Treatment of refractory epilepsy with the modified Atkins diet

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ABSTRACT
The modified Atkins diet (MAD) is an alternative therapeutic diet for the treatment of drug-resistant epilepsy. It consists of a diet with 60% energy from fat, 30% from protein, and 10% from carbohydrates. The objective of this article is to present a series of nine patients diagnosed with refractory epilepsy of different etiologies treated with the MAD at our hospital. In our group of nine patients, results obtained were similar to those published by other authors, with adequate adherence, tolerance and response. Of all patients, two achieved a reduction of more than 90% in the number of seizures; four experienced a reduction of 50-90%; two had a reduction of less than 50% in seizure control; and only one patient did not respond to the MAD. No patient had an increase in the number of seizures, and the diet was well-tolerated in all cases.
Key words: *refractory epilepsy, modified Atkins diet, ketogenic diet, tolerance, effectiveness.*

http://dx.doi.org/10.5546/aap.2014.eng.348

INTRODUCTION

Refractory epilepsy is a condition that occurs in approximately 30% of all patients with epilepsy.[1] It is defined as the lack of response to two treatment schedules (adequate and well-tolerated), either as monotherapy or combined, so that patients are continuously seizure-free.

The classic ketogenic diet (CKD) is an alternative therapeutic diet that has been used for more than 90 years for the treatment of drug-resistant epilepsy.[2] The CKD may have an anticonvulsant effect by means of specific mechanisms of action on neurotransmitters and metabolites.[3] The CKD is a strict diet where 90% of energy comes from fat, occasionally leading to difficulties with compliance and adherence.[4]

The Atkins diet was developed in the 1970s by Dr. Robert Atkins for the treatment of obesity. It was formulated as a high fat diet with a variable carbohydrate intake depending on the patient's weight.

At the end of the 1990s, the modified Atkins diet (MAD) was developed, with an adequate calorie intake distributed as follows: 60% fat, 30% protein, and 10% carbohydrates, with no protein restriction, therefore making its adherence and tolerance easier for patients.[4-6] In 2008, the results of the first randomized, controlled study were published, which described the effectiveness of the ketogenic diet as a treatment for refractory epilepsy in the pediatric and adult populations.[7]

DESCRIPTION OF CASES

A series of cases of children with refractory epilepsy treated with the MAD at our hospital between January 2008 and December 2012 is presented. Medical records of nine patients with refractory epilepsy treated with the MAD were reviewed. Clinical characteristics of patients are described in *Table 1*. One of the patients had started the CKD and switched to the MAD due to intolerance. In all cases, patients were evaluated before starting the diet, including the nutritional history, a daily record of seizure type and frequency, a clinical and anthropometric exam, and a lab test panel. Follow-up was performed with scheduled visits at one, three and six months after starting the diet, where adherence, tolerance and the seizure diary were evaluated.

Treatment effectiveness was measured at six months after starting the diet by establishing the number of seizures suffered. Such clinical control was classified as follows: 1) *excellent control:* if seizure control was absolute (100%); 2) *very adequate control*: a reduction of more than 90% in the number of seizures; 3) *adequate control*: a reduction between 50-90% in the number of seizures; 4) *regular control*: a reduction of <50% in the number of seizures; 5) *no effect*: no change

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Conflict of interest: None.

Received: 3-27-2013
Accepted: 2-5-2014

in the number of seizures; and 6) *negative effect*: increased number of seizures.[8]

If patients showed a reduction of more than 50% in the number of seizures at six months, the diet was considered effective and they remained on it for two years; then patients were controlled at 12, 18 and 24 months. Those patients who did not show this reduction were immediately withdrawn from the diet.

Out of the nine patients, two had a very adequate control of seizures, four had an adequate control, two had a poor control, and only one had no response. No patients worsened compared to diet initiation. *Table 1* shows seizure characteristics for each patient and the absolute frequency of seizures prior to the MAD and at six months after having started it.

The response observed by type of epileptic syndrome was as follows:

- Of patients with focal seizures (six): one had a very adequate control, three had an adequate control, one had a regular control, and one had no effect; therefore, no significant difference was observed in seizure control in this group.
- Of patients with Lennox-Gastaut syndrome (two): one had a very adequate control and one had a regular control.
- The patient with Dravet syndrome had an adequate control of seizures.

Out of nine patients, six had seizure reduction of at least 50%. Patients who achieved a reduction in the number of seizures continued with no modifications observed in the different follow-ups over the two year treatment with the MAD.

Adverse events included weight loss, hypercholesterolemia, sporadic self-limited diarrhea, and hypokalemia. These events were reverted and none represented an indication for diet discontinuation (see *Table 1*).

Four patients are currently on the MAD and three completed two years on the MAD with no relapse after treatment discontinuation. Two patients were on the MAD for six months only because they showed no response; and diet compliance was adequate in all patients.

