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Establishing an Adult Epilepsy Diet Center: Experience, efficacy and challenges

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ABSTRACT

Objectives: Over 250 medical centers worldwide offer ketogenic diets to children with epilepsy; however, access to these therapies has been extremely limited for adults until recent years. We examine our 5-year experience creating and implementing a dedicated Adult Epilepsy Diet Center designed to provide adults with epilepsy access to ketogenic diets.

Material and methods: Outpatients seen at the Johns Hopkins Adult Epilepsy Diet Center from August 2010 thru September 2015 age 18 years and older were enrolled in a prospective open-label observational study. Patients that also enrolled in ongoing clinical diet trials were excluded from this study. Participant demographics, diet type, urine and/or serum ketones, laboratory studies, seizure frequency, diet duration, reason for discontinuing diet therapy, and side effects were recorded. A subgroup analysis of participants that met International League Against Epilepsy (ILAE) criteria for drug-resistant epilepsy (DRE) and were treated de novo with a Modified Atkins Diet (MAD) was performed to compare outcomes with the current literature regarding efficacy of other antiseizure treatments for DRE.

Results: Two hundred and twenty-nine adults attended the Adult Epilepsy Diet Center, and 168 met inclusion criteria. Two-thirds (n = 113, 67%) were women with an age range of 18–86 years at the initial visit. Thirty-five participants (21%, n = 133) were already on a therapeutic diet while 79% (n = 133) were naïve to diet therapy at the time of the initial visit. Diet-naïve participants were typically prescribed MAD (n = 130, 98%), unless unable to intake adequate oral nutrition, in which case they were prescribed KD (n = 1) or a combination of oral MAD and ketogenic formula (n = 2). Twenty-nine of 130 (22%) participants prescribed MAD elected not to start or were lost to follow-up, and 101 (78%) began MAD.

A subgroup analysis was performed on one hundred and six participants naïve to diet therapy that met International League Against Epilepsy criteria for DRE, were able to tolerate oral nutrition, and were prescribed a MAD. Relative to the number of enrolled participants who had reliable follow-up results for a given duration (including those that ultimately elected not to start or were later lost to follow-up), at 3 months, 36% of these participants responded (≥50% seizure reduction) to diet therapy, and 16% were seizure-free. At 1 year, 30% responded, and 13% were seizure-free. At 4 years, 21% responded, and 7% were seizure-free.

Hyperlipidemia was the most common side effect (occurring in 39% of screened participants, including those on a therapeutic diet prior to the initial visit). Weight loss was also common (occurring in 19% of all participants treated with a ketogenic diet therapy) yet was often an intended effect.

Significance: This study, the largest series of adults with epilepsy treated with ketogenic diet therapies to date, provides evidence that ketogenic diets may be feasible, effective, and safe long-term in adults, although long-term adherence was limited and further adequately controlled studies are necessary to determine the efficacy of ketogenic diets in the treatment of adults with epilepsy.

1. Introduction

Although ketogenic diets are widely implemented for children (in over 250 medical centers worldwide) with drug-resistant epilepsy (DRE) and certain electroclinical syndromes [1], few epilepsy centers worldwide offer these therapies to adults [2,3]. New antiseizure drugs, devices for neurostimulation, and epilepsy surgery continue to be utilized for refractory epilepsy in the adult population. In addition, diet

Abbreviations: KD, ketogenic diet; MAD, Modified Atkins Diet; AEDC, Adult Epilepsy Diet Center.

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therapies may be perceived as restrictive for adults, especially the Classic (4:1 ratio of fat to carbohydrates and protein grams combined) Ketogenic Diet.

Recently, several circumstances have been identified in which the Classic Ketogenic Diet (KD) and other ketogenic diet therapies (Modified Atkins Diet (MAD) [4,5], Medium-Chain Triglyceride (MCT) Diet [6], and the Low Glycemic Index Treatment (LGIT) [7,8]) may be beneficial for adults. First, children on ketogenic diets transitioning out of pediatric neurology clinics require ongoing care by an adult neurologist and registered dietitian [9]. Second, many adults with DRE carry diagnoses of electroclinical syndromes for which diet treatments have been shown to be effective in childhood such as Rett syndrome [10,11], tuberous sclerosis complex [12], Lennox–Gastaut syndrome [13], and juvenile myoclonic epilepsy [14,15]. Third, adults with drug-resistant focal epilepsy who are surgical candidates but not ready to pursue surgery and adults who are not surgical candidates may be seeking an alternative to trying additional antiseizure drugs. Fourth, many adults wish to reduce antiseizure drugs because of side effects. Finally, recent retrospective studies have shown potential benefit of ketogenic diets in adults with refractory and super-refractory status epilepticus who may require long-term diet treatment after recovery, though prospective randomized trials are needed [2,16,17].

