Use of the Modified Atkins Diet in Intractable Pediatric Epilepsy

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Background and Purpose: The modified Atkins diet is a less restrictive alternative to the ketogenic diet (KD), allowing unlimited protein, fat, calories, and fluid intake. Moreover, it can be started on an outpatient basis without requiring a fast. This study evaluated the efficacy, tolerability, and compliance of the modified Atkins diet in intractable pediatric epilepsy.

Methods: We retrospectively reviewed the medical records of 26 pediatric patients (10 males and 16 females) with intractable epilepsy who were treated using the modified Atkins diet at Samsung Medical Center from January 2011 to March 2017.

Results: The mean age at initiation of the modified Atkins diet was 10.9 (range, 2-21) years. The diet was continued for a mean duration of 5.9 (range, 1-16) months. After 6 months, 10 (38.5%) remained on the diet, of whom six (60%) had > 50% seizure reduction and two (20%) became seizure free. Four of 26 patients (15.4%) reported side effects of the diet, including constipation (n = 2) and lipid profile elevations (n = 2). Mean body mass index (BMI) was reduced from 22.6 to 20.9 kg/m² (p < 0.05) in 13 patients who continued the diet for ≥ 3 months. Four of these patients (30.8%) were overweight (BMI > 25 kg/m²) before initiating the diet and were satisfied with their BMI changes from a mean of 30.3 to 27 kg/m² (p < 0.05). Food refusal (n = 3) and poor parental compliance (n = 3) were the common reasons cited for cessation.

Conclusions: The modified Atkins diet may be an alternative treatment option for children with intractable epilepsy who are unable to tolerate KD because of food intake-related restrictiveness or adverse effects. The continuous support of healthcare professionals and families plays a key role in diet maintenance.

Key words: Atkins, Ketogenic diet, Epilepsy, Children

Introduction

Approximately 20% of pediatric epilepsy patients do not respond well to antiepileptic drugs (AEDs) and are considered medically intractable. The ketogenic diet (KD), a high-fat, low-carbohydrate, and low-protein diet, has been proven to be effective for intractable epilepsy. Despite its effectiveness in the management of seizures, previous studies have demonstrated poor compliance as a critical obstacle for its use. Freeman et al. noted that only 55% of children who started KD continued the diet after one year; the rest of the patients terminated the diet because of decreased oral tolerability, adverse effects, and lack of efficacy.

The modified Atkins diet is a less restrictive diet therapy based on the same principles as those of KD. Kossoff et al. first described the use of the modified Atkins diet for treating refractory epilepsy in 2003. The modified Atkins diet differs from KD because the former permits the free intake of protein, fat, calories, and fluids. Fat-to-protein and carbohydrate ratios in the modified Atkins diet are on average 1:1, whereas those in KD are 3:1. This diet can be started on an outpatient basis without the need to maintain fasting conditions. As the modified Atkins diet is less restrictive and more palatable than KD, it may be associated with a greater compliance by both patients and parents.

Since the appearance of the first report, many prospective and retrospective studies on the modified Atkins diet in intractable epilepsy patients have been published. The effect of the modified Atkins diet compared with that of KD remains controversial. Several studies have demonstrated that the modified Atkins diet is as effec-
tive as KD for intractable epilepsy. However, other studies have suggested that KD has an overall superior response rate. Because of variable sample sizes and studies producing inconsistent results, a thorough investigation on the efficacy of the modified Atkins diet is warranted. In addition, most studies have reported only short-term seizure outcomes after the modified Atkins diet initiation.

In this study, we aimed to delineate the efficacy, tolerability, and compliance of the modified Atkins diet in intractable pediatric epilepsy. We also evaluated the outcomes beyond 6 months and identified patient groups that benefitted from the modified Atkins diet.

Methods

Patients

A retrospective medical chart review was performed of the intractable epilepsy patients and with the modified Atkins diet at Samsung Medical Center (Seoul, Korea). Subjects were recruited from January 2011 to March 2017. According to the International League Against Epilepsy (ILAE), intractable epilepsy was defined as the failure of adequate trials of two tolerated, appropriately chosen, and used AED schedules. During diet therapy, adjustments of AED dosage were allowed at the physician’s discretion.

