

# Is a Fast Necessary When Initiating the Ketogenic Diet?

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## ABSTRACT

The purpose of this study was to determine time of onset of ketosis and efficacy when the classic ketogenic diet is initiated at full calories without a prior fast in children with epilepsy. A retrospective hospital and neurology clinic chart review was done of all 14 children commenced on the classic ketogenic diet at full calories without a prior fast between January 1, 1997, and May 31, 2001, to determine time to ketosis, time to good ketosis (urine ketones  $\geq 80$  mg/dL), and success of the ketogenic diet. Median age at diet initiation was 63 months (25th–75th percentile 47–149 months). There were 7 girls and 7 boys. Four had symptomatic generalized epilepsy, whereas the remainder had partial seizures  $\pm$  secondary generalization. Twelve of 14 children suffered seizures on a daily basis prior to the ketogenic diet. Six were commenced on the diet as outpatients, whereas 8 were admitted to hospital. No patients were fasted. All admitted patients were started on a 1:1 ketogenic ratio at full calories for the first 24 hours and advanced to a 3:1 or 4:1 ratio over 3 to 4 days, while outpatients were started on a 1:1 or 2:1 ratio and similarly advanced. Thirteen of 14 patients were successfully started on the diet, with 1 developing vomiting and food refusal during the initial hospitalization but after ketosis was established. One child was lost to follow-up after initial hospital discharge. Information regarding time to ketosis was determined for all inpatients. Mean time to onset of ketosis was 33 hours (range 17 to 48) and to good ketosis, 58 hours (range 40 to 84). Five of 12 children (42%) experienced success with the ketogenic diet, and all of these had their antiepileptic medications either withdrawn ( $n = 3$ ) or decreased ( $n = 2$ ). The ketogenic diet can be effectively initiated without a fast in children with epilepsy. Time to ketosis and diet efficacy are similar to protocols that use a fast. (*J Child Neurol* 2002;17:179–182).

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The treatment of epilepsy with the ketogenic diet dates back over 75 years to a time when only phenobarbital and bromides were available.<sup>1–7</sup> This diet mimics the changes of starvation. Neurons use ketone bodies rather than glucose as a metabolic substrate, and although the exact mechanism of action of the diet is not known, it has been suggested that chronic ketosis may control seizures by increasing the cerebral energy reserves in the brain, thus promoting neuronal stability.<sup>8</sup>

Traditionally, children beginning on the ketogenic diet have been fasted for 1 to 2 days, until ketosis is seen, are then started on one-third calories for 24 hours and then two-

thirds calories for the next 24 hours, and finally are advanced to a full diet.<sup>9</sup> The fasting period is often a difficult time for young children and their families.

In our center, we have started the ketogenic diet without the initial fast, commencing at a 1:1 to 2:1 ratio and advancing to a 3:1 or 4:1 ratio over 3 to 4 days. We review our results in 14 children who were begun on the ketogenic diet in this fashion to determine time of onset of ketosis and outcome of the diet.

## METHODS

Between January 1, 1997, and May 31, 2001, 17 children were initiated on the classic ketogenic diet at the Alberta Children's Hospital. Of these, no children were fasted, 3 were initiated on reduced (one-third) calories and increased to full calories over a 3-day period, and 14 were initiated on full calories, beginning with a 1:1 to 2:1 ketogenic ratio and advancing to a 3:1 or 4:1 ketogenic ratio over 3 to 4 days. The charts of these 14 patients commenced on the diet at full calories were reviewed to determine the time to keto-

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**Table 1. Study Population Demographic Data**

Study No.	Sex	Age at Diet Onset	Age at Seizure Onset	Seizure Type	Seizure Frequency	No. of AEDs Previously Tried	Outcome
1	F	3 yr, 8 mo	1 yr, 6 mo	P	Daily	6	Lost to follow-up after discharge
2	M	5 yr, 5 mo	Birth	P	Daily	7	Recurrent vomiting; diet stopped in hospital
3	M	1 yr, 0 mo	3 wk	P	Daily	10	Continues diet; 50–99% seizure reduction
4	F	12 yr, 5 mo	8 yr	P	Daily	7	Discontinued for food refusal; 50–99% seizure reduction
5	M	5 yr, 2 mo	6 mo	P	Daily	10	Discontinued for persistent vomiting; 50–99% seizure reduction
6	M	2 yr, 6 mo	4 mo	P	Daily	10	Discontinued for food refusal; <50% seizure reduction
7	M	4 yr, 10 mo	3 yr	SG	Daily	8	Continues seizure free
8	F	7 yr, 3 mo	6 mo	SG	Daily	9	Discontinued for food refusal; 50–99% seizure reduction
9	F	8 yr, 2 mo	5 mo	P	Weekly	5	Weaned off; after 2 years seizure free
10	F	14 yr, 4 mo	9 yr	P	Daily	6	Discontinued for food refusal; 50–99% seizure reduction
11	F	3 yr, 11 mo	1 yr, 11 mo	SG	Weekly	6	Continues diet; 50–99% seizure reduction
12	F	16 yr, 9 mo	10 yr	P	Daily	7	Discontinued for lack of efficacy
13	M	2 yr, 2 mo	4 mo	SG	Daily	4	Continues diet; seizure free
14	M	15 yr, 0 mo	6 mo	P	Daily	6	Discontinued for lack of efficacy

