RESEARCH ARTICLE

A MODIFIED ATKINS DIET FOR INTRACTABLE CHILDHOOD EPILEPSY

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Abstract

Objective

The aim of the present study was to evaluate the efficacy and tolerability of a modified Atkins diet for intractable childhood epilepsy.

Materials & Methods

Twenty one children with medically intractable epilepsy were enrolled in the study. Inclusion criteria were at least four seizures per month and a trial of at least three anticonvulsants without becoming seizure-free. The subjects received the diet over a 6-month period.

Results

Three months after diet initiation, 15 patients (71.4%) remained on the diet and 12 (57.1%) had >50% seizure reduction. Eleven patients (52.4%) completed the 6-month study and 8 (38.1%) chose to remain on the diet afterward. At 6 months, 9 patients (42.8%) had >50% seizure reduction. The diet was more effective in cryptogenic epilepsy (p=0.032). Most complications were transient and successfully managed by careful follow-up and conservative strategies.

Conclusion

The modified Atkins diet is an effective and well- tolerated therapy for intractable childhood epilepsy.

Keywords: Atkins diet, ketogenic diet,intractable epilepsy, children

Introduction

The majority of people with epilepsy become seizure-free with antiepileptic medications, but approximately 20-30% will have refractory epilepsy, i.e. seizures persist despite accurate diagnosis and carefully monitored treatment with antiepileptic drugs (1, 2). The chance of responding to medications falls dramatically after failure of two drugs (3). Non pharmacological approaches for children with uncontrolled epilepsy include epilepsy surgery, the vagal nerve stimulation (VNS) and diet therapies. Unfortunately, surgery and VNS are not easily available in developing countries; therefore, dietary therapies represent a potentially valuable adjunct to other epilepsy treatment.

The ketogenic diet (KD), which is a high fat, adequate protein and very low-carbohydrate diet, has been used for many years to treat intractable epilepsy in children. The KD has been shown to be effective in retrospective, prospective and randomized controlled studies (4-7). Since its introduction in 1921, the traditional KD has not changed considerably (8). The KD, however, seems to be difficult to introduce to older children and adolescents, and requires highly motivated parents in order to successfully maintain this very strict diet.

The Modified Atkins Diet (MAD) induces ketosis, but without fluid, calorie, or protein restriction, nor the requirement for fasting, food weighing or hospitalization (9). Recently, this diet was shown to be effective and well tolerated in children with intractable epilepsy (10-11).

The aim of the present study was to evaluate the tolerability and efficacy of treatment with the Modified Atkins Diet for six months in children and adolescents with medically intractable epilepsy.

Materials & Methods

Twenty-one patients were treated prospectively in a hospital based ambulatory clinic at Tabriz Children Hospital, Iran, from March 2006 to August 2008. The subjects were 21 children in the age range of 4-17 years, with intractable epilepsy. These children were experiencing more than four seizures per month which could not be controlled by any combination of three or more antiepileptic drugs (AEDs). Patients with evidence of metabolic disorders were excluded. Neuroimaging and electroencephalogram (EEG) findings were reviewed. The subjects were treated with the Modified Atkins Diet protocol (Table1) (11).

For statistical analysis, the etiologies were defined as cryptogenic or symptomatic, because a detailed classification would reduce the number of patients in each category and would reduce the statistical significance of each. Antiepileptic drugs were not changed during the diet. To measure the outcome, seizure control was assessed based on seizure calendars provided by the patients and parents. Efficacy was evaluated based on the comparison between the average monthly baseline seizure frequency (3 months before diet initiation) and seizure frequency after 6 months of using MAD. Control was optimal if patients achieved ≥90% reduction in seizure frequency and the diet was considered effective if seizure control was higher than 50%, compared to previous baselines. Because of natural fluctuations in these seizure disorders, improved seizure control had to be evident for more than 4 weeks.

Although EEG was obtained from all patients in the beginning of diet, response was determined only through seizure diary. Differences between proportions were statistically tested by Chi-square Fisher's exact test. All other numerical or quantitative comparisons were performed using student's unpaired t-test or Mann-Whitney U test. All values were two tailed and were considered statistically significant at $P \leq 0.05$ level. Oral and written informed consent was obtained from all families prior to the initiation of the study. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences.

Results

The 21 enrolled patients (11 males, 10 females) had a mean (±SD) age of 10.1(±3.8) years at the beginning of the diet and the mean age at seizure onset was 5.9 (±3.5), ranging from 0.2 to 13 years. The mean number of AEDs tried before diet initiation was 6.9 (±2.5). At diet initiation, every child was receiving at least two AEDs. Characteristics of patients are shown in Table 2.

Thirteen patients (61.9%) had cryptogenic and 8 patients (38.1%) had symptomatic epilepsy.

