Original Article

Efficacy of the Atkins Diet as Therapy for Intractable Epilepsy in Children

Seyed Hassan Tonekaboni MD•[1,2], Parvin Mostaghimi[3], Parvin Mirmiran[1], Ali Abbaskhanian MD[4], Fatemeh Abdollah Gorji[5], Mohammad Ghofrani MD[2], Fereidoun Azizi MD[1]

Abstract

Background and Aims: The ketogenic diet is an effective medical therapy for intractable childhood epilepsy. However, it has drawbacks in that it restricts calories, fluids and protein. The Atkins diet may also induce ketosis without those restrictions. Our objective was to evaluate the efficacy of a modified Atkins diet in children with intractable childhood epilepsy.

Methods: This clinical trial was conducted in 51 epileptic children aged 1 – 16 years with refractory seizures from Feb. 2004 to Oct. 2006. Outcome measures included seizure frequency and adverse reactions. Twenty-seven patients left the study for various reasons, leaving 24 who continued the Atkins diet for a minimum of three months. Carbohydrates were initially limited to 10 g/day and fats constituted 60% of the total energy requirement. All participants received vitamin and calcium supplementation.

Results: Following three months of treatment with the Atkins diet, 16 patients (67%) had >50% decrease in seizure frequency, and 6 (25%) had >90% improvement, of whom 5 were seizure-free. Mean seizure frequency after the first, second and third months of treatment were significantly lower than at baseline (*P* values <0.001, 0.001 and 0.002, respectively).

Conclusion: The Atkins diet can be considered as a safe and effective alternative therapy for intractable childhood epilepsy. Atkins diet was well tolerated in our patients with rare complications and it appears to demonstrate preliminary efficacy in childhood refractory epilepsy.

Keywords: Atkins diet, children, epilepsy

Introduction

Epilepsy is defined as two or more seizures of unknown cause. Despite the appropriate use of multiple anticonvulsants, 10% to 30% of children with epilepsy will continue to have seizures.[1,2]

Authors' affiliations: [1]Research Institute of Endocrine Sciences, Shahid Beheshti Medical University (SBMU), Tehran, [2]Department of Pediatric Neurology, Mofid Children's Hospital, Shahid Beheshti Medical University (SBMU), Tehran, Iran. [3]Department of Nutrition, Mofid Children's Hospital, Shahid Beheshti Medical University (SBMU), Tehran, Iran. [4]Mazandaran Medical University, Sari, [5]Clinical Research Development Center, Mofid Children's Hospital, Shahid Beheshti Medical University (SBMU), Tehran, Iran.
•**Corresponding author and reprints:** Seyed Hassan Tonekaboni MD, [1]Research Institute of Endocrine Sciences, Shahid Beheshti Medical University (SBMU), [2]Mofid Children's Hospital, Shariati Ave., Tehran 15468-15514, Iran. Telefax: +98-212-290-9559, Email: shtonekaboni@yahoo.com
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The ketogenic diet is an individually calculated and rigidly controlled high-fat, low protein, and low carbohydrate diet used for the treatment of difficult-to-control seizures.[3] This classic ketogenic diet, developed at Johns Hopkins, contains a 4:1 ratio of fats to carbohydrates. The amount of protein is adjusted such that approximately 90% of calories are derived from fat with total calories restricted to 75% of the recommended daily allowance.[4] In the Johns Hopkins Hospital protocol and in the German consensus protocol, patients are admitted to the hospital and ketosis is initiated by fasting.[5]

The Atkins diet also restricts carbohydrates, but unlike the ketogenic diet, it does not restrict consumption of calories or proteins. In the last few years there have been reports that the Atkins diet can induce ketosis and can be potentially used to treat seizures.[6]

The purpose of this study was to evaluate the clinical efficacy, adverse effects, and tolerability of the Atkins diet for refractory epilepsy in children.

Patients and Methods

For this study, 51 children, aged 1 to 16 years, who suffered from ongoing seizure disorders and referred to the Pediatric Neurology Clinic of Mofid Children's Hospital from February 2004 to October 2006 were enrolled. Treatment with at least three appropriate anti-epileptic drugs had failed to control seizures in all patients. Those with neurodegenerative disorders, brain neoplasm and children whose mothers were illiterate were excluded from the study.

