Ketogenic Diet Underused For Control of Seizures

Biology is not understood, but studies show the high-fat, low-carb diet is effective for epilepsy patients.

BY GREG MUIRHEAD
Contributing Writer

MAUI, HAWAII — A high-fat ketogenic diet is effective in helping epilepsy patients control their seizures, but it is underused because it is misunderstood, said Dr. Eileen P.G. Vining.

The diet is not difficult. It can be palatable, adaptable, and inexpensive, she explained at a meeting sponsored by the University Childrens Medical Group and the American Academy of Pediatrics.

It has been estimated that the diet is initiated in only about 2,500 patients each year, based on a rough calculation of published data, while approximately 100 million people worldwide have epilepsy, according to the World Health Organization, she said.

The ketogenic diet is a high-fat, low-carbohydrate diet that provides adequate protein (1 g/kg per day), but greatly restricts carbohydrate intake, Dr. Vining said at the meeting, also sponsored by California Chapter 2 of the AAP. The effect of the diet is to mimic ketosis. The ketogenic diet's fat-to-carbohydrate and protein ratio may range from 2:1 (less strict) to 4:1 (very strict), with an average of 3:1. At a 3:1 ratio, fat intake accounts for 80%-90% of calories.

"We know the diet is effective for a wide variety of seizures," said Dr. Vining, director of the John M. Freeman Pediatric Epilepsy Center at the Johns Hopkins Hospital, Baltimore.

She admitted, however, that "we don't understand the biology of the ketogenic diet."

About 46% of patients on the diet have greater than 90% control of seizures at 12 months, she said. For those using the diet, medications often can be decreased, although for patients helped by just two or three medications, it may make sense to continue them.

But a study on more "aggressive" discontinuation of medications found good results even within 1 month (Epilepsy Behav. 2004;5:499-502). "There are some 'superresponders' who become seizure free within the first 2 weeks," added Dr. Vining, who is also professor of neurology and pediatrics at Johns Hopkins University.

The diet emerged in the 1920s, when it was discovered that a person who is fasting becomes ketotic, she explained.

Researchers at the Mayo Clinic developed the idea that changing the nutrient structure of a diet would mimic fasting. By using the ketogenic diet, a person is put in a constant state of ketosis. The diet was popular until phenytoin came on the market and was seen as easier to use than maintaining the diet, she said. But the diet has had a resurgence since the mid-1990s. It is comparable to the popular Atkins diet for weight loss (Epilepsia 2006;47:421-4).

Prior to beginning the diet at Johns Hopkins' clinic, children fast for 24 hours and are seen in the clinic on Monday morning. They are then admitted to the clinic for 4 days (Monday-Thursday), where they are given eggnog to increase the fat in their diet from one-third to two-thirds of the full calories, and finally to a full percentage of calories using regular food. Individual adjustments are made to maintain 80-160 mmol urinary ketosis and to avoid significant weight gain or loss.

Dr. Vining cited several studies in support of the effectiveness of the diet.

A large prospective study that was conducted at Johns Hopkins enrolled 150 children with a mean age of 5.3 years and a mean monthly seizure rate of 410. The children used a mean of 6.2 antiepileptic drugs prior to initiating the diet. At 3 months, 83% remained on the diet, and 34% experienced greater than 90% reduction in seizures. At 12 months, 55% of the children remained on the diet, and 27% had greater than 90% reduction in seizures. The diet appeared to work across a wide spectrum of ages and seizure types.

Another study found that after 1 year of being on the diet, 74% of pediatric patients were able to reduce their medications, with the number on two medications was reduced from 79% to 23%. No medications were needed by 48%. There was a 67% reduction in medication costs, resulting in an average savings of about $1,000 per child per year (J. Child. Neurol. 1999;14:469-71).

A downside to the diet is impaired growth. A study conducted by Dr. Vining of 237 children ranging in age from 2 months to 9 years and 10 months found at 1 year that weight had not substantially increased and linear growth had also been reduced (Dev. Med. Child. Neurol. 2002;44:796-802).

Another study by Dr. Vining and her associates found that use of the diet for as long as 2 years resulted in elevated triglycerides, total cholesterol, and LDL cholesterol levels but no rise in HDL cholesterol levels (JAMA 2003;290:912-20). Also, acidosis is seen routinely.

Kidney stone risk was found to increase to 5.4% (6/112), with a calcium/creatinine ratio greater than 0.2 being an important risk factor in one study (Epilepsia 2000;43:1168-71). But treatment with Polycitra-K (an oral potassium citrate supplement) appears to reduce this risk, she said.