Efficacy and tolerability

Patients maintained on the Modified Atkins Diet for a mean of 5.1 (±3.3) months. Although the diet could be discontinued at parents' discretion whenever they felt the burden of the diet exceeded its benefits, we urged a trial of the diet for at least 4 weeks. Seizure outcome of the patients on diet is shown in Table 3.

One patient discontinued diet before the end of the first month. Six patients (28.6%) discontinued the diet within three months. However, a total of 10 patients (47.6%) discontinued the diet within 6 months and only 8 patients (38.1%) maintained on the diet beyond six months. Of the 21 patients, nine (42.9%) showed >50% reduction in seizure frequency after sixth months of diet. At the end of the 3rd month, the Modified Atkins Diet was more effective in patients with cryptogenic epilepsy (P=0.032). However, it was not significant at the end of the sixth month.

The major reasons for discontinuing the diet were being ineffective in 7 patients (33.3%) and strictness of the diet in 3 patients (14.3%). No patient discontinued the diet due to abnormal laboratory results or adverse effect of the diet. Significant constipation was reported in four (19%) patients but resolved with diet modification. No patient developed abnormalities of white blood cell count, hematocrit, platelet count, BUN, creatinine, liver

function tests, calcium, magnesium, phosphorus or uric acid. Two patients showed hyperlipidemia (cholesterol levels of 542 mg/dL and 615 mg/dl) within the first month, but it was transient.

Table 1: Modified Atkins Diet protocol

- Carbohydrates described in detail and restricted to 10 g/day for the first month with planned increases after 1 month to 15 g, then 20-30 g/day as tolerated based on seizure control
- Use of fats (e.g., 36% heavy whipping cream, oils, butter, mayonnaise) encouraged
- Cereal, carbohydrate-free fluids not restricted
- Low-carbohydrate multivitamin and calcium 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 (non-liquid) preparations
- Low-carbohydrate, store-bought (e.g., shakes, candy bars, baking mixes) discouraged for at least the first month
- Children evaluated in clinic after being on the diet for 1, 3, and 6 months
- Complete blood count, complete metabolic, creatinine, urea, liver function tests, uric acid, calcium, phosphorus, alkaline phosphatasis, fasting lipid profile and EEG evaluated at baseline, 3, and 6 months.

Table 2: Characteristics of the patients

Patient No	Gender	Epilepsy Onset (year)	Etiology of the epileptic syndrome	Age onset diet (year)	Number of previous AEDs	Diet time (months)	Concomitant AEDs at start
1	F	1.5	LGS-symptomatic post vaccinal (pertussis)	12.2	7	3	VPA-PB-CNZ
2	M	2.9	Symptomatic-Meningitis	5.1	5	3	TPM-VPA-CBZ
3	M	1.5	Symptomatic-Cerebral Palsy	5.8	9	2	PB-VPA
4	M	6.3	Cryptogenic	8.2	9	8	VPA-PRM
5	F	5.8	Cryptogenic	7.8	6	6	PB-VPA-CNZ
6	M	3.4	Symptomatic -Hypoxic ischemic encephalopathy	7.5	7	1	VPA-PB-LTG
7	F	8.6	Cryptogenic	11.4	9	6	CBZ-PRM-VPA
8	M	13.00	Juvenile Myoclonic Epilepsy	14.1	5	2	VPA-LTG
9	M	3.9	Cryptogenic	9.2	4	12	CBZ-CNZ
10	M	7.5	Cryptogenic	14.3	8	9	PB-VPA-CNZ
11	F	8.1	Cryptogenic	15.4	5	7	CBZ-PRM-VPA
12	F	10.10	Juvenile Myoclonic Epilepsy	13.3	4	8	VPA-LTG-ETM
13	F	6.7	Cryptogenic	9.00	6	7	CBZ-PB-CNZ
14	F	11.2	Cryptogenic	17.00	6	6	CBZ-PB-TPM
15	M	11.00	Symptomatic-encephalitis(HSV)	15.8	4	4	VPA-LTG
16	F	6.7	Crypotogenic epilepsy	9.2	7	10	PB-CBZ
17	F	2.9	Symptomatic- Cortical dysplasia	4.7	5	3	VPA-PB-CNZ
18	M	3.1	Symptomatic-Angelman syndrome	8.5	6	1	PB-NZP-LTG
19	M	0.2	LGS-symptomatic-Tuberosis Sclerosis	4.00	11	7	PRM-NZP-VGB
20	F	6.3	Cryptogenic	11.1	14	1	VPA-LTG-NZP
21	M	4.1	Myoclonic Astatic Epilepsy of Doose	7.9	8	1	PB-VPA-NZP