Several case series and reviews suggest that the efficacy of ketogenic diets in adults with epilepsy is comparable with that in children [2,3,18–31]. The largest retrospective study to date of the KD from 1930 reported results in 19 adolescents and 81 adults, including patients with both drug-naïve and drug-resistant seizures, of which 56% "derived benefit" [31]. A more recent prospective study of 12 adults treated with a 3:1 ratio ketogenic diet showed a response rate (≥50% seizure reduction) of 44% at 4 months [18] while another study of 9 adults reported completion of a 12-week diet treatment in only 2 participants; both of whom had a greater than 50% seizure reduction [25]. One prospective study examining the efficacy of the MAD in 30 adults showed that 47% achieved a ≥50% seizure reduction at one and three months and 33% at 6 months [20], and another prospective study of 18 adults reported a 28% responder rate at 6 months [22]. Despite these promising results with regard to efficacy, access to these diets remains limited worldwide, and concerns persist regarding adherence in adults.

Because of increasing demand, we created a multidisciplinary Adult Epilepsy Diet Center (AEDC) in 2010 in order to provide ketogenic diets to adults with epilepsy. The purpose of this study was to determine whether ketogenic diets are a feasible and efficacious treatment option when provided to adults as part of a multidisciplinary, outpatient clinic.

2. Methods and materials

Consecutive patients age 18 years and older seen in the Adult Epilepsy Diet Center (AEDC) at Johns Hopkins Hospital from August 2010 thru September 2015 and not eligible for ongoing clinical diet trials (NCT01796574, NCT01834482, or NCT02426047) were enrolled in this prospective, open-label, observational study. The study was approved by the Johns Hopkins Institutional Review Board. Written consent to participate in the study was obtained by all patients or a legally authorized representative for patients not capable of providing informed consent.

At scheduling, patients were mailed or e-mailed a packet of written instructions including a tracking calendar and were asked to record seizures daily (type and frequency) until the first clinic visit (1 or more months prior to the initial visit) to establish a baseline seizure frequency as part of standard clinical care. Patients already on ketogenic diets at the time of scheduling were also asked to record biweekly urine ketones prior to the initial visit.

At the time of enrollment, participants were scheduled for a 60-minute new-patient clinic visit with an adult epileptologist [MCC], followed by a one-on-one interview with a registered dietitian [BJH]. Medical records were reviewed, and participant interviews were conducted to determine seizure characteristics. Electroencephalography findings and neuroimaging were used to classify seizure types and electroclinical syndromes [32]. Medical records were also reviewed for any evidence of an underlying metabolic disorder that might be contraindicated [33,34] as well as cardiovascular risk factors, history of diabetes, nephrolithiasis, anorexia, pancreatitis, cholecystectomy, osteopenia/osteoporosis, and orthostatic hypotension, and at-risk patients were counseled regarding potential risks of exacerbation or recurrence. Baseline vital signs and laboratory studies were obtained per the AEDC protocol (Table 1).

Participants not already on a form of diet therapy at the time of the first visit and able to tolerate oral nutrition attended a group instructional session (typically 60–90 min) on how to begin and continue a 20 g per day net carbohydrate limit MAD per protocol (Table 1). Increased fat intake was encouraged, but a specific target number of fat grams per day was not prescribed. Participants were provided a manual containing a summary of the materials presented in the teaching session, recommended micronutrient supplements, shopping lists, sample menus, potential side effects and management, recipes, websites, and books for reference (Supplementary material).

Those participants who were unable to tolerate oral nutrition were prescribed a formula-based 4:1 ratio KD. Participants aged 21 years or younger were first started on KD with admission to the Johns Hopkins Pediatric Ketogenic Diet inpatient service (before establishing care in

Table 1
Johns Hopkins Adult Epilepsy Diet Center Modified Atkins Diet protocol.

Prediet
Nutrition evaluation
Height and weight, calculation of body mass index
Three-day food record to calculate prediet caloric intake
Food preferences/practices (ex. religious)/prior diets, allergies, intolerances, aversions
Laboratory evaluations
Comprehensive metabolic panel, complete blood count, fasting lipid profile, vitamin D
Antiepileptic drug levels (if applicable)
Urine calcium, creatinine, human chorionic gonadotropin (premenopausal woman)
Diagnostic studies
EEG/Epilepsy Monitoring Unit evaluation (if diagnosis is unclear)
MRI with epilepsy protocol (if applicable)
Screening for cardio- and cerebrovascular risk factors, history of nephrolithiasis
Prediet calendar of daily seizures, start and end of menses (premenopausal women)
Initiation
Diet prescription
20 g net carbohydrates per day (subtracting fiber) Modified Atkins Diet
Liberal fat intake to satiety
Daily multivitamin, calcium and vitamin D supplement (low carbohydrate brand)
Maintain adequate hydration
Monitoring (documented on a calendar)
Seizures daily
Urine ketones daily until reaching 40 mg/dL, then biweekly
Weights weekly
Start and end of menses (premenopausal women)
Follow-up
Clinic visits at 3 and 6 months then annually
Monitoring
Seizure frequency
Urine ketones
Food records/compliance
BMI changes
Side effects
Laboratory evaluations (annual unless otherwise specified)
Comprehensive metabolic panel, complete blood count, fasting lipid profile (at 3 months and more frequent if elevated)
Antiepileptic drug levels
Vitamin D, zinc, selenium levels, free and total carnitine levels
Diagnostic studies
Renal ultrasound (if nephrolithiasis suspected)
ECG (if history of heart disease)
Carotid ultrasound (if prolonged fasting lipid elevation)
Bone density scan (every 5 years, minimum)