

Risk of Liver Dysfunction in the Ketogenic Diet

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Background

- The ketogenic diet is a well-established non-surgical therapy that can be used for the nearly 30% of patients with epilepsy who do not respond to medical therapy.
- The ketogenic diet has resulted in total seizure resolution in 16% of patients and greater than 90% reduction of seizures in 32% of patients who have failed medical therapy.
- It has been observed in mouse models that a high fat, low-carbohydrate diet causes significant lipid infiltration into the liver, consistent with non-alcoholic fatty liver disease (NAFLD).
- Indeed, hepatitis is a known side effect of the ketogenic diet; however, the prevalence and risk of liver dysfunction is unknown.
- We do not know whether patients on the ketogenic diet who exhibit mild elevations in transaminases are at high risk for progressing to frank liver dysfunction or cholestasis.
- Given that NAFLD is quickly becoming one of the leading causes of liver transplantation, there is a critical need to understand the prevalence and degree of hepatitis as well as nutritional/metabolic abnormalities associated with the ketogenic diet.

Objectives

- The overall objectives of this project are to assess the prevalence of liver dysfunction with the ketogenic diet, and to identify predictors (e.g. increased transaminases, nutritional deficiencies, weight gain) of those at risk. Answering these questions will increase our understanding of the risks of long term use of the ketogenic diet on liver health and identify patients in whom early discontinuation of the diet should be considered.

Aims

- Define the prevalence of elevated transaminases in the medication-refractory epilepsy patients managed on the ketogenic diet.
- Review other nutritional and metabolic markers such as carnitine, cholesterol, BMI to determine if there are additional deficiencies associated with the ketogenic diet that could contribute to development of liver dysfunction.
- Develop a statistical model to predict which patients are at risk of developing liver dysfunction while on the ketogenic diet for medication refractory epilepsy.

Methods

- We will perform a retrospective chart review of over 200 patients followed in the UCLA Department of Neurology Ketogenic Diet Clinic for up to 10 years.
- We will collect transaminases before the ketogenic diet was initiated and trend them throughout duration of participation. We will collect GGT, Indirect and Conjugated Bilirubin to assess development of non-alcoholic fatty liver disease or cholestasis.
- Carnitine and vitamin D deficiency, hypercholesterolemia, and weight gain are also associated with the ketogenic diet, and could potentially contribute to NAFLD and liver disease; therefore, we will collect surveillance levels drawn throughout therapy and trend growth at each visit.

Next Steps/Policy Implications/Significance

- While the ketogenic diet offers great therapeutic potential for some patients with seizures, we do not know whether we are putting these patients at risk for severe liver disease. Thus, the contribution of this study is significant because understanding the prevalence of hepatitis associated with the ketogenic diet in the pediatric population is a critical step in ultimately discovering the mechanism of action of liver injury and developing protocols for surveillance in order to prevent progression to fibrotic liver disease and cirrhosis.

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