Diet initiation and monitoring

The modified Atkins diet was a nearly balanced diet comprising 60% fat, 30% protein, and 10% carbohydrates by weight. Carbohydrates were restricted to 10 g/day but were allowed to be increased by 5 g/day to a maximum of 10% carbohydrates per day by weight at intervals of at least 1 month depending on tolerance. The carbohydrate content of various food items was explained to the parents and exchange lists were provided. The intake of fat was actively encouraged. Protein intake was not restricted. There was no calorie restriction. The total caloric intake was determined based on patients’ age, height, weight, and degree of daily activity. The diet was started on an outpatient basis without the need to maintain fasting conditions.

Regular outpatient visits were recommended at monthly intervals, during which any reduction in seizure frequency, patients’ tolerance to the diet, and adverse effects related to diet therapy were recorded. Patients were asked to check urine ketone levels on a weekly basis using reagent sticks. Laboratory evaluations were performed during the course of the modified Atkins diet intake. The modified Atkins diet protocol is summarized in Table 1.

Clinical analysis

Demographic, clinical, and laboratory data were recorded, including sex, age at seizure onset, seizure types and frequency, AED profiles, age at diet initiation, diet duration, brain magnetic resonance imaging findings, electroencephalogram patterns, serial biochemical analysis results, and diet-related complications.

The patients were evaluated with respect to the following seizure reduction parameters after following the diet for 1, 3, and 6 months: 1) seizure freedom, 2) seizure reduction ≤ 50%-99%, 3) seizure reduction < 50%, and 4) no improvement.

All statistical analyses were performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA) for Windows. Pearson’s chi-square and Fisher’s exact tests were used to compare clinical characteristics between groups and differences were considered statistically significant for p-values < 0.05.

Results

Patient characteristics

We identified 26 patients (10 males and 16 females) with intract-
able epilepsy who were treated with the modified Atkins diet. The mean age of seizure onset was 5 years (range, 0.1-14). The mean seizure frequency prior to diet initiation was 22 times per week (range, 0.25-112). An average of 6.8 AEDs (range, 3-9) had failed before enrollment of these patients into our study. Of the 26 patients, one (3.8%) had undergone epilepsy surgery. The children were receiving a mean of 4.2 AEDs (range, 1-7) at the time of diet initiation. The mean age at the beginning of diet therapy was 10.9 (range, 2-21) years.

The most common diagnoses were Lennox-Gastaut syndrome (8/26 patients, 30.8%) and West syndrome (2/26 patients, 7.6%). Of the 26 patients, 17 (65.5%) had structural etiologies of epilepsy, including focal cortical dysplasia, hypoxic-ischemic encephalopathy, schizencephaly, and band heterotopia and two had genetic mutations, including those in the SCN1A gene in one patient and in DCX (band heterotopia) in another (Table 2).

### Efficacy

A total of 26 enrolled patients completed ≥1 month on the diet. Twenty-one (80.8%) and 10 (38.5%) patients remained on the diet for >3 and >6 months, respectively. Seizure reduction in children who continued with the diet is summarized in Table 3. At 1 month and 3 months, seven (26.9%) and 11 (52.4%) patients had experienced >50% reduction in seizure frequency, respectively. However, changes in the mean number of administered AEDs were not observed (p = 1.00). After undergoing the modified Atkins diet for 6 months, six patients (60%) had >50% improvement and two (20%) became seizure-free after 6 months of diet therapy. Of the 10 patients who continued the modified Atkins diet beyond 6 months, six (60%) showed increased alertness and improved functional performance.

