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A Modified Atkins Diet Is Effective for the Treatment of Intractable Pediatric Epilepsy

Eric H. Kossoff, Jane R. McGrogan, Renee M. Bluml, Diana J. Pillas, James E. Rubenstein, and Eileen P. Vining

The John M. Freeman Pediatric Epilepsy Center, Departments of Neurology and Pediatrics, The Johns Hopkins Medical Institutions, Baltimore, Maryland, U.S.A.

Summary: *Purpose:* The Atkins diet may induce ketosis as does the ketogenic diet, without restrictions on calories, fluids, protein, or need for an inpatient fast and admission. Our objective was to evaluate the efficacy and tolerability of a modified Atkins diet for intractable childhood epilepsy.

Methods: Twenty children were treated prospectively in a hospital-based ambulatory clinic from September 2003 to May 2005. Children aged 3–18 years, with at least three seizures per week, who had been treated with at least two anticonvulsants, were enrolled and received the diet over a 6-month period. Carbohydrates were initially limited to 10 g/day, and fats were encouraged. Parents measured urinary ketones semiweekly and recorded seizures daily. All children received vitamin and calcium supplementation.

Results: In all children, at least moderate urinary ketosis developed within 4 days (mean, 1.9). Sixteen (80%) completed the 6-month study; 14 chose to remain on the diet afterward. At 6 months, 13 (65%) had >50% improvement, and seven (35%) had >90% improvement (four were seizure free). Mean seizure frequency after 6 months was 40 per week ($p = 0.005$). Over a 6-month period, mean serum blood urea nitrogen increased from 12 to 17 mg/dl ($p = 0.01$); creatinine was unchanged. Cholesterol increased from 192 to 221 mg/dl, ($p = 0.06$). Weight did not change significantly (34.0–33.7 kg); only six children lost weight. A stable body mass index over time correlated with >90% improvement ($p = 0.004$).

Conclusions: A modified Atkins diet is an effective and well-tolerated therapy for intractable pediatric epilepsy. **Key Words:** Atkins diet—Ketogenic diet—Epilepsy—Children.

The ketogenic diet is an effective medical therapy for intractable childhood epilepsy (1). Since its introduction in 1921, the ketogenic diet has not changed considerably (2). A medium-chain triglyceride oil diet was introduced in the 1950s to allow more carbohydrates, but this diet leads to bloating and abdominal discomfort (3).

The traditional ketogenic diet has drawbacks. It restricts calories and fluids, which requires weighing of foods. Protein is generally restricted to 1 g/kg/day, with the majority of remaining calories in the form of fat. In some parts of the world, especially eastern and southern Asia, the dependence on rice has made the diet difficult to administer (4). Although recent publications have debated the tradition of a 48-h fast at diet initiation, they still advocate a 3- to 4-day admission to educate families (5,6). Side effects of the diet include kidney stones, constipation, acidosis, diminished growth, weight loss, and hyperlipidemia (7–9). Although most of these side effects are manageable, often by increasing protein, dietitians rarely will permit less than a 3:1 ratio (fat: protein and carbohydrates).

In 2003, we reported our experience with using a modified Atkins diet in the treatment of six children and adults with intractable epilepsy (10). This diet has several advantages over the traditional ketogenic diet, most notably no restriction on protein, calories, or fluids. One key similarity is its ability to create ketosis.

METHODS

Patients, ages 3–18 years, with prior use of at least two anticonvulsants (AEDs) and at least three seizures per week, were included. All seizure types were permitted. No child with prior exposure to either the ketogenic or the Atkins diet was enrolled, nor were patients with known hypercholesterolemia, kidney dysfunction, or heart disease.