A 2004 study found that the ketogenic diet is used at 80 centers in the United States and at 70 centers in 41 countries. Continued use in patients has ranged from 1 to 45 years, with a median of 8 years. The average number of people per country using the diet was 71.6, with 5.4 started per year—with a range of 0-40 (Epilepsia 2004;45:1163). ■

Basal Ganglia Abnormalities Seen in Neuropsychiatric Lupus

BY DAMIAN McNAMARA
Miami Bureau

BIRMINGHAM, ENGLAND — Metabolic changes in the basal ganglia that can be detected with magnetic resonance spectroscopy may precede irreversible changes from neuropsychiatric lupus, according to a pilot study.

"Why look at basal ganglia? They are highly prone to hypoxic damage and have recently been linked with the frontal lobe regarding cognitive function," Dr. Pamela L. Peterson said at the annual meeting of the British Society for Rheumatology. In Parkinson disease "and other diseases, there is increasing recognition of the role of basal ganglia."

Lupus patients had a statistically significant correlation between decreases of *N*-acetylaspartate in the basal ganglia and frontal white matter.

There are at least four circuits that link the basal ganglia to the cerebral cortex. Although less common, movement disorders are a well-accepted complication of neuropsychiatric systemic lupus erythematosus (NPSLE) and may be mediated by the basal ganglia, said Dr. Peterson, a rheumatology fellow at St. George's Hospital, London.

Clinicians more commonly order MRI scans to detect abnormalities in the periventricular region and subcortical white matter of patients with NPSLE. However, magnetic resonance spectroscopy of the basal ganglia might prove to be useful for earlier clinical intervention,

"Magnetic resonance spectroscopy is noninvasive, cheap, and easily added to an MRI protocol," Dr. Peterson said.

Preliminary findings of the study are based on 24 patients who have NPSLE, 8 patients with active lupus but without neurologic symptoms, and 4 healthy controls. Participants are recruited for the ongoing study from St. George's University of London; St. Thomas' Hospital, London; and University College London. The age range is 17-54 years.

Blood tests indicated absolute concentrations of *N*-acetylaspartate (NAA), choline, creatine, and myoinositol. The metabolite NAA is a marker for neuronal loss or dysfunction, Dr. Peterson said. Study participants had a combination of MRI, magnetic resonance spectroscopy, and diffusion tensor imaging, as well as an interview, clinical assessment, and psychometric testing.

The researchers found a statistically significant correlation between decreases in NAA in the basal ganglia and frontal white matter. Also, levels were significantly lower in these regions, compared with healthy controls. "There was a step-wise deterioration in NAA with worsening neurologic effects," Dr. Peterson said.

Participants with non-neuropsychiatric lupus also had decreases in the metabolite, but the reductions were not significantly different, compared with controls.

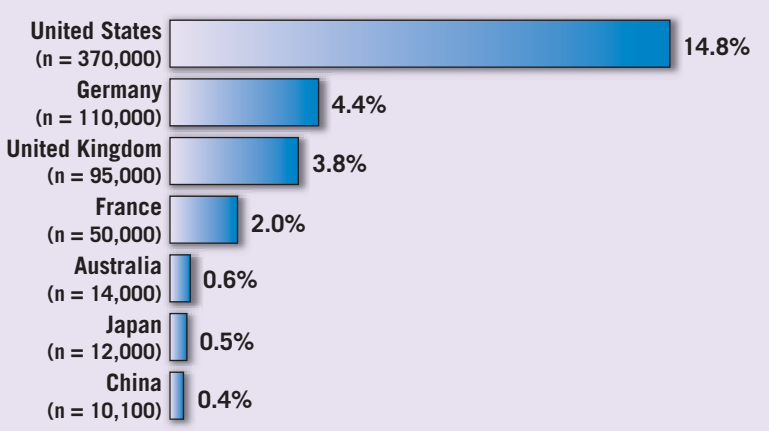
"This correlation may simply indicate a global reduction of NAA in patients with NPSLE or it may reflect abnormalities in the circuits connecting the frontal white matter with the basal ganglia," the researchers noted. NPSLE may alter the cortical striatal fibers that connect basal ganglia and frontal lobe, Dr. Peterson added.

Although the pilot data from the study included only magnetic resonance spectroscopy findings, Dr. Peterson said changes in myoinositol in these two regions also appear to be correlated. In addition, initial psychometry results suggest "a possible relationship between NAA reduction in the basal ganglia and processing speed."

"My results are tentative. This is a small data set," Dr. Peterson said. "We want bigger numbers in the future." ■

DATA WATCH

Prevalence of Multiple Sclerosis in Selected Countries As Percentage of World Cases



Note: Based on 2006 data from the World Health Organization.
Source: Kalorama Information