To determine the factors related to the favorable effects of the test diet therapy, we compared the characteristics of the patients who

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**Table 2.** Patient characteristics

| Characteristic                                      | Value (n = 26) |
|----------------------------------------------------|----------------|
| Female: male                                       | 16:10          |
| Age (years) at seizure onset                       | 5 (0.1-14)     |
| Age (years) at diet initiation                     | 10.9 (2-21)    |
| Number of previously administered antiepileptic drugs (AEDs) | 6.8 (3-9)     |
| Current number of AEDs                             | 4.2 (1-7)      |
| Seizure frequency per week                         | 22 (0.25-112)  |
| Seizure type                                       |                |
| Myoclonic                                          | 1 (3.8)        |
| Simple partial                                     | 2 (7.6)        |
| Complex partial                                    | 5 (19.3)       |
| Epileptic spasms                                  | 1 (3.8)        |
| Multiple                                           | 17 (65.5)      |
| Epilepsy syndromes                                |                |
| Lennox-Gastaut syndrome                            | 8 (30.8)       |
| West syndrome                                      | 2 (7.6)        |
| Dravet syndrome                                    | 1 (3.8)        |
| Epilepsy, not otherwise specified                 | 15 (57.8)      |
| Etiology                                           |                |
| Structural/Metabolic                               | 17 (65.5)      |
| Unknown                                            | 7 (26.9)       |
| Genetic                                            | 2 (7.6)        |

Values are presented as mean (range) or number (%) unless otherwise indicated.

**Table 3.** Seizure reduction in patients continuing with the modified Atkins diet at 1, 3, and 6 months

| Seizure reduction                     | 1 month (n = 26) | 3 months (n = 21) | 6 months (n = 10) |
|---------------------------------------|------------------|-------------------|-------------------|
| Seizure free                          | 3 (11.5)         | 2 (9.5)           | 2 (20)            |
| 50-99% improvement                   | 4 (15.4)         | 9 (42.9)          | 6 (60)            |
| 1-49% improvement                    | 7 (26.9)         | 7 (33.3)          | 2 (20)            |
| No improvement                        | 12 (46.2)        | 3 (14.3)          |                   |

Values are presented as number (%).
maintained the diet after 6 months and achieved >50% seizure reduction with those who had <50% improvement or who discontinued the diet before 6 months due to poor tolerance or side effects. More than one type of generalized seizure was predominantly observed in the former group ($p < 0.05$). The patients who continued the diet beyond 6 months and achieved >50% improvement in seizure frequency had several different types of generalized seizures, including generalized tonic-clonic and atonic (n = 2); generalized tonic, myoclonic, and atonic (n = 1); generalized tonic and absence (n = 1); and atonic and absence (n = 1). In contrast, the patients who had <50% seizure reduction or who terminated the diet before 6 months showed generalized tonic, myoclonic, and absence (n = 1); generalized tonic and myoclonic (n = 1); and myoclonic and tonic seizures (n = 1). Except for this, sex, age at first seizure, age at diet initiation, number of current and previously administered AEDs, and etiologies of epilepsy did not influence the likelihood of good outcomes.

Of the 26 patients, two (7.6%) had previously undergone KD before transitioning to the modified Atkins diet due to food intake-related restrictiveness. They had favorable outcomes with a >50% reduction in seizure frequency owing to KD and maintained seizure control after switching to the modified Atkins diet.

**Effect on weight or body mass index (BMI)**

Thirteen of 21 patients (61.9%) who continued the modified Atkins diet for >3 months lost weight, from a mean of 44 kg at baseline to 40.9 kg at the 3-month visit ($p = 0.052$). BMI was reduced from a mean of 22.6 to 20.9 kg/m$^2$ in these patients ($p < 0.05$). For the remaining eight patients, data regarding height, weight, and BMI were not available. Four of 13 patients (30.8%) were overweight (BMI > 25 kg/m$^2$) before initiating the diet and were satisfied with significant BMI changes from a mean of 30.3 to 27 kg/m$^2$ ($p < 0.05$) after diet therapy. Except for two patients whose data could not be obtained, eight patients (80%) who remained on the diet for >6 months did not show significant changes in weight or BMI. Their weight and BMI changed from a mean of 34.2 to 32.8 kg ($p = 0.561$) and from 18.8 to 18 kg/m$^2$ ($p = 0.406$), respectively.

**Tolerability and adverse effects**

Four (15.4%) of 26 patients, including two patients who maintained the diet for >6 months, reported side effects that could be potentially attributed to the modified Atkins diet. These adverse effects included constipation (n = 2) and increased cholesterol (n = 1) and triglyceride (n = 1) levels from 217 to 460 mg/dL and from 107 to 281 mg/dL, respectively. No medication was prescribed and the abnormal values improved after lifestyle modification. When laboratory values were assessed, no significant differences were observed between the baseline values and the values obtained at the final visit (Table 4). None of the patients reported kidney stones, bone fractures, or other complications that were occasionally reported in patients on long-term KD.

