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A randomized, crossover comparison of daily carbohydrate limits using the modified Atkins diet

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Abstract

The modified Atkins diet is a dietary therapy for intractable epilepsy that mimics the ketogenic diet, yet does not restrict protein, calories, and fluids. The ideal starting carbohydrate limit is unknown. Twenty children with intractable epilepsy were randomized to either 10 or 20 g of carbohydrates per day for the initial 3 months of the modified Atkins diet, and then crossed over to the opposite amount. A significantly higher likelihood of >50% seizure reduction was noted for children started on 10 g of carbohydrate per day at 3 months: 60% versus 10% ($P = 0.03$). Most parents reported no change in seizure frequency or ketosis between groups, but improved tolerability with 20 g per day. A starting carbohydrate limit of 10 g per day for children starting the modified Atkins diet may be ideal, with a planned increase to a more tolerable 20 g per day after 3 months.

Keywords: Atkins diet; Ketogenic; Carbohydrates; Intractable; Epilepsy; Children

1. Introduction

The modified Atkins diet is a nonpharmacologic therapy for intractable childhood epilepsy that was designed to be a less restrictive alternative to the traditional ketogenic diet [1,2]. This diet is started as an outpatient without a fast, allows unlimited protein and fat, and does not restrict calories or fluids. Early studies have demonstrated efficacy and safety [1,2].

As clinicians use this diet, a major unanswered question concerns the ideal starting daily carbohydrate limit. In children receiving the traditional ketogenic diet, carbohydrates are restricted to approximately 5–10 g per day; therefore, our modified Atkins diet used this limited amount [3]. However, 10 (50%) of 20 children in our prospective study increased carbohydrates to 15 g per day after the first month, and one child increased to 20 g per day after the fourth month [2]. Only one of these children reported a reduction in efficacy as a result, and none described decreased levels of urinary ketosis. In a study of a low-glycemic-index dietary treatment, carbohydrates were even less restricted, with efficacy noted at 40–100 g of low-glycemic-index carbohydrates per day, despite the majority having nearly no urinary ketosis [4].

This study was designed to identify the ideal starting limit of carbohydrates on the modified Atkins diet to maximize efficacy, ketosis, and tolerability. A crossover design was employed to evaluate carbohydrate amounts for both the overall population response and each individual child. In addition, we attempted to clarify typical calorie, fat, and protein compositions of children receiving the diet.

2. Method

A prospective, randomized, crossover study design was employed. The parents of the 20 children with epilepsy consented after an initial evaluation of their children in the Johns Hopkins Hospital outpatient pediatric epilepsy clinic by the primary investigator (E.K.). The study was approved by the Johns Hopkins institutional review board.

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Inclusion criteria included age 3–18 years, prior use of at least two anticonvulsants, and at least daily, countable seizures. No child with prior use of the Atkins diet for more than 7 days was enrolled, nor were patients with known hypercholesterolemia, kidney dysfunction, or heart disease. Patients significantly underweight (body mass index <3% for age) were also not included. No child who had recently used or was currently on the traditional ketogenic diet was enrolled; however, use of the ketogenic diet >1 year prior to enrollment was allowed.

Children were evaluated at baseline, 3 months, and 6 months on the diet in the Johns Hopkins Hospital outpatient neurology clinic by both a physician (E.K.) and dietitians (Z.T. and R.B.), with frequent contact via phone and e-mail at 1 month on the diet. Families confirmed their understanding of the study protocol at the end of the initial visit using a five-question quiz. A baseline complete blood count, fasting lipid profile, comprehensive metabolic profile (liver and kidney functions), and urine calcium and creatinine levels were obtained by the families. Families were asked to mail in a 3-day food record of typical prediet meals. Diet composition was analyzed using Food Processor for Windows, EHSA Research, Salem, OR, USA. Copies of *Dr. Atkins New Diet Revolution* [5] and *The CalorieKing Calorie, Fat and Carbohydrate Counter* [6] were given to all families.

Children were randomized to 10 or 20 g of carbohydrates per day in two equal groups. The diet was explained to families in an hour-long visit. All families were provided with a prescription for a carbohydrate-free multivitamin and calcium supplement. Although protein sources were not restricted, families were counseled to provide significant quantities of fats (e.g., butter, mayonnaise, oils, 36% heavy whipping cream) with all meals. A monthly calendar was provided, with instructions to document seizures daily, ketones (using urine dipsticks) semiweekly, and weight weekly. Low-carbohydrate products (e.g., shakes, candy bars, baking mixes) were not recommended for the initial month only.

