RESEARCH ARTICLE

THE EFFECT OF THE KETOGENIC DIET ON THE GROWTH AND BIOCHEMICAL PARAMETERS OF THE CHILDREN WITH RESISTANT EPILEPSY

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Abstract

Objective

The aim of this study was to evaluate the effect of the ketogenic diet on the growth parameters of the children with resistant epilepsy.

Materials & Methods

A total of 36 children with resistant epilepsy who were 2 to 7 year old were put on the ketogenic diet. Their growth and biochemical parameters were studied at the beginning of the study and after 3 months.

Results

Weight decreased in all patients. Serum levels of hemoglobin, calcium, and blood sugar decreased significantly but remained in the normal range. Creatinine did not change, but BUN showed a significant increase.

Conclusion

We can lower the complications of ketogenic diets by using more unsaturated fat, more water, and more minerals.

Keywords: ketogenic diet, epilepsy, growth parameters, biochemical parameters, children

Introduction

Epilepsy means recurrent attacks with or without epileptic movements due to local or generalized discharges in the brain. According to the studies performed in this regard, the frequency of the single or recurrent epilepsies (except for the febrile convulsions) is about 5.2 to 8.1 in 1000 (1).

About 60% of the patients achieve control of their epilepsy with first drug therapy (2), About 10 to 20 % of the epileptic patients do not respond to the epileptic drugs in their therapeutic doses and are considered as those with resistant epilepsy which is defined when there is no response to at least 2 first-line anti-epileptic drugs (including carbamazepine, sodium valproate, phenytoin, Phenobarbital) and 2 second-line anti-epileptic drugs (such as benzodiazepines, vigabatrine, lamictal) within one or more years (2,3).

On the other hand, the side effects of these drugs are very annoying for the patients and their families. These side effects include some degrees of drowsiness, vertigo, hyperactivity, weight gain, learning difficulties, and mental power decrease (4).

During the past decades, it was discovered that using a high-fat and low-carbohydrate diet can cause sustained ketosis in patients that can control the epileptic convulsions (5,6,7). This was named the ketogenic diet. The fat level of this diet is about 3 to 5 times more than carbohydrates and proteins. In three fourth of the patients, this diet

controls the epileptic convulsions and in half of them, the convulsions completely disappear (4,8).

Electroencephalography of these children also shows a significant improvement (9). This method has been used in the neurology department of Mofid Children Hospital; however, since the fat level of this diet is high, changes in the total cholesterol, HDL, VLDL, LDL, and triglyceride ensue and as a result, the risk of cardiovascular diseases increase. Thus, better evaluation of the treatment is needed. Additionally, due to the little amount of water and liquids, kidney problems should be viewed as a probability. Some growth retardation due to the low level of calcium is also possible.

In this study, we evaluated the children with resistant epilepsy who were hospitalized and treated by the ketogenic diet in Mofid Children Hospital to assess the changes in their growth parameters.

Materials & Methods

In this study, a total of thirty-six 2- to 7-year old children with resistant epilepsy who had been on the ketogenic diet for at least 3 months were evaluated between April 1999 and September 2001. Those with acute or chronic diseases (including metabolic, cardiac, kidney, liver, or gastro-intestinal diseases), malnutrition (BMI $<5^{th}$ percentile for age and sex), less ducated parents (who could not correctly manage the diet), or the patients who did not follow the diet for at least 3 months were excluded.

Before hospitalization and after 3 months of follow-up, an electroencephalography and measurement of creatine phosphokinase (CPK), biochemistry lab tests, cholesterol, triglyceride, serum lipoproteins, and weight and height were performed. At each visit, morning height and weight (average of 3 measurements) was obtained using stadiometer (for height) and seca (for weight). On the day before hospitalization, the child had to eat low-carbohydrate foods, and prescribed drug(s) was changed to tablets if the patient was using the syrup form, according to the classic protocol of John's Hopkins University (10). The calorie needed was measured by the ideal body weight (70 to 75 kilocalorie /kg). Then, total calorie was measured by the ratio of 4 to 1 (fat to carbohydrate and protein). A total of 80% of the needed body daily calorie, was gained from the fat. The total carbohydrate used did not exceed 30 g/day and was not less than 10 g/day and one gram of protein per kilogram of bodyweight existed in the diet(8). Water was also limited in this diet. The amount of water used was 50 cc/day at the beginning of the diet which increased to 500 to 800 cc/day (65cc/kg at the most). The specific gravity of the urine did not exceed 1030.

The child fasted at the beginning of the diet for 24 hours execpt above mentioned amount of water. During this period, vital signs and plasma sugar, and urine ketones were measured twice daily. After losing 15% of the body weight and reaching a level of 3+ to 4+ of urine ketones, the food started from the third day.

On day one, 2, and 3, the daily meals were served 1, 2, and 3 times per day, respectively. All analyses were made using the SPSS statistical software package and a probability value of less than 0.05 was considered statistically significant. Data was expressed as mean ± SD. Paired-sampled T-test was used to compare variables before and three months after the ketogenic diet.