The protocol for this study is described in Table 1. Children were evaluated at baseline, and after 1, 3, and 6 months on the diet in the Johns Hopkins Hospital outpatient neurology clinic by both a physician (E.K.) and dietitians (J.M. and R.B.). Laboratory values were obtained

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Address correspondence and reprint requests to Dr. E.H. Kossoff at Jefferson 128, The Johns Hopkins Hospital, 600 North Wolfe Street, Baltimore, MD 21287-1000, U.S.A. E-mail: ekossoff@jhmi.edu

TABLE 1. *Modified Atkins diet protocol*

- Copy of Dr. *Atkins' New Diet Revolution* provided (20)
- Carbohydrates described in detail and restricted to 10 g/day for the first month
- Fats (e.g., 36% heavy whipping cream, oils, butter, mayonnaise) encouraged
- Clear, carbohydrate-free fluids not restricted
- Low-carbohydrate multivitamin (Unicap M) and calcium (Calcimix) supplementation prescribed
- Calendar provided to document seizures daily, urine ketones semiweekly, and weight weekly
- Medications unchanged for at least the first month, but changed if necessary to tablet or sprinkle (nonliquid) preparations
- Low-carbohydrate, store-bought products (e.g., shakes, candy bars, baking mixes) discouraged for at least the first month
- Children evaluated in clinic at 1, 3, and 6 months on the diet
- Complete blood count, complete metabolic profile (SMA-20), fasting lipid profile at baseline, 3, and 6 months; urine calcium and urine creatinine obtained at 3 and 6 months

at baseline and at 3 and 6 months. Carnitine and selenium levels were not obtained, nor were routine electrocardiograms (ECGs) performed. Urine ketones were measured by parents semiweekly.

Clinic visits were compensated by a grant from the Dr. Robert C. Atkins Foundation. This study was approved by the Johns Hopkins Committee for Clinical Investigation. Categoric data were analyzed by Pearson's χ^2 for independence of rows and columns. Means were compared with a Wilcoxon two-sample test. The significance level for all tests was $p = 0.05$.

RESULTS

Overall

Twenty children (11 girls) were enrolled and treated from September 2003 until May 2005. The mean age at diet onset was 8.1 years (range, 3–16 years). The average age at seizure onset was 3.5 years (range, 1 month–9 years). An average of 6.5 AEDs had failed before enrollment (range, two to 14); three patients had an operational vagus nerve stimulator (VNS). Children were receiving a mean of 1.8 AEDs at diet onset (range, none to four), and four patients were taking no medications. No patient had prior resective epilepsy surgery or a corpus callosotomy. Seizure frequency averaged 163 times per week (range, four to 470) in the month before diet initiation. Seizure types included multiple (10), absence (five), complex partial (three), atonic (one), and myoclonic (one).

Treatment duration

All but one of the 20 patients enrolled completed ≥1 month on the diet. Eighteen (90%) remained on the diet after 3 months, and 16 (80%) after 6 months.

Fourteen (88%) of the 16 children who completed the 6-month study chose to remain on the modified Atkins diet. To date, 11 (55%) remain on the diet, with a mean duration of 10.3 months (range, 7–14 months). One child was switched to the traditional ketogenic diet after 9 months because of perceived improvement during in the study during periods of higher levels of ketosis. No clinical change was found for the following 1 year.

TABLE 2. *Seizure reduction in patients remaining on a modified Atkins diet at 1, 3, and 6 months*

	1 mo (n = 19)	3 mo (n = 18)	6 mo (n = 16)
Seizure free	1 (5%)	3 (17%)	3 (19%)
>90% improvement	3 (16%)	2 (11%)	3 (19%)
50–90% improvement	10 (53%)	9 (50%)	6 (37%)
1–49% improvement	2 (11%)	2 (11%)	3 (19%)
No improvement	3 (16%)	2 (11%)	1 (6%)

Seizure reduction

Seizure reduction for children remaining on the diet is summarized in Table 2. With an intent-to-treat analysis, at 1 month, 14 (70%) had >50% reduction in seizure frequency, and four (20%) had >90% improvement. At 6 months, 13 (65%) had >50% improvement, and seven (35%) had >90% improvement. The average seizure frequency was reduced from 163 to 40 per week over the 6-month period ($p = 0.005$). Four patients became seizure free by 6 months. Four of the five patients with <50% improvement at 6 months chose to remain on the diet after the study period for reasons including medication reduction, increased alertness, and decreased seizure severity.