DISCUSSION

The Atkins diet was developed in the 1970s by Dr. Robert Atkins for the treatment of obesity. Since it was similar to the principles proposed by the CKD, but less stringent, the Johns Hopkins Epilepsy Center started using it for the first time in 2001 for drug-resistant epilepsy.

The first publications on the MAD are from 2003 and 2006,[5,7] and describe series of cases with a favorable effect on the control of seizures. In 2006,[5] a prospective study was conducted; it included 16 patients treated with the MAD, with a mean age of 6.5 years old. After six months on the MAD, the percentage of seizure control was evaluated. Results showed that 12 patients had a seizure reduction of over 50%, and of them, six had a reduction of over 90%. The effectiveness of the MAD was assessed in a recent publication of a double-blind study on patients with refractory epilepsy on the diet. Patients were randomly enrolled for three months on the MAD or on a normal diet; subsequently, results showed that the MAD had been effective in reducing the number of seizures with a few adverse events, with a statistically significant difference between both groups.[9]

The differences between the CKD and the MAD basically lay on their nutrient composition and, therefore, their tolerability. Fat intake in the MAD is 60%, while it accounts for 90% of total energy intake in the CKD. Unlike the CKD, no hospitalization is required in order to start the MAD. Foods are measured using carbohydrate tables, making it unnecessary to actually weigh foods, which should be strictly done with the CKD. Family members are trained on how to implement the MAD during outpatient visits. On the MAD, proteins are freely consumed, therefore preventing non compliance with the diet due to lack of satiety. The MAD can be a treatment option forthose patients (adolescents and adults) who cannot access a ketogenic diet center or who have behavioral disturbancesthat prevent them from starting or remaining on the CKD (lack of satiety, dietary transgression, anorexia).[8-13]

The MAD could be considered a second-line option for patients who showed poor adherence to the CKD (poor tolerance to calorie restriction) and who also comply with some of the previously described criteria, and for those patients who have epileptic encephalopathies,[13] such as West syndrome, Lennox-Gastaut syndrome, Dravet syndrome, and symptomatic focal seizures.

The implementation of both the CKD and the MAD requires a multidisciplinary medical team made up of nutrition and neurology specialists to adequately follow-up patients and to achieve an suitable treatment adherence.

In our group, nine patients had similar results to those published by other authors in terms of adequate adherence, tolerance and control of seizures. None of the patients had severe adverse

TABLE 1. *Sample clinical characteristics*

Case	Age (years)/sex	Type of seizure	Drugs	Monthly seizures before/after the MAD	Reduction in the number of seizures	Adverse events	Time on MAD
1	5 / Female	- Focal motor - Generalized (tonic-clonic)	Topiramate Levetiracetam Valproic acid	240/90	50-90%	No	2 years
2	12 / Male	Generalized - Atonic - Tonic - Atypical absence	Clobazam Lamotrigine Topiramate Levetiracetam Rufinamide	60/40 900/450	0-50%	Mild hypokalemia	2 years
3	20 / Female	- Focal motor - Focal, secondarily generalized	Levetiracetam Clobazam Felbamate Clobazam	150/30	50-90%	Weight loss, BMI= 23, previous= 26	Ongoing (total: 3 years)
4	20 / Female	Focal motor - Focal, secondarily generalized	Felbamate Lamotrigine	6/6	0%	Weight loss, BMI= 19, previous= 21	6 months
5	21 / Male	- Focal motor	Diphenylhydantoin Clobazam Oxcarbazepine	8/6	0-50%	No	6 months
6	15 / Female	Generalized - Myoclonic - Absence - Tonic-clonic	Valproic acid Levetiracetam	90/20	50-90%	No	Ongoing (total: 1 year)
7	15 / Female	Generalized - Atypical absence - Tonic-clonic	Phenobarbital Diphenylhydantoin Oxcarbazepine Lamotrigine Valproic acid	200/10	+ 90%	No	Ongoing (total: 1 year)
8	9 / Female	- Focal motor - Focal, secondarily generalized	Lacosamide Topiramate Phenobarbital Valproicacid	150/5 2/0	+ 90%	Weight loss BMI = 17, previous 20, diarrhea	Ongoing (total: 1 year)
9	17 / Male	- Focal motor	Phenobarbital Lamotrigine Clobazam Valproic acid Topiramate	20/8	50-90%	Increased cholesterol	Ongoing (total: 1 year)

events. Those patients who succeeded with the diet were able to complete the treatment after two years. No patients worsened during treatment.

We believe that the MAD should be considered a treatment option, especially in adolescents and adults with refractory epilepsy. ■

Acknowledgments

To Luis Panico, M.D., who introduced and promoted this treatment in Argentina, for his selfless and patient help.

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