Results

Mean age of the patients was 4.1 years (range: 2 to 7 years). They included 14 girls (38.8%) and 22 boys (61.2%). Twelve (33.4%), 13 (36.1%), 6 (16.7%), and 5 (13.8%) patients had generalized tonic-clonic, myoclonic, partial, and mixed seizures, respectively. Comparison of the studied parameters before the initiation of the diet and 3 months later showed that weight, hemoglobin level, calcium, and blood sugar significantly decreased (Table). Mean height growth velocity was 2/5cm per year that showed a decrease in comparison with the normal growth velocity chart for age (-1/6 ±1/7 SDscore; mean ± SD). Patients' height, serum creatinine, and LDL/HDL and total cholesterol/HDL ratios did not change significantly, but the levels of cholesterol, VLDL in all patients, and BUN in some of them significantly increased (Table1).

Table1. Changes of the Biochemical and Growth Parameters of the Patients with Resistant Epilepsy Receiving the Ketogenic Diet

Change / Parameters	At the beginning of the study	3 months after the study	P value
Height	101.8 ± 11.7	102.4 ± 11.75	0.095
Weight	17.07 ± 5	16.4 ± 4.9	0.011
Hemoglobin	11.8 ± 1.18	11.3 ± 1.08	<0.001
Calcium	9.36 ± 1.08	8.7 ± 0.72	<0.001
BUN	13.4 ± 4.1	16.2 ± 3.2	<0.001
Creatinine	0.59 ± 0.22	0.72 ± 0.13	<0.01
Cholesterol	92.7 ± 12.3	221.6 ± 24.5	<0.001
Triglyceride	95.6 ± 14	463.4 ± 91.9	<0.001
VLDL	18 ± 3.1	92.9 ± 21.2	<0.001
LDL/HDL	1.7 ± 0.6	3.2 ± 3. 3	0/002
Cholesterol/HDL	4.5 ± 0.5	5.5 ± 0.64	0/003
Blood sugar	87.8 ± 17.3	59.4 ± 8.7	<0.001

Discussion

Since 70 years ago, the ketogenic diet has been tried as a treatment in children with drug-resistant epilepsy and is used by many pediatric neurologists nowadays (11, 12, 13). In one study, 60% of the patients became seizure free, and another 35% benefited from a halving in their seizure frequency. Although many studies have proved the efficacy of this diet in the treatment of drug-resistant epilepsy, it is used as the last mode of treatment because of its limitations including the problems of supplying food articles and its unknown side effects. However, it is quite efficient especially in developing countries where supplying epileptic drugs confronts economical problems. On the other hand, there are some side effects including constipation, hypotonia, and spasticity. Kidney calculi and loss of appetite are seen in less than 5 to 10% of the patients. Starting the diet at a younger age is accompanied by hypercalciuria and higher risk of calculus formation (14) The diet may be accompanied by gastrointestinal reflux, low grade acidosis , hypoglycemia (6) bruising, small bleedings in younger ages, increased bleeding time, low platelet aggregation, increased long-chain fatty acids, increase or decrease in carnitine, prolonged QT period, and increased liver function tests (15,16,17,18).

Use of this diet is prohibited in patients with acute intermittent porphyria and seizure, mitochondrial dysfunction, and use of drugs such as topiramate which results in dehydration and acidosis (10).

According to our results, the patients' height did not statistically change but their mean weight, hemoglobin, calcium, and blood sugar levels decreased significantly. Significant increases were detected in the level of cholesterol, triglyceride, VLDL and the LDL/HDL and cholesterol/HDL ratios. Thus, this treatment, in the long time, may be associated with the risk of cardiovascular diseases. However, in other studies, no significant increase was observed in the level of patients' cholesterol which is possibly due to the use of unsaturated fats in their setting. Thus, more evaluation of the treatment is needed. In another study performed in United States, 21 children on the ketogenic diet were evaluated between 1994 and 1996. In a 6-month follow-up, no significant change was detected in the level of hemoglobin, calcium, creatinine,

and cholesterol of the patients but a significant increase was detected in the height and weight of the cases and a significant decrease in the blood urea nitrogen (18).

It can be concluded that some minerals such as iron and calcium could not be completely obtained by our patients in our center, probably due to the abridgement of the parents. In addition, in the mentioned study, no significant increase was detected in the level of patients' cholesterol which is possibly due to the use of unsaturated fats in their setting. Another point was the increase in the level of BUN in our patients which was because of little water intake.

In conclusion, since seizures may be well controlled by the ketogenic diet, we can lower its complications by using unsaturated fats and standard use of minerals and water and recommend both parents and doctors to use it. On the other hand, although no significant change was detected in the weight / height ratio of the children in our study, the study period was too short to conclude that the diet would not change the growth parameters of the children and more studies with longer follow-up periods are suggested.

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