Seizure reduction improved over the 6-month study period. Of those patients followed up for 3–6 months, 10 (56%) of 18 had improved seizure control, and four (22%) of 18 maintained the seizure reduction noted after 1 month. The five children with absence epilepsy had a particularly good response, with four (80%) having a >50% reduction in seizures, and three had seizure-free periods of >1 month. Age at diet onset, age at first seizure, gender, initial body mass index (BMI), number of current and previously tried medications, and seizure frequency did not influence likelihood of a >90% improvement.

Ketosis

All children were at least moderately ketotic within 4 days of diet initiation (mean, 1.9 days; range, 1–4 days). Because urine ketones were not checked daily during this study, however, ketosis could have occurred even sooner. Fourteen (74%) had consistently large ketosis at the 1-month visit, but only four (29%) were able to maintain this level afterward. In the 10 patients with gradually decreasing ketones, seizures worsened in only two.

The presence of large ketosis at 1 month correlated with likelihood of >50% seizure reduction (12 of 14 children), when compared with children with moderate or less ketosis (two of five; $p = 0.04$). For all other periods, however, large ketosis was not predictive of better outcome. At 6 months, three of the five patients with zero to trace ketosis were >90% improved, and a fourth patient was 50–90% improved.

Medications

Ten families chose to reduce medications because of a diet-induced reduction in seizure frequency, three (30%) before 3 months, and the remaining seven afterward. In two of these 10 patients, seizures worsened as a result. One family increased the dose to the previous amount, with subsequent improvement; the second did not, remained on one AED, and seizures stabilized after 1 month. Four patients had their medication doses increased during this study, only one with subsequent improvement (lamotrigine). Three children were able to discontinue all AEDs. The mean number of medications was reduced from 1.8 to 1.4 over the study period ($p = 0.35$).

Restrictiveness

Eighteen families chose to increase carbohydrates to 15 g/day during the study; one increased to 20 g/day. Of these children, only one child had increased seizures as a consequence, and carbohydrates were reduced back to 10 g/day with resultant improvement. Eighteen children used low-carbohydrate prepared foods; five (28%) reported a subsequent increase in seizures.

Even at 15 g/day, finding creative recipes and meals was problematic for many parents. Many of the patients' families contacted each other independently and shared advice, support, and recipes at an Internet chat room. The family of one of the children recently created a website: http://www.atkinsforseizures.com.

Side effects

The mean weight was 34.0 kg at baseline and 33.7 kg at the 6-month visit ($p = 0.95$). Six children lost weight, with a median of 2.7 kg (range, 0.3–8.7 kg), three of whom were the heaviest in the cohort at baseline (range, 50.9–87.5 kg); 13 gained weight, with a median of 1.2 kg (range, 0.6–9.1 kg). Height increased in all but two of the 18 children with ≥3 months' follow-up; both were 13 years old at diet onset. The average height increased over the 3- to 6-month period from 131.1 cm to 133.9 cm, with both a mean and median increase of 2.0 cm.

BMI changed from a mean of 18.5 to 18.1 ($p = 0.84$). BMI-to-age percentile also did not change significantly, 65.4% to 64.4% ($p = 0.82$). A stable BMI over time correlated with outcome; all four children with a change in BMI <0.3 had >90% improvement (three seizure free) compared with three of 14 with a BMI change >0.3 ($p = 0.004$). Overall level of ketosis did not correlate with weight or BMI change.

Laboratory changes at baseline and at the last visit are listed in Table 3. No child had abnormalities of white blood cell count, hematocrit, or platelet count at baseline or during the study. The urine calcium-to-creatinine ratio was elevated above 0.2 in eight patients, and all were started on oral polycitrates to prevent kidney stones (7). Of note, clear fluids were encouraged throughout the study, and in no child did kidney stones develop. Significant constipation was reported in four (20%). One child was hospitalized overnight with acidosis after 2 weeks on the diet, but the diet was not stopped, and she remains on the diet to date.