This is a before and after clinical trial which was approved by the Ethics Committee of the Research Institute for Endocrine Sciences (RIES), of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

During the first meeting, the dietitian explained the Akins diet and the goals of the study to the families of participants, using simple comprehensible terms. Following parental agreement, they gave informed consent forms and subjects were enrolled in the study.

Prior to beginning the diet, parents of participants were asked to register the frequency of their child's seizures (number/day) for a period of one week in a diary. The Atkins diet was adapted to the cultural and financial status of the families. The diet was initiated with fats comprising 60% of recommended calories for age and ideal weight, protein 30%, and carbohydrates initially limited to 10 g/day; these proportions were then changed, according to patient status. The mother recorded frequency of her child's seizures for three consecutive months. Children were evaluated by both a neuropediatrician and dietitian, at baseline and after one, two and three months in the Mofid Pediatric Neurology Outpatient Clinic. Assessment of seizure control was based on the percentage in reduction of a patient's seizure frequency as recorded in the patient's seizure diary by the parents at each of the three visits, i.e. after the first, second, and third months.

Anti-epileptic drug therapy remained unchanged for at least the first three months, but if necessary, was changed to nonliquid preparations. Low carbohydrate multivitamins and calcium supplementation were prescribed for all children. Urinary ketones were measured once weekly, for the first two months, and lipid profiles were assessed at the end of the second and third months. The minimum follow up was three months and after that, if the diet was effective, the regimen was continued.

Data on seizure frequency, age of the child at the onset of epilepsy, age at time of initiation of the Atkins diet, length of time the child stayed on the diet, classification of seizures, medication profile, EEG pattern, brain imaging findings, demographic information, and results of serial biochemical analysis were abstracted from their files and diaries, and entered into an SPSS data base for analysis.

Differences in seizure frequency and other data were assessed using the non-parametric Wilcoxon and repeated measures test. The significance level for all tests was $P<0.05$.

Results

Of the initial 51 children enrolled for treatment, 27 left the study during the first few weeks because some of the families were unable to continue the diet or their children had minimal side effects. Therefore, the investigation continued with 24 patients, including 7 girls and 17 boys, who followed the diet instructions appropriately for a minimum of three months. At initiation of the Atkins diet, the average age of patients was 53.3±31.7 months (range 12 to 138 months). Syndromic classification of epilepsies included 66.7% symptomatic, 20.8% idiopathic, and 12.5% cryptogenic.

Seizure types included generalized tonic clonic in 8.3%, generalized tonic in 4.2%, myoclonic in 12.5%, complex partial seizure in 4.2% and the remaining patients (70.8%) had a mixed type seizure. Seventy-five percent of children had no prenatal complication, while 16.7% of them had birth asphyxia and one patient had neonatal hypoglycemia. For one child, no prenatal history could be obtained.

Twenty patients had a brain MRI, of which 45% of them were normal; 25% had generalized brain atrophy; in 25%, a focal lesion was found and in one (5%) case periventricular leukomalacia was observed.

Electroencephalography (EEG) abnormalities were high voltage slow wave discharges in 50%; sharp waves in 79.2%; spike wave in 33.3% and 16.7% of the patients had hypsarrythmia.

The mean seizure frequency of patients, before starting the diet, was 13.0±11.8 seizures/day (range

Table 1. Seizure reduction in patients maintained on the Atkins diet at 1, 2, and 3 months duration of treatment compared to baseline

	1 mo (*n*=24) (*P*<0.001)	2 mo (*n*=24) (*P*<0.001)	3 mo (*n*=24) (*P*<0.002)
Seizure-free	4(16.7)*	3(12.5)	5(20.8)
90 – 99%	1(4.2)	1(4.2)	1(4.2)
50 – 89%	9(37.5)	11(42.8)	10(41.7)
1 – 49%	4(16.7)	1(4.2)	0(0)
No improvement	6(25)	8(33.3)	8(33.3)
*Number in parenthesis denote percentage			

2 – 50/day). The mean seizure frequency at the end of the first, second, and third months of the Atkins diet was 7.2±10.7; 6.7±10.3 and 6.6±10.5; $P<0.001$, 0.001 and 0.002, compared to baseline (using the Wilcoxon test), respectively. Repeated measures were used to compare the four above observations, which showed significant difference in decrease in seizure frequency ($P<0.001$).