Of 26 patients, 12 (46.2%) were withdrawn from diet therapy after a median of 3 months on the diet (range, 1-7). The most common reasons for cessation were food refusal (n = 3) and poor parental compliance (n = 3). Two patients discontinued the diet because the parents felt that the seizure reduction was not enough to motivate a continuation of the diet therapy. The remaining four patients could not maintain the diet due to medical conditions unrelated to the diet, including infection (n = 2), sudden unexpected death in epilepsy (n = 1), and loss to follow-up (n = 1). After 6 months of receiving the modified Atkins diet, four patients (40%) stopped the diet due to refusal of food intake (n = 2), difficulties faced by the parents in adhering to the diet (n = 1), and ineffectiveness (n = 1). For the 12 patients who discontinued the modified Atkins diet, none reported persistent side effects potentially attributable to the diet therapy.

| | Baseline | Final visit | p-value |
|---|---|---|---|
| Alanine aminotransferase (AST) | 25.1 (14-50) | 21.4 (12-35) | 0.051 |
| Aspartate aminotransferase (ALT) | 16.3 (9-44) | 14.2 (7-33) | 0.305 |
| Total protein | 6.9 (5.9-7.8) | 7 (6.3-7.8) | 0.266 |
| Blood urea nitrogen | 10.6 (3.8-17.8) | 14.2 (5.7-22) | 0.013 |
| Creatinine | 0.6 (0.1-1.18) | 0.5 (0.11-1.11) | 0.074 |
| Total cholesterol | 173.5 (73-245) | 208.2 (120-460) | 0.052 |
| High-density lipoprotein cholesterol (HDL) | 72.5 (59-77) | 60 (57-63) | 0.344 |
| Low-density lipoprotein cholesterol (LDL) | 123 (49-174) | 142 (65-219) | 0.598 |
| Triglycerides | 117.5 (44-191) | 193 (101-281) | 0.121 |

Values are presented as average mg/dL (range).
Discussion

Based on the results of this study, the modified Atkins diet appears to be an effective and generally well-tolerated therapy in the management of children with intractable epilepsy. Despite the widespread acceptance of KD, its excessive restrictions with regard to the intake of certain food constituents make it difficult for patients to continue with the diet. The modified Atkins diet, a less restrictive alternative to KD, induces a state of ketosis by providing high fat and low carbohydrate content, suggesting that this diet may control seizures by a mechanism similar to that of KD. One of the prominent findings of this study is that the modified Atkins diet was an effective alternative dietary option for children with intractable epilepsy who were unable to tolerate KD due to either food intake-related restrictiveness or adverse effects. The modified Atkins diet can also be used as a transitional diet after successful KD therapy. As reported in other studies, patients can maintain seizure control after switching from KD to the modified Atkins diet. Because most previous studies have demonstrated short-term seizure outcomes after diet initiation, we attempted to delineate the outcomes of patients who were on the modified Atkins diet for > 6 months.

Six months after initiating the modified Atkins diet, more than one-third of the patients (38.5%) continued with the diet, more than half of the patients (60%) had > 50% seizure reduction, and 20% became seizure-free. These findings were consistent with those reported previously by Kossof et al., in which 65% of study participants had a > 50% response and 19% became seizure-free after 6 months. The results were comparable to the results associated with the short-term administration of the modified Atkins diet. This finding is similar to that of a large-scale prospective study on KD, in which 51% of subjects achieved a > 50% decrease in seizure frequency beyond 6 months. Keene also reported that after complying with KD therapy for ≥ 6 months, 48.6% of subjects had > 50% seizure reduction, of which 15.6% were seizure-free. Based on the present and previous studies, the efficacy of the modified Atkins diet as a treatment option for drug-resistant epilepsy is comparable to that of KD.