TABLE 3. *Laboratory changes over time*

	Baseline	Final visit[a]	p Value
ALT	21 (6–41)	26 (10–59)	0.30
AST	27 (17–40)	28 (18–45)	0.54
Bicarbonate (CO_2)	23 (16–31)	22 (15–29)	0.36
Total protein	7.3 (6.3–8.0)	7.7 (6.8–8.5)	0.16
Blood urea nitrogen	12 (6–22)	17 (7–29)	0.01
Creatinine	0.5 (0.3–0.9)	0.5 (0.3–1.5)	0.92
Total cholesterol	192 (128–299)	221 (165–302)	0.06
High-density lipoprotein cholesterol (HDL)	65 (41–92)	69 (53–103)	0.79
Low-density lipoprotein cholesterol (LDL)	108 (54–201)	130 (79–211)	0.15
Triglycerides	82	84	0.56

Values reported as average mg/dl (range); ALT, alanine aminotransferase; AST, asparate aminotransferase.

[a]At the 6-month visit in 14 patients, 3-month visit in three.

DISCUSSION

A modified Atkins diet appears to be an effective and well-tolerated therapy for children with intractable epilepsy, based on results from this small, open-label prospective study. At the 6-month period, 65% had a >50% response, and 35% had a >90% response. A striking similarity exists to a large published prospective study of the traditional ketogenic diet, in which 51% had a >50% response and 32% had >90% seizure reduction, with an intent-to-treat analysis (11). Also in that study, 71% were able to stay on the diet for 6 months, similar to the 80% in this study.

This study raises important questions on the current use of the traditional ketogenic diet. The first is whether higher ratios with more fat, less protein, and fewer carbohydrates are truly necessary for efficacy. Our results also question whether ketosis is as important as previously reported (10,12). Eighty percent of children with a loss of large urinary ketosis over the study period did not lose seizure control, and the same percentage with trace or zero ketosis at 6 months were still improved. Preliminary efficacy of a low–glycemic index diet with lower levels of ketosis also suggests this may be accurate (13). Last, this study confirms that ketosis can occur rapidly without a fast (5,6).

Side effects overall were limited in this limited number of patients. Weight loss was minimal, except in patients who were significantly overweight at onset. A lack of change in BMI correlated with success. Although exact calories were not measured, this surprising finding is in contrast to the proposed mechanism of calorie restriction for the efficacy of the ketogenic diet (14–16). In no child did kidney stones develop, but in this limited study of 20 patients, the expected incidence with the ketogenic

diet (5.5%) would have been only one child (7). Although cholesterol increased slightly, the mean increase was 29 mg/dl over a 6-month period, exactly half of the reported increase with the ketogenic diet (58 mg/dl) (8).

This study has several limitations, which we hope to address in future studies. For example, detailed food records were not obtained to confirm that families were providing the specific carbohydrate amounts recommended. Specific calorie amounts were not recorded. In addition, no formal quality-of-life scales were used to measure the tolerability of this lifestyle change. Last, all seizure counts were recorded by home parental observation, and half the subjects had multiple seizure types with very frequent and occasionally subtle seizures.

We suspect that the Atkins diet will be useful for adolescents and adults previously offered the traditional ketogenic diet only sporadically (17–19). A study at our institution is currently evaluating a modified Atkins diet for patients older than 18 years with intractable epilepsy. In theory, a modified Atkins diet should also be helpful in patients unable to tolerate the ketogenic diet because of either restrictiveness or side effects. A modified Atkins diet may also be useful in centers with limited nutrition resources or abilities to admit children regularly for diet initiation. A modified Atkins diet, with its relative ease of initiation and maintenance, might be used for newer-onset, less-intractable epilepsies than those typically treated with the ketogenic diet.

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