

Use of a Modified Atkins Diet in Intractable Childhood Epilepsy

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Summary: *Purpose:* To evaluate the efficacy, safety and tolerability of a modified Atkins diet in intractable childhood epilepsy.

Methods: Fourteen children with epilepsy were treated prospectively with a modified Atkins diet. Outcome measures included seizure frequency, adverse reactions and tolerability to the diet; blood β -hydroxybutyrate and urine ketones were also measured.

Results: Six months after diet initiation, seven (50%) remained on the diet, five (36%) had >50% seizure reduction, and three (21%) were seizure free. The diet was well tolerated by 12 (86%)

patients. Most complications were transient and were successfully managed by careful follow-up and conservative strategies. A consistently strong ketosis (β -hydroxybutyrate of >3 mmol/L) seemed to be important for maintaining the efficacy of the diet therapy.

Conclusions: The modified Atkins diet was well tolerated and sometimes a modified Atkins diet can be substituted for the conventional ketogenic diet. Serious complications were rare, but long-term complications remain to be determined. **Key Words:** Atkins diet—Intractable childhood epilepsy.

The ketogenic diet (KD) has been used worldwide for the treatment of intractable childhood epilepsy (Kossoff and McGrogan, 2005). However, the KD is not yet a convenient therapy, especially in older children and adolescents (Freeman et al., 1998; Kang et al., 2004). The Atkins diet induces a state of ketosis by providing a high fat content and few carbohydrates, suggesting that this diet may control seizures by a mechanism similar to that of the KD (Stafstrom, 2004). Recently, a modified Atkins diet was shown to be effective and well tolerated in children with intractable epilepsy (Kossoff et al., 2006). We also aimed in this study to evaluate the efficacy, safety and tolerability of a modified Atkins diet in 14 children with intractable childhood epilepsy.

METHODS

The subject cohort consisted of 14 patients with intractable childhood epilepsy who had been experiencing more than four seizures per month, which could not be

controlled by any combination of three or more antiepileptic drugs. They were treated prospectively with a modified Atkins diet and were followed for at least more than 6 months since the diet had been tried at a tertiary care referral epilepsy center.

The modified Atkins diet consisted of a nearly balanced diet (60% fat, 30% protein, and 10% carbohydrates by weight), without the restriction of recommended daily calories according to patient age, and substituting the initial stepwise caloric increase of the nonfasting protocol for initial fasting and fluid restriction (Fig. 1). As suggested by Kossoff et al. (2006), for the first month, carbohydrates were restricted to 10 g/day, but were permitted to increase by 5 g/day at intervals of at least 1 month if the child was having difficulty with the restriction of carbohydrates, to a maximum of 10% carbohydrates per day by weight. Following the start of the diet, all patients were advised to remain in the hospital for 3 or 4 days to ensure adequate diet adaptation and to have their blood ketosis carefully monitored; a qualified dietician also educated the caregivers/parents about preparation of the diet at home. Multivitamins, calcium and vitamin D2 were given as supplements throughout. Regular outpatient visits were recommended at monthly intervals, during which blood β -hydroxybutyrate, any reduction in seizure frequency, the patient's toleration of the diet and any complications

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FIG. 1. A typical daily portion of a modified Atkins diet, allowing large amounts of protein (30% by weight) with the restriction of carbohydrates to 10 g/day. From the upper and right corner to the lower and left corner, boiled chicken, roasted fish, fresh tomato, kimchi (Korean pickled vegetables), milk, bean sprouts, anchovy soup and olive oil.

associated with diet therapy were recorded. In addition, we recommended frequent measurements of urine ketones at home, especially when seizures occurred or seizure frequency increased. Regularly scheduled assessments of the tolerability and complications of the modified Atkins diet, including laboratory evaluations, were according to the protocol of the Sanggye Paik Hospital for the conventional KD (Kang et al., 2004). Statistical Package for the Social Science (version 10.0) (SPSS Korea, Seoul, Korea) was used for all statistical analyzes and a p -value < 0.05 was regarded as statistically significant. This study was approved by the Sanggye Paik Hospital's Committee for Clinical Investigation.