P = Partial with or without secondary generalization; AED = antiepileptic drug; SG = symptomatic generalized.

sis (defined as the time from the last regular meal to the first urinalysis demonstrating any degree of ketosis), time to good ketosis (defined as the time from the last regular meal to the first urinalysis documenting at least 8 mmol/L [80 mg/dL] for ketones), and success of the diet (defined as either remaining on the diet with at least a 50% reduction in seizure frequency at follow-up or discontinuing after a successful course, with at least a 50% reduction in seizure frequency and no significant side effects). Patients were included if they were commenced on the ketogenic diet either as inpatients or as outpatients. Those who were admitted began the ketogenic diet at lunch or supper and had regular meals up until that time. Families who commenced the ketogenic diet as an outpatient had approximately 4 hours of teaching by the dietitian prior to its commencement. Although families were not observed preparing meals, they were asked to calculate sample meal plans and were instructed on the use of the scale. Site of initiation of the diet was determined by team and family.

Potential predictors of success of the diet were studied, including age at diet initiation, sex, seizure type (primary generalized versus focal onset), number of prior antiepileptic agents used, and site of diet initiation (inpatient versus outpatient). Potential predictors of time to ketosis were also assessed, including age at diet initiation, sex, seizure type, number of prior antiepileptic agents used, and eventual ketogenic ratio achieved.

## RESULTS

Demographic data from the study population are shown in Table 1. The median age at initiation of the ketogenic diet in our 14 patients was 63 months (25th–75th percentile 47–149 months).

Six patients were commenced on the diet as an outpatient, whereas 8 patients were admitted to hospital. All patients initiated on the diet since January 2000 were

admitted. Prior to January 2000, 3 children were started as inpatients: 1 child who was only 30 months of age and 2 older children who were admitted with increasingly frequent seizures. All patients admitted to hospital were started on a 1:1 ketogenic ratio at full calories for the first 24 hours and were increased to a 2:1 ratio for the next 24 hours and to a 3:1 ratio for the third 24 hours. Six of 8 inpatients remained on a 3:1 ratio, whereas 2 were further increased to a 4:1 ratio after an additional 24 hours. Outpatients were started on either a 1:1, 1.5:1, or 2:1 ketogenic ratio at full calories and advanced at a similar rate to a 3:1 ( $n = 2$ ), 3.5:1 ( $n = 1$ ), or 4:1 ratio ( $n = 3$ ). Thirteen of 14 patients were successfully started on the diet. One child developed recurrent vomiting and refused the ketogenic diet during the initial hospitalization, but after ketosis was established. One child was lost to follow-up following initial hospital discharge on the ketogenic diet. Data from these two patients were used in determining time to ketosis and time to good ketosis but were excluded in determining predictors of success of the diet.

Information regarding time to ketosis was available for all 8 inpatients but for none of the outpatients. For inpatients, urine was checked for ketones two to three times daily. The mean time to onset of ketosis was 33 hours (range 17–48 hours) and to good ketosis was 58 hours (range 40–84 hours). Review of clinic notes indicated that all outpatients were in good ketosis by 3 to 10 days; however, the exact timing of onset of ketosis could not be established accurately.

Success of the diet was determined for all children except the one who discontinued the diet during the initial hospitalization and the other who was lost to follow-up after initiation of the diet. Overall, 5 of 12 (42%) experienced success. Four of 12 (33%) children remain on the diet at follow-up, after a mean duration of 19 months (range

2–47 months). Two of these children are seizure free, and 2 experienced a 50 to 99% reduction in seizure frequency. All children remaining on the diet are felt by their parents to be more alert, 2 have been weaned off all antiepileptic drugs, and the remaining 2 have had their seizure medications decreased. One child had a favorable response to the ketogenic diet and was maintained on the diet as monotherapy for 2 years. She was then weaned off and has had only one seizure in the past 2 years, and continues off antiepileptic medication.