F: Female, M: Male, LGS:Lennox Gastaut Syndrome, HSV: Herpes Simplex Virus VPA: Valproic Acid, PB: Phenobarbital, CNZ: Clonazepam, TPM: Topiramate, CBZ: Carbamazepine, PRM: Primidone, LTG: Lamotrigine, ETM: Ethosuxamide NZP: Nitrazepam, VGB: Vigabatrine

Table 3: Condition of diet and seizure control of patients

Seizure Reduction	Duration of diet		
	At first month	At third month	At sixth month
	N=20(95.2%)	N=15(71.4%)	N=11(52.4%)
Optimal >90%	9(42.8%)	7 (33.3%)	7 (33.3%)
Effective > 50-90 %	6(28.6%)	5(23.8%)	2(9.5%)
ineffective < 50 %	5 (23.8%)	3(14.3%)	2(9.5%)

Discussion

The Modified Atkins Diet (MAD) was created at Johns Hopkins Hospital as an attempt to create a more palatable and less restrictive dietary treatment primarily for children with behavioral difficulties and adolescents in whom parents and neurologists were reluctant to start the traditional ketogenic diet (KD). Since there was only limited evidence that high ratios of calorie and fluid restriction, fasting, and an inpatient diet initiation were necessary for ketogenic diet (12-13), the MAD was designed to induce ketosis while providing similar foods but with unlimited quantities of fat and protein. Kossoff et al., 2003, first reported a case series of six children and adults with intractable epilepsy who were treated with the Modified Atkins Diet. Half of these patients showed at least a 50% reduction in seizures (10).

We showed that the Modified Atkins Diet could be a dietary alternative for the classic KD in children with intractable epilepsy. Six months after initiating the modified Atkins Diet, 52.4% of the patients remained on the diet and 42.9% experienced > 50% reduction in seizures.

Our overall results are similar to a study from South Korea on 14 children aged 2-14 years with intractable epilepsy, demonstrating that six months after the initiation of the diet, 50% of the patients remained on the diet and 36% experienced > 50% reduction in seizures (14). However, the first formal prospective study on the use of Modified Atkins Diet for epilepsy reported much better results since 80% of the patients were able to stay on the diet, 65% experienced > 50% response, and 19% became seizure- free after 6 months (11). Results of a study in Iran on 24 children with intractable epilepsy showed that three months after diet initiation, 67% of the patients had >50% decrease in seizure frequency which was more than our study. This finding could be explained by the longer duration of diet in our study (15). In a prospective open-label study on 30 adult patients with an age range of 18 to 53 years, 47% of the patients experienced >50% seizure reduction after 1 and 3 months of diet and 33% of the patients showed >50% seizure reduction after 6 months (16). Porta et al retrospectively compared the KD and MAD in 27 children with intractable epilepsy and concluded that both the KD and MAD had similar efficacy in children with intractable epilepsy in a 6-month period; however, the MAD was better tolerated (17). Although characteristics of the patients have not been predictive of diet response in most studies, we noted that patients with cryptogenic epilepsy had a better outcome (P=0.032).

Although the results of most studies regarding the efficacy of the Modified Atkins Diet as therapy for intractable epilepsy are average, the seizure reduction induced by the diet is similar to most trials of new adjunctive anticonvulsants for adults with intractable epilepsy with 33-47% of patients having >50% seizure reduction over the study period (18). Unfortunately, the costs and the lack of availability of the new anticonvulsants in developing countries can be problematic.

The most common reason for discontinuing the diet was neither the lack of acceptance (or tolerance) of the diet nor the difficulty of diet preparation, but because the diet was not sufficiently effective in 33.3% of our patients. If seizures substantially reduced (>50%), the probability

of remaining on the diet at 6 months was high. If seizure control was <50%, it correlated with a decreasing percent of patients remaining on the diet in the course of time. Virtually, most (80%) of those who remained on the diet for 6 months had >50% seizure control; and virtually all of those who had good seizure control remained on the diet.

The MAD appears to be tolerable with limited adverse effects in recent studies. The increase in total cholesterol, blood urea nitrogen and urine calcium/creatinine ratio have been previously reported but usually do not lead to diet discontinuation (11, 14, 19). In our study, two patients showed hyperlipidemia which was transient and successfully managed by careful follow-up and conservative strategies. Weight loss may occur in children and adults who are predominantly overweight and may be desired.

Unlike the KD, the long-term side effects of the MAD are not clear. Considering the increased protein and decreased fat content, it is possible that the risk of growth impairment, kidney stones, dyslipidemia, and gastroesophageal reflux be less compared to the KD.

It can be concluded that the Modified Atkins Diet is a safe and effective alternative therapy for intractable childhood epilepsy. This diet can replace the conventional KD, especially in older children and adolescents.

Conflict of interest

The authors have no relationship (including financial) with people or organizations that could pose a conflict of interest in connection with the present work (A modified Atkins Diet for Intractable childhood Epilepsy).

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