rates of 17% [47]. Our low rates of constipation at follow-up may be due to the heavy focus on importance of fiber from nutrient dense (fiber rich) vegetables, nuts, and seeds based on the structure of our diets (MKD-15 and MKD-50). Additionally, we did not assess reported constipation at baseline consistently, thus, we did not report the baseline values. It is possible that those reporting constipation at follow-up may have also had constipation at baseline.

There were no reports of kidney stones at follow-up, though it is possible that this is due to the short duration of the study period. One of the patients included in this sample did go on to develop kidney stones approximately 2 years into MKD therapy; however, was also receiving a medication that may increase risk for development of kidney stones.

In theory, low free carnitine may reduce efficacy of KD therapy due to the inability to efficiently shuttle fatty acids into the mitochondria for beta-oxidation. Low free carnitine values at baseline were higher than expected in the current study, for which patients received carnitine therapy of approximately 50 mg/kg/day until values were within normal limits. Interestingly, one of the two patients with follow-up low free carnitine values had normal values at baseline and was not on any AEDs known to deplete serum carnitine stores, while the other patient with low values at follow-up did not complete carnitine labs at baseline and was receiving valproic acid. Researchers have recently reported that higher baseline acetyl carnitine is positively associated with greater efficacy of KD therapy [48]; however, this analysis was not conducted in the current study because of limited availability of acetyl carnitine laboratory values. Future studies are needed to confirm this association.

Limitations of the current study are similar to those of most retrospective literature, including short duration, small sample size, lack of blinding or randomization or intent to treat analysis, lack of control group, and self-reported data—which are comparable with most KD research. Blinding is extremely difficult in nutrition-based research for obvious reasons. Additionally, the retrospective nature of the current study limited the ability to use validated tools to assess seizure severity and QOL changes, as well as to evaluate the long-term efficacy, compliance, and potential side effects.

This study suggests several intriguing new findings among different populations of patients with epilepsy, as well as adds to the evidence that both MKDs, including the MKD-15 and MKD-50, are effective in improving seizure control and QOL in adults with DRE.

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Kelly Roehl authored an introduction to a ketogenic cookbook and received a one-time contract fee but does not receive royalties; she otherwise has no conflicts of interest. Jessica Falco-Walter and Bichun Ouyang have no conflicts of interest. Antoaneta Balabanov

has served as an advisory board member for SK Life Science, Inc. and Nutricia.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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