Seizure reduction for patients on the Atkins diet is summarized in Table 1. After three months, five (20.8%) children were seizure free; six (25%) children had over 90% reduction in seizures and 16 (66.7%) had over 50% reduction in seizures. In eight (33.3%) patients there was no improvement.

Mean serum cholesterol and triglyceride levels at the end of the first month were 227.38±81.59 mg/dL and 126±48.03 mg/dL, respectively.

No serious complication was observed during the trial; however, in some of the 27 patients who discontinued the diet, minor side effects such as nausea, vomiting, and loss of appetite were the probable causes. All of our patients took more than five antiepileptic drugs before starting the diet. Seizure classification was based upon seizure types. Definite syndromatic classification which needed more sophisticated laboratory techniques could not be applied. Urinary ketones were measured weekly during first two months, but assessment of serum concentration of ketone bodies (acetoacetate and beta-hydroxybutyrate) was not performed.

Table 2 shows different variables in our study (descriptive statistics) including age of onset of epilepsy, age of initiation of Atkins diet, sex, parent's education, epilepsy classification, brain imaging findings, electroencephalographic abnormalities, and previous anti-epileptic drug regimen and rate of decrease in seizure frequency, three months after starting the Atkins diet.

Discussion

This open label, prospective clinical trial has shown that the Atkins diet appears to be an effective and well tolerated treatment for children with refractory seizures. At the end of the third month, 66.7% of patients had >50% response, 25% had >90% decrease in seizure frequency and 20.8% were seizure free.

In the first prospective study of the efficacy of a modified Atkins diet for six months in 20 children with daily, intractable seizures, resistant to at least two anticonvulsants, Kossoff et al.[6] reported that 65% of children had >50% reduction in seizure frequency and 35% of patients had >90% seizure reduction, with 5% seizure-free. In this study, as seen in the present report, none of the demographic features had any correlation with a higher likelihood of seizure reduction.

A very similarly designed study from South Korea (14 children, aged 2 – 14 years) reported that 7 out of 14 had >50% reduction in seizure frequency and four (28.6%) of the patients became seizure-free at the three month evaluation. At six months, seven patients (50%) remained on the diet and five (35.7%) had >50% reduction in seizures, including three (21.4%) who became seizure free.[7] The dropout rate at six months in this study was similar to ours at the beginning of the Atkins diet.

In Kossoff's excellent review of eight prospective and retrospective studies conducted on the modified Atkins diet used in refractory epilepsy both in children and adults,[8] 45% of the patients had a 50 – 90% seizure reduction and 28% had >90% seizure reduction. The overall rate of seizure reduction in these studies was very similar to ours.

Table 2. Frequency of seizure reduction in patients remaining on the Atkins diet after 3 months, based on demographic, clinical and paraclinical data*

		Seizure-free	90 – 99%	50 – 89%	No improvement
Age at initiation of diet (years)	<2	4.2	0	4.2	4.2
	2-5	16.7	4.2	16.7	16.7
	>5	0	0	20.8	12.5
Age at convulsion onset (years)	<1	12.5	4.2	29.2	20.8
	1-2	4.2	0	8.3	8.3
	2-5	4.2	0	4.2	4.2
Sex	Female	12.5	0	33.3	25
	Male	8.3	4.2	8.3	8.3
Mother›s education	≤ High school diploma	16.7	4.2	25	25
	< BS	4.2	0	16.7	8.3
	≥ BS	0	0	0	0
Type of seizure	Tonic colonic	4.2	0	4.2	0
	Generalized	0	0	0	0
	Tonic generalized	4.2	0	4.2	0
	Myocolonic	0	0	0	8.3
	CPS	0	0	4.2	0
	Mixed	12.5	4.2	29.2	25
Type of epileptic syndrome	Cryptogenic	0	0	8.3	4.2
	Idiopathic	8.3	0	8.3	4.2
	Symptomatic	12.5	4.2	25	25
MRI findings	Normal	10	5	10	20
	Focal lesion	10	0	5	10
	Atrophy	5	0	10	10
	PVL◊	0	0	5	0
CT scan findings	Normal	5.3	5.3	21	15.8
	Focal lesion	0	0	5.3	0
	Atrophy	10.5	26.3	0	10.5
EEG findings	High voltage slow wave	12.5	4.2	16. 7	16.7
	Sharp wave	20.8	4.2	33. 3	20.8
	Spike wave	4.2	0	20.8	8.3
	Hypsarrhythmia	0	0	4.2	12.5
Drugs used before Atkins diet	2–0	0	0	0	0
	4–3	0	0	0	0
	≥ 5	20.8	4.2	41.7	33.3
Urinary ketones					
After 1 month	0	4.2	0	0	0
	+1	4.2	0	25	20.8
	+2	8.3	4.2	16.7	12.5
	+3	4.2	0	0	0
After 2 months	0	4.8	0	0	0
	+1	0	0	33.3	14.3
	+2	9.5	4.8	9.5	9.5
	+3	9.5	0	4.8	0
After 3 months	0	0	0	5.6	0
	+1	16.7	0	11.1	11.1
	+2	5.6	5.6	16.7	5. 6
	+3	5. 6	0	11.1	5.6