RESULTS

Patient characteristics

The 14 enrolled patients (nine males, five females) had a mean (\pm SD) age at the beginning of the diet of 89.1 (\pm 39.9) months, and were maintained on the modified Atkins diet for a mean of 5.1 (\pm 3.6) months. Classifications of the patients' epilepsies and underlying etiologies are presented in Table 1.

Treatment efficacy

One month after initiating the diet, 11 patients (78.6%) remained on the diet and eight (57.1%) showed a $>50\%$ reduction in seizure frequency, including five patients (35.7%) who became seizure-free. At 3 months, 9 patients (64.3%) remained on the diet and seven (50.0%) had a $>50\%$ reduction in seizure frequency, including four

(28.6%) who became seizure-free. At 6 months, seven patients (50%) remained on the diet and five (35.7%) had a $>50\%$ reduction in seizures, including three (21.4%) who became seizure-free. Two patients have maintained the diet for about 1 yr. One (patient 1) displayed a rare presence of seizures and the second (patient 7) did not obtain favorable seizure outcome but showed improved cognitive function. Of the 14 patients, six (patients 1–6) showed a $>90\%$ reduction in seizure frequency, whereas eight patients (patients 7–14) experienced a $<50\%$ reduction. When we compared these two groups, we could not find any differences between their clinical profiles (Table 1).

Blood ketosis

The results of blood β -hydroxybutyrate are presented in Fig. 2. Ten patients achieved high blood ketosis (of >3.0 mmol/L), whereas the remaining four did not. In six patients, β -hydroxybutyrate was over 3 mmol/L within 2 or 3 days of starting the modified Atkins diet. The other eight patients left the hospital without experiencing β -hydroxybutyrate of >3 mmol/L. Although patients 4 and 6 did not reach this level of blood β -hydroxybutyrate, both became seizure-free, suggesting that blood ketosis was not absolutely correlated with positive seizure outcomes. However, the other four patients (patient 1, 2, 3, and 5) who showed favorable response maintained consistent blood β -hydroxybutyrate over 3 mmol/L (Fig. 2A). In addition, the degree of blood β -hydroxybutyrate fluctuated widely in patients with unfavorable seizure outcomes, sometimes falling below 2.0 mmol/L (Fig. 2B). The caregivers/parents checked urine ketones randomly on 58 occasions when seizure frequencies increased, finding that urine ketones were low (trace or 1+ or 2+) on 42 of these occasions.

Tolerability and complications

All patients but two (patients 3 and 4) were older than 6 yr of age when starting the modified Atkins diet, and all patients had already refused the conventional KD or found it too restrictive. Most patients reported good or very good tolerance of the modified Atkins diet. Only two patients (patients 4 and 8) stopped this diet due to intolerance.

During their first month on the modified Atkins diet, six patients experienced gastrointestinal disturbances, such as vague abdominal pain, constipation, vomiting and diarrhea. Only one patient (patient 2) had symptomatic hypoglycemia, less than 40 mg/dL, during the initial period of the stepwise increase of calories. Two patients (patients 2 and 10) showed hyperlipidemia respectively with 379 mg/dL of cholesterol and 475 mg/dL of triglyceride within the first month, but it was transient. Urinary calcium oxalate was also detected in one patient (patient 7) after 3 months. patient 2 had recurrent episodes of vomiting, symptomatic hypoglycemia and transient hypercholesterolemia; despite a reduction in seizures, this patient

TABLE 1. Clinical profiles of 14 patients in whom a modified Atkins diet was tried

No. of Pt/ Sex	Epilepsy diagnoses (p ^a = 0.63)/ main seizure type (p ^a = 0.84)	Etiology (p ^a = 0.35)	Age ^b (yr.month)/(duration ^c (month)	Process of the diet therapy	Efficacy of the AD (reduction of of seizure frequency, %)	Most recent status	Adverse events
Pt 1/M	LGS/atonic	Suspicious MC	8.0/12	AD	100	Maintained	Constipation
Pt 2/M	LGS/GT	Cortical dysplasia	3.10/5	AD	90	Stopped	Symptomatic hypoglycemia, vomiting, hypercholesterolemia, aspiration pneumonia, anemia
Pt 3/M	LGS/atyp ABS	HIE	4.5/6	AD	100	Maintained	Vomiting
Pt 4/F	PS/clonic	HIE	6.0/2	KD->AD	100	Stopped	Intolerance
Pt 5/M	PS/staring	Cryptogenic	11.2/6	KD->AD	100	Maintained	
Pt 6/M	PS/secondary GTC	Encephalitis	4.1/6	AD	100	Maintained	Abdominal pain, diarrhea
Pt 7/F	PS/secondary GTC	Encephalitis	8.1/12	AD	25	Stopped	Urinary calcium oxalate
Pt 8/M	PS/staring	HIE	11.3/1	Previous KD	0	Stopped	Intolerance
Pt 9/M	Doose syndrome /atonic	Cryptogenic	14.4/7	AD	25	Maintained	Vomiting
Pt 10/M	PS/clonic	Encephalitis	6.8/6	AD	25	Maintained	Hypertriglyceridemia
Pt 11/F	LGS/atonic	Cryptogenic	5.11/3	AD	25	Stopped	
Pt 12/M	GS/GT	Cryptogenic	2.6/2	AD	0	Stopped	
Pt 13/F	LGS/GTC	Trauma	9.2/>1	AD->KD	0	Stopped	
Pt 14/F	LGS/atonic	Encephalitis	9.6/2	AD	25	Stopped	Vomiting

No., number; Pt, patient; M, male; F, female; LGS, Lennox-Gastaut syndrome; GT, generalized tonic; atyp ABS, atypical absence; PS, partial seizures; GTC, generalized tonic and clonic; MC, mitochondrial cytopathy; HIE, hypoxic ischemic encephalopathy; KD, ketogenic diet; AD, a modified Atkins diet.

^aStatistical analysis for the data between the favorable group (a reduction of seizure frequency >90%) (patients 1-6), and the unfavorable group (with <50% seizure reduction) (patients 7-14).

^bAge at beginning a modified Atkins diet.

^cDuration of a modified Atkins diet.

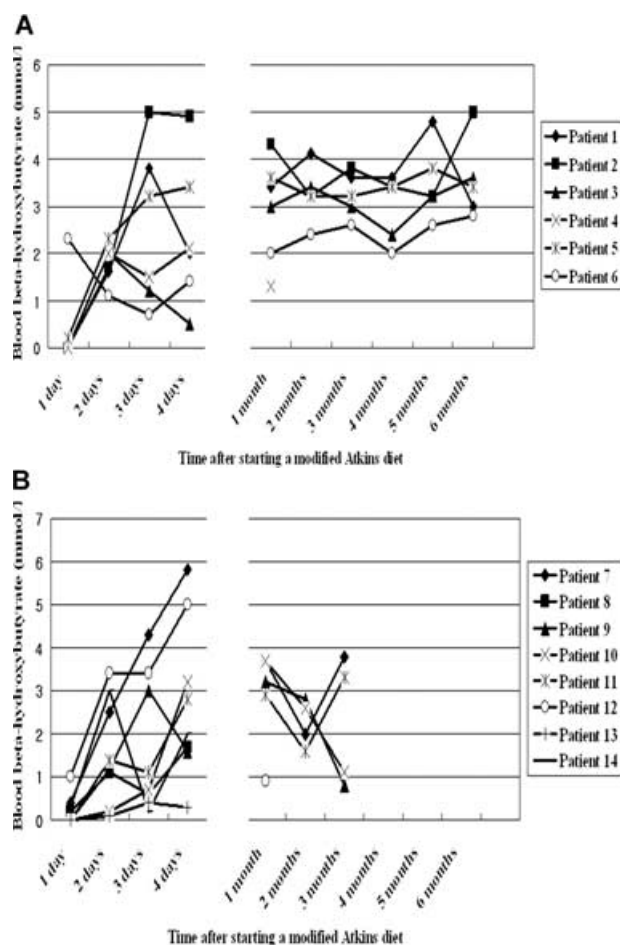


FIG. 2. Blood β -hydroxybutyrate during the modified Atkins diet in 14 patients with intractable childhood epilepsy. **(A)** Patients 1–6, who showed a $>90\%$ reduction in seizure frequency. **(B)** Patients 7–14, who showed a $<50\%$ reduction in seizure frequency.

stopped the Atkins diet due to the development of aspiration pneumonia after 5 months. Patient 2 had diffuse cortical dysplasia without any laboratory evidence of underlying metabolic diseases. Body mass index changed from a mean of 18.6 to 17.7 ($p = 0.25$). A fall in weight percentile was not observed in any of the patients (Table 1).

DISCUSSION

We have shown here that sometimes a modified Atkins diet could substitute for the classic KD in children with intractable epilepsy. Six months after initiating the modified Atkins diet, 50% of the patients remained on the diet, 36% had a $>50\%$ reduction in seizures, and 21% became seizure-free. These findings were somewhat lower than those of the first formal prospective study to use a modified Atkins diet for epilepsy, which found that 80% of the patients were able to stay on the diet, 65% had a $>50\%$ response, and 19% became seizure-free after 6-months (Kossoff et al., 2006), and which showed a striking simi-

larity to large prospective and retrospective studies of the conventional ketogenic diet (Freeman et al., 1998; Kang et al., 2005).

The extent of ketosis was not always proportionately correlated with better seizure outcomes as the previous report suggested (Kossoff et al., 2006). However, in most patients on the modified Atkins diet, lower ketosis was not sufficient to completely control intractable seizures and patients who showed unfavorable seizure outcomes had wider fluctuations in blood β -hydroxybutyrate. There was also an association between low urinary ketones and an increase in seizure frequencies.

The Atkins diet was modified for patients with intractable epilepsy to obtain a high ketosis, by reducing carbohydrates to less than 10 g/day for the first month and permitted to increase by 5 g/day at intervals of one month according to the patients' tolerability to maximum of 10% carbohydrate per day by weight (Kossoff et al., 2003; Stafstrom, 2004; Kossoff et al., 2006). But the diet provided more liberal total carbohydrate and protein and so it was more difficult to maintain consistently strong ketosis on the Atkins diet than with the conventional KD. Besides, patients often attempt to eat protein (which may be more appetizing than lipid constituents) constituents first and then later refuse or vomit the lipid constituents. Patients should be more strictly encouraged to have all of those constituents together and ketosis should be monitored more frequently and carefully when patients are on the Atkins diet than on the conventional KD (Kang et al., 2004).

Although all patients enrolled in this study had previously shown reluctance to use the KD or could not tolerate it, most caregivers/parents reported good or very good ability to tolerate the modified Atkins diet, suggesting that a modified Atkins diet could definitely increase the tolerability of diet therapy. We did, however, observe various complications with the modified Atkins diet, similar to those reported with the conventional KD (Kang et al., 2004). These complications were transient or well controlled by conservative management derived from experience with the KD (Kang et al., 2004). Only one patient, who had aspiration pneumonia, gave up the diet for safety reasons. Ironically, although the Atkins diet was created as a means to combat obesity (Foster et al., 2003), a fall in weight percentile was not observed in any of our patients. However, the most serious complications that occurred after 6 months were also experienced while on the KD (Wheless and Ashwal, 1999; Kang et al., 2004), and long-term complications remain to be determined.

In summary, the ability of these patients to tolerate the modified Atkins diet was encouraging, suggesting that sometimes this diet can replace the conventional KD, especially in older children and adolescents. Serious complications were rare, whereas long-term complications require further determination. Consistently strong ketosis

(β -hydroxybutyrate of >3 mmol/L) seems to remain important to obtain favorable seizure outcomes from diet therapy.

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