Seven of 12 (58%) children did not experience success and discontinued the diet after a mean of 5 months (range 1–18 months). Reasons for discontinuation included food refusal ( $n = 3$ ), persistent vomiting ( $n = 1$ ), lack of efficacy ( $n = 2$ ), and lack of efficacy combined with food refusal ( $n = 1$ ). Although no patient who discontinued the diet became seizure free, 4 did have a 50 to 99% reduction in seizure frequency. Only 3 children who discontinued the diet were felt by their parents to have an improvement in their alertness while on the ketogenic diet.

Age at initiation predicted success with the diet with 4 of 5 (80%) children who were less than 5 years versus 1 of 7 (14%) who were 5 years or older at diet initiation being successfully treated ( $P < .05$ ). Seizure type also tended to predict success. Three of 4 (75%) children with primarily generalized seizures versus only 2 of 8 (25%) with partial-onset seizures were successfully treated on the ketogenic diet ( $P = .15$ ). Although our numbers were small in each group, patients admitted to hospital did not have a significantly higher likelihood of success with the ketogenic diet compared with those initiated as outpatients.

No predictors for time of onset of ketosis were found.

## DISCUSSION

In this study, we have clearly shown that ketosis can be achieved without fasting when initiating the ketogenic diet in children with epilepsy. Furthermore, the mean time to achieve good ketosis was 58 hours, which is comparable to when the diet is initiated following a fast.<sup>9</sup>

It has long been the assumption that a fast is necessary for the timely induction of ketosis. However, this assumption is incorrect. Initiating a diet high in fat and low in carbohydrate without a fast can readily induce ketosis as is evident on reviewing the biochemical pathways responsible for carbohydrate and fat metabolism.<sup>10</sup>

Fats are metabolized via their acyl coenzyme A (CoA) derivatives to acetyl-CoA, which may then either enter the citric acid cycle or condense with a second molecule of acetyl-CoA to form ketone bodies. Entry of acetyl-CoA into the citric acid cycle is dependent on the availability of oxaloacetate. Oxaloacetate is predominantly synthesized from pyruvate (by the action of pyruvate carboxylase), which is derived from glucose through the glycolytic pathway. Smaller amounts of oxaloacetate are also formed by the metabolism of excess four-carbon amino acids, such as aspartate. If fat and carbohydrate metabolism are appro-

priately balanced, acetyl-CoA enters the citric acid cycle by combining with oxaloacetate to form citric acid. However, if carbohydrate intake is relatively deficient compared to fat intake, the concentration of oxaloacetate is decreased because of inhibition of glycolysis (which results in decreased production of pyruvate and hence oxaloacetate) and enhanced gluconeogenesis (which results in increased conversion of oxaloacetate to phosphoenolpyruvate). In the absence of adequate oxaloacetate, acetyl-CoA does not enter the citric acid cycle, but, instead, two molecules of acetyl-CoA condense to form acetoacetyl-CoA, which is further metabolized to form ketone bodies (acetoacetate, acetone, and  $\beta$ -hydroxybutyrate). Although fasting will lead to glucose depletion and breakdown of fat stores, with production of ketone bodies, the same result can be obtained without fasting by delivery of a diet relatively deficient in carbohydrate compared to fat. This imbalance will lead to depletion of oxaloacetate, thereby shunting acetyl-CoA into ketone body production.

Avoiding a fast when initiating the ketogenic diet in children can be preferable for a number of reasons. First, a young child has a small amount of glycogen reserve, and with fasting, hypoglycemia is a real risk.<sup>11</sup> For this reason, blood glucose is usually monitored at least every 6 hours, during the fast and until the child is tolerating at least two-thirds calories,<sup>9</sup> which translates into a significant number of blood-letting procedures. Furthermore, if hypoglycemia does occur, most protocols recommend giving orange juice,<sup>9</sup> which will provide carbohydrate but again will delay onset of ketosis. By initiating the diet at full calories, we avoided the need to test blood glucose. Second, most children who are begun on the diet are too young to comprehend the rationale for fasting. Parents and caregivers often find the concept of fasting their children very difficult psychologically. Third, avoidance of the fast may allow for outpatient initiation of the diet, or if the child is hospitalized, may decrease hospitalization time and the cost of this treatment. In most current protocols, the child fasts until the second hospital day, then begins one-third caloric intake for 24 hours, increases to two-thirds caloric intake for the next 24 hours, and finally proceeds to full calories, usually necessitating a 5-day hospital stay.<sup>9</sup> Our patients are started at full calories on a 1:1 ratio, and the ratio is increased to 3:1 or 4:1 over 3 to 4 days, thereby allowing discharge 1 to 2 days earlier.