*No patient had 1 – 49% reduction in seizure frequency after 3 months, ◊Periventricular leukomalacia

A striking similarity exists between the results obtained by the use of the modified Atkins diet and the traditional ketogenic diet in an updated systematic review[9] on the use of the ketogenic diet in childhood epilepsy. Keene analyzed 26 studies, including 972 patients and found that after six months compliance with the ketogenic diet, 48.6% had >50% seizure reduction, of which 15.6% were seizure-free.

Based on previous meta analyses, the traditional ketogenic and the Atkins diets have almost similar effects in seizure reduction as we can conclude; however, the Atkins diet has several advantages over the traditional ketogenic diet, most notably its relative ease of initiation and maintenance with no need for hospitalization and no restrictions on protein, calorie, and fluids.

Despite our sample size being too small to reach a definite conclusion, we did not find any relation between the age of seizure initiation, age of beginning the Atkins diet, epileptic syndrome, brain imaging findings, EEG abnormalities, urinary ketone level, seizure form, and rate of decrease in seizure frequency. No such relation has been found in other studies investigating the Atkins diet.[6–8] Some authorities believe that certain epilepsy syndromes may be particularly well-treated by the traditional ketogenic diet, including infantile spasms, Dravet syndrome, tuberous sclerosis complex, and myoclonic astatic epilepsy (Doose syndrome).[10]

All our patients had urinary ketone evaluation two weeks after starting the diet. Because urinary ketones had not been checked daily during the research, ketosis could have occurred sooner. There was no relation between the urinary ketone levels and seizure reduction, which was similar to the Kossoff studies.[6,7]

This study has a few limitations. First, 27 of our 51 patients (53%) discontinued the Atkins diet during the first month of the diet; this dropout rate is higher than any other study which investigated the Atkins and traditional ketogenic diets. Kossoff had a 20% dropout rate in his pediatric patients[6] and 33% of his adult patients with intractable epilepsy discontinued the modified Atkins diet before the three month assessment point.[11] Sixty-seven (44.7%) out of 150 children with refractory epilepsy discontinued the traditional ketogenic diet within one year of initiation[12] and 23 of these 67 families discontinued the diet before three months; 33 of 67 parents who discontinued the diet believed the diet was ineffective, while 19 found it too restrictive; 13 others stopped because of illness and 2 discontinued for other reasons. Secondly, although we did not observe any side effects in our patients during a three month follow up, the long-term side effects of the Atkins diet in childhood refractory epilepsy have not been established, unlike the traditional ketogenic diet.[13]

The Atkins diet seems to be as effective as the traditional ketogenic diet in reducing seizures in children with refractory seizures. The Atkins diet does have some advantages over the ketogenic diet, most notably its ease of initiation and maintenance and no restriction or protein, calories, or fluids, thus making it an effective and tolerated therapy for refractory seizures in children. A longer follow up is required to document the potential side effects of the Atkins diet. Other limitations included the lack of assessment of lipid profiles before starting the diet and low number of children enrolled in the research.

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