Clinical Research Reports

Manipulation of Types of Fats and Cholesterol Intake Can Successfully Improve the Lipid Profile While Maintaining the Efficacy of the Ketogenic Diet

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Abstract: *The ketogenic diet (KD) is a dietary therapy that effectively treats intractable epilepsy in children. Hyperlipidemias are common side effects of KD and have been reported in approximately 30% to 50% of patients on this diet. Fats comprise 90% of the calories, and saturated fats are often used as 50% of the fat intake. The purpose of this study was to investigate whether alterations of the dietary fat sources can improve the lipid profiles while maintaining seizure control in the ketogenic diet. Using a retrospective chart review, the authors evaluated their practices of treating hyperlipidemias in 6 children on the KD who developed elevated lipid profiles. All had normal or mildly elevated lipid profiles before beginning the KD. The elevated lipid levels were detected after an average of 7 months of KD treatment. Changing the dietary fat types to mainly oils (polyunsaturated fats) and decreasing the use of protein foods high in saturated fats and cholesterol resulted in a normalized or baseline lipid profile in all 3 months later. Seizure control was unaffected. Hyperlipidemia is not a cause for discontinuing the KD and can be managed by changing the dietary fat sources.*

Keywords: ketogenic diet; hyperlipidemia; saturated fat; unsaturated fat; cholesterol

The ketogenic diet (KD) is a high-fat, low-protein, and very low-carbohydrate diet that effectively treats intractable epilepsy in children.[1] For the classic KD, 90% of the calories are provided as fat, whereas carbohydrate and protein only make up 10% of the total caloric intake. Composition of the classic KD is represented in terms of the ratio of weight in grams of ketogenic food to weight in grams of antiketogenic food. The classic 4:1 ratio refers to the total grams of daily fat intake in comparison to total daily grams of protein and carbohydrate intake combined. To make the KD diet palatable, 80% to 90% of the fat content is typically saturated fats (40% butterfat heavy cream, butter, and high-fat processed meats and cheeses). The other 10% to 20% fats are unsaturated fats such as margarine, oils, and nuts.

"Our case series indicates that by minimizing the intake of saturated fats while maintaining the high ketogenic ratio, patients can improve their lipid profiles."

Hypercholesterolemia and hypertriglyceridemia are frequent side effects of the KD as reported by Kwiterovich et al[2] and Kang et al.[3] In the general population, these types of hyperlipidemias may

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lead to an increased risk of heart disease, pancreatitis, and stroke. The long-term effects of a 90% fat diet on the cardiovascular system are unknown. Typical KD treatment at The Children's Hospital of Philadelphia is a 2-year full diet treatment followed by a 1-year gradual wean. We report 6 children who developed hyperlipidemias while being treated with the KD. