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Long-term health consequences of epilepsy diet treatments

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SUMMARY

The ketogenic diet (KD) typically provides a marginally healthy diet and in recent years has been used for more protracted courses of therapy. This results in concern about the impact of the diet on the general health of the child. Studies have demonstrated poor growth, dyslipidemia, kidney stones, and numerous other problems seen less frequently. Major areas of concern are reviewed as well as some emerging evidence of more beneficial long-term health consequences beyond the expected control of seizures.

KEY WORDS: Ketogenic diet, Epilepsy.

Dietary therapy for control of seizures, such as the ketogenic diet (KD), has existed for millennia. In its more modern context, the KD has been used for short periods of time—typically about 2 years (Livingston, 1972). However, in the past decade, as interest in the KD has increased and its effectiveness has been found to exceed that of many modern antiepileptic drugs (AEDs), children may be using the KD for longer periods of time. Thus, such children are at higher risk for long-term impact upon their health.

The literature suggests that many problems and areas for concern do arise, both in the short and long term. These include growth, lipid levels, cardiac function, kidney stones, disordered bone metabolism, nutritional adequacy, and hematologic/immunologic concerns. On the other hand, some literature suggests that the KD (or similar diets) can be beneficial to overall health. Finally, the diet can lead to improved function and quality of life. All of these factors must be considered in weighing the risk:benefit ratio of continuing these therapeutic diets.

A number of studies have discussed the various short- and long-term complication of the KD. In one study of 52 children treated for 22 months, five patients had significant complications, including two with hypoproteinemia, one with Fanconi's renal tubular acidosis, and two with increased liver enzymes (Ballaban-Gil et al., 1998). Four of these children were on valproic acid. In the Korean experience, 199 children were followed for variable periods of time (Kang et al., 2005). Twenty-five had complications: nine had gastrointestinal problems, five had serious infections, three had lipoid pneumonia, and a variety of other problems were seen in individual patients. There were four deaths related to cardiomyopathy, lipoid pneumonia, or serious infections. The patients who died generally were very ill prior to diet initiation, which is typical of other studies as well. The most recent overall review of long-term use of the diet reported on 28 patients who had been treated for 6–12 years. Twenty-four of these children had experienced more than 90% reduction in seizures, an obvious reason for continuing the therapy. Growth was a major problem with 10 of the children being below the 10th percentile for height at diet onset, but 22 of them below the 10th percentile at follow-up. Seven of the children had experienced kidney stones and six had skeletal fractures. Dyslipidemia was seen with mean cholesterol 201 mg/dl, LDL 129 mg/dl, triglycerides 97 mg/dl, and HDL 54 mg/dl (Groesbeck et al., 2006). Many practitioners with long experience using the KD are aware of patients remaining on the diet for more than 20 years. A recent patient presented to the group at Hopkins, having "self-managed" the diet for decades. He had no hunger issues, kidney stones, constipation, or acidosis, and he had a DEXA scan that predicted a low risk for fracture and a normal carotid ultrasound. He did have dyslipidemia. His family clearly wished to continue the diet and was able to obtain new guidance regarding nutrition and vitamin supplementation (Kossoff et al., 2007).

The nutrition community has long recognized the problems concerning growth of children who are treated with

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the KD. Livingston acknowledged this, but also reported that when patients were examined 15–20 years after completing the KD, their physical growth was within normal limits for their age. More recently, Williams followed 21 children and noted that the height percentiles dropped in 86% (Williams et al., 2002). In a larger, prospective study of 237 children under 10 years of age, 135 patients remained on the KD for at least 1 year (Vining et al., 2002). At 1 year, weight had not increased substantially and was generally at lower centiles. Children had remained within normative values for age, but those under 1 year of age were impacted more severely. Linear growth appeared less affected over this period of time. Two groups were more susceptible to poor weight gain (i.e., greater decline in weight Z score): those who were nonambulatory or noncommunicating. On the other hand, clinicians are very familiar with children who have become overweight while on various anticonvulsants and who successfully normalize their weight when placed on the KD. Prescribing physicians and dietitians are beginning to more carefully evaluate whether restriction of weight gain, especially in very young children is necessary.

There are no definitive long-term studies on the cardiovascular impact of the KD. Livingston (1972) reported on patients seen in follow-up at age 40–50 years who had been on the KD as youngsters. There was no evidence of arteriosclerosis; blood pressure readings were normal, as were ECGs. Blood cholesterol levels typically were normal. A prospective study of 141 children on the KD for at least 6 months (the majority on a 4:1 ratio) were found to have dyslipidemia with elevated cholesterol, triglyceride, apolipoprotein B, very low density lipoproteins (VLDL) and low density lipoproteins (LDL). Only 1/6 had either cholesterol or triglyceride in an acceptable range. The functional impact of these findings remains to be evaluated. Typically, diets are managed by changing to more polyunsaturated fats and adding medium chain triglycerides when lipid values become excessive (Kwiterovich et al., 2003).

Kidney stones occur in 5–7% of children on the KD. Risk factors include young age, family history of kidney stones, and a urine Ca/Cr ratio of >0.2 (Furth et al., 2000). Oral potassium citrate significantly decreased the prevalence of stones and increased the mean time on the diet before occurrence (Sampath et al., 2007).

A variety of other medical problems have been seen in children on the KD, including Vitamin D deficiency, low carnitine levels, acute pancreatitis, prolonged QT intervals, and excessive bruising. Often it is not clear what the relationship is to the KD, medications, or other complicating medical issues.

There is a small, but important literature emerging that suggests that a KD or a diet low in carbohydrates may actually be beneficial to health, beyond control of seizures. A group of adults placed on a KD for more than a year showed significant decrease in BMI as well as improved lipid studies (Dashti et al., 2006). Another study compared a low carbohydrate KD to a low fat diet and demonstrated greater weight loss on the KD as well as improvement in some lipoprotein subclasses (Westman et al., 2006). In a comparison of a variety of weight loss diets, the Atkins diet (a modified form of which is used for seizure control) showed the most weight loss and a more favorable overall impact on various metabolic profiles (Gardner et al., 2007).

Finally, studies are emerging that support Livingston's observation that behavior and disposition were better on the KD. Pulsifer et al. showed that the mean developmental quotient significantly improved on the KD and that there was significant behavioral improvement in attention and social functioning (Pulsifer et al., 2001). Another study of 18 children on the KD showed improved quality of life and attention that may correlate with increased rapid eye movement (REM) sleep (Hallbook et al., 2007).

Although the KD was not originally intended for prolonged use, many children have such vastly improved seizure control and quality of life that they remain on it for many years. The long-term consequences of this marginally adequate nutritional state must be evaluated. Less caloric restriction with more careful attention to healthy weight gain and less fluid restriction have become standard. Vitamin supplementation and assessment of bone function is critical. In the future, understanding the relationship of dyslipidemia to functional effect on the cardiovascular system will be important to study. Research will hopefully allow us to optimize the factors of the diet that are critical to seizure control, while eliminating the factors that lead to negative consequences.

Acknowledgment

I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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