During clinic visits, calendars and laboratory values were reviewed and changes in the carbohydrate limit and medications made by joint physician–parent decisions. Seizure improvement was compared with baseline and classified as seizure-free, >90% improvement, 50–90% improvement, and <50% improvement. Urine ketones were checked in children who were continent at the 3- and 6-month visits by the primary investigator (E.K.) as well as with documentation by monthly calendars. Repeat serum and urine laboratory test results were also obtained at the 3- and 6-month visits.

At the 3-month clinic visit, children were crossed over to the opposite carbohydrate amount. A return to the prior carbohydrate amount after 2 weeks was allowed by parental choice if seizures were reported as significantly worse with the change. Medication changes were allowed only after 2 weeks, if requested by parents. Families were subsequently asked, by phone or e-mail, which carbohydrate amount was the most tolerable, was the most efficacious, and led to higher urinary ketosis. At the 6-month clinic visit, the families were given the option to continue on the modified Atkins diet at their choice of carbohydrate amount with periodic visits to our center or to discontinue the diet.

Power calculation revealed a minimum enrolled patient number of 20 to show a response difference of 30% between groups, assuming a 40% early discontinuation rate. Categorical data were analyzed using the Fisher exact test, and medians were compared using a Wilcoxon two-sample test. Means were compared using a paired two-sample t test. The significance level for all tests was $P = 0.05$.

3. Results

3.1. Patient demographics

Twenty patients enrolled in the study. One family chose not to start their child on the diet after the initial consultation and consent, but was included in the analysis as intention to treat. Information on prediet patient characteristics for both groups is provided in Table 1. Etiologies included idiopathic (15), Rett syndrome (2), cortical dysplasia (2), and tuberous sclerosis complex (1). Thirteen (65%) had either generalized or multifocal epilepsy. There was no statistically significant difference between the treatment arms with respect to median age, gender, age at seizure onset, number of anticonvulsant drugs attempted, number of current anticonvulsant drugs, seizure frequency, seizure type, and baseline weight.

Table 1
Baseline patient demographics for each treatment arm[a]

	Initial 10 g of carbohydrate/day ($n = 10$)	Initial 20 g of carbohydrate/day ($n = 10$)	P value
Age	7.5 (4.0–15.0)	9.8 (3.0–16.0)	0.41
Age at first seizure	2.2 (0.3–6.0)	3.0 (0.5–11.0)	0.36
Gender (male)	6 (60%)	4 (40%)	0.33
Current anticonvulsants	2 (0–5)	2 (1–5)	0.27
Number of anticonvulsants attempted	6 (3–13)	6 (4–11)	0.85
Seizure frequency (per week)	41 (7–350)	55 (10–1050)	0.60
Seizure type (partial)	2 (20%)	5 (50%)	0.18
Baseline weight (kg)	27.1 (17.1–47.0)	27.3 (15.8–100.0)	0.97
Baseline body mass index	17.0 (13.6–21.2)	17.0 (13.8–32.6)	0.68

[a] Values are either medians (range) or numbers (%).

Four patients had been started previously on the ketogenic diet with no reported improvement, with the most recent 5 years prior to beginning the modified Atkins diet. Two were randomized to a starting carbohydrate limit of 10 g per day, and two to 20 g per day. All patients had reported minor improvement during the generally brief periods on the ketogenic diet, with no reported side effects. No child had previously attempted the modified Atkins diet.

3.2. Overall efficacy

Sixteen patients (80%) were on the diet at 3 months; 12 (60%) completed the 6-month trial. Using an intent-to-treat analysis, after 1 month, 10 (50%) had a >50% reduction in seizures, 1 of whom improved >90%. Seven (35%) had a >50% reduction at 3 months; 3 (15%) improved >90%. At the end of the 6-month study, 10 (50%) had improved >50%; and 7 (35%), >90%. Two children became seizure-free by 6 months. Of the 12 patients who completed the study, 9 (75%) decided to remain on the modified Atkins diet afterward. The median diet duration to date is 6 months (range, 0–22 months).

There was a slight trend toward reduced efficacy at 3 months for children with complex partial seizures, with 1 of 7 (14%) experiencing >50% seizure reduction compared with 6 of 13 (46%) with generalized seizures ($P = 0.18$). Similar to published evidence, 2 (40%) of 5 children with concurrent vagus nerve stimulation experienced >90% seizure reduction [7]. Of the four patients who had previously