In our study, no association was observed among sex, age of seizure initiation, age at initiation of the modified Atkins diet, the number of current and previously administered AEDs, etiologies of epilepsy, and the rate of decrease in seizure frequency. No such relationship has been found in other studies on the use of the modified Atkins diet in intractable epilepsy. The patients who continued the diet for > 6 months and had > 50% seizure reduction tended to have several different types of generalized seizures. However, considering that the sample size in this study was too small to reach a definite conclusion, further studies are required to demonstrate the associations between demographic factors and favorable seizure outcomes.

In addition to the effect of the modified Atkins diet on the number and severity of seizures, we noted improved functional status and quality of life. We found that more than half of the patients (60%) who continued with this diet for 6 months showed decreased lethargy and increased levels of alertness. This is particularly important in intractable epilepsy patients because uncontrolled seizures and treatment with multiple anticonvulsants can lead to deleterious cognitive and behavioral consequences, sedation, and concentration and memory impairments. Taking into account that the mean number of AEDs was not altered after the diet therapy, these cognitive improvements may be attributed to well-controlled seizures. These findings were consistent with those of previous studies that reported cognition, alertness, attention, or social function improvement in patients administered KD.

The modified Atkins diet is likely to have a low occurrence of side effects. In most children, the adverse effects of the diet were transient and well-controlled by conservative management and did not necessitate discontinuation of the diet. A common side effect reported in association with the diet was constipation, which is also a typical complication reported in KD. In our study, the total cholesterol and triglyceride levels increased during the course of the modified Atkins diet and have also reportedly been higher in studies involving the modified Atkins diet. In addition, weight loss and BMI reduction were minimal, except in patients who were significantly overweight at diet initiation. Four of the patients who began the diet met the diagnostic criterion for being overweight (i.e., BMI > 25 kg/m²). After 3 months of diet, these patients no longer met this diagnostic criterion. Considering the fact that some antiepileptic medications promote weight gain during treatment, the modified Atkins diet may act as a beneficial co-therapy for intractable epilepsy patients who are overweight or obese.

In the present study, at 6 months, 10 of the 26 (38.5%) patients were able to continue with the diet. Although the retention rate for the modified Atkins diet was lower in our patients than in those in other studies, the diet therapy was generally well-tolerated. The most common reasons for discontinuing the diet were food refusal and poor parental compliance when maintaining the diet became burdensome. Because meals provided at schools are not similar to...
low-carbohydrate diets, patients or their parents find it difficult to continue this diet therapy. In addition, the stigma associated with epilepsy being easily noticed by peers when school-aged or adolescent patients carry a modified Atkins diet meal is a major factor contributing to poor compliance. The other reason for cessation of the modified Atkins diet was uncertain effects on seizure control because the duration of the diet was not sufficient. No patient discontinued the diet because of adverse effects including abnormal laboratory results or increased seizure frequency.

The modified Atkins diet is a less restrictive alternative to KD because patients and their families can control the diet at their own discretion as opposed to the strict control exerted by a dietician for KD. For this reason, the support of healthcare professionals and networking between families are imperative for achieving high compliance and favorable seizure outcome using the modified Atkins diet.

The retrospective nature of this study presents several limitations. The accuracy of the data was affected by incomplete medical records and recall biases from practitioners and the parents of the patients. The small sample size and the heterogeneity of the enrolled patients also likely influenced the lack of statistical significance. In addition, the higher dropout rate compared to those of other studies may have influenced the seizure outcomes. Thus, larger prospective studies or collaborative trials are warranted to identify the definite therapeutic roles of the modified Atkins diet in patients with intractable pediatric epilepsy.

In conclusion, the modified Atkins diet seems to be effective and generally well-tolerated in children with intractable epilepsy. The diet has several advantages over KD; most notably, it is relatively easier to initiate and maintain with no need for hospitalization and no restriction on protein, calorie, and fluid intake. Therefore, it may serve as an alternative treatment option for patients in resource-constrained settings or for those who are unable to tolerate KD due to either food intake-related restrictiveness or associated side effects.

Acknowledgements

We would like to thank the dietician So-Young Yoo at our institution for providing information regarding the modified Atkins diet and educating the parents involved in this study.

Conflicts of Interest

All the authors declare no conflict of interests.

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