If fasting can be avoided, outpatient initiation of the ketogenic diet is feasible provided that a number of conditions can be met. First, both the family and dietitian must be willing to make the large time commitment needed to allow for adequate teaching regarding meal preparation and monitoring for ketones. Second, families need to stay in close proximity to the hospital for several days at the time the diet is initiated, to facilitate travel to hospital for this detailed teaching and to seek medical attention in the unlikely event that their child should develop difficulties when starting the diet. Rarely, vomiting and food refusal may occur. The ketogenic diet may also alter the metabolism and

protein binding of certain antiepileptic agents.<sup>12</sup> However, in our experience, these complications are uncommon. Third, adequate facilities must be available to allow for teaching on an outpatient basis. Ideally, these facilities would include a kitchen area in which the family can learn hands-on meal preparation under the supervision of the dietitian.

There are a number of limitations to our study. Our patients were identified retrospectively, and data regarding exact time of onset of ketosis were unavailable for the six subjects initiating the diet on an outpatient basis. Despite our small patient numbers, we are confident that a fast is unnecessary as none of our subjects had difficulty achieving good ketosis in a timely manner. The success of the ketogenic diet has recently been reported in two large studies,<sup>13,14</sup> and, overall, 40 to 50% of children had a 50% or greater reduction in seizure frequency and showed good tolerance to the diet. Our success rate of 42% is similar, suggesting that elimination of the fast did not impact on the success of the diet.

We strongly feel that fasting a child prior to initiation of the ketogenic diet is unnecessary, places them at risk for hypoglycemia, and probably leads to increased hospital stay. We have shown that children do achieve prompt ketosis when started on a classic ketogenic diet at full calories, with advancing of the ketogenic ratio from 1:1 to 3:1 or 4:1 over several days. Possibly, with avoidance of the fast, we can move toward outpatient initiation of the ketogenic diet.

## References

1. Guelpa G, Marie A: La lutte contre l'épilepsie par la desintoxication et par la reeducation alimentaire. *Rev Ther Med Chir* 1911;78:8-13.
2. Conklin HW: Cause and treatment of epilepsy. *J Am Osteopath Assoc* 1922;26:11-14.
3. Geyelin HR: Fasting as a method for treating epilepsy. *Med Rec* 1921;99:1037-1039.
4. Peterman MG: The ketogenic diet in the treatment of epilepsy: A preliminary report. *Am J Dis Child* 1924;28:28-33.
5. Peterman MG: The ketogenic diet in epilepsy. *JAMA* 1925;84:1979-1983.
6. Helmholtz HF: Treatment of epilepsy in childhood: Five years experience with the ketogenic diet. *JAMA* 1927;88:2028.
7. Wilkins L: Epilepsy in childhood: III. Results with the ketogenic diet. *J Pediatr* 1937;10:341-357.
8. DeVivo DC, Leckie MP, Ferrendelli JS, McDougal DB Jr: Chronic ketosis and cerebral metabolism. *Ann Neurol* 1978;3:331-337.
9. Freeman JM, Kelly MT, Freeman JB: *The Epilepsy Diet Treatment: An Introduction to the Ketogenic Diet*, 2nd ed. New York, Demos, 1996.
10. Stryer L: *Biochemistry*, 2nd ed. San Francisco: WH Freeman and Company, 1981.
11. Haymond MW: Hypoglycemia, in Rudolph AM (ed): *Pediatrics*, 19th ed. Norwalk, CT, Appleton and Lange, 1991:323-331.
12. Swink TD, Vining EPG, Freeman JM: The ketogenic diet: 1997. *Adv Pediatr* 1997;44:297-329.
13. Vining EPG, Freeman JM, Ballaban-Gil K, et al: A multicenter study of the efficacy of the ketogenic diet. *Arch Neurol* 1998;55:1433-1437.
14. Freeman JM, Vining EPG, Pillas DJ, et al: The efficacy of the ketogenic diet—1998: A prospective evaluation of intervention in 150 children. *Pediatrics* 1998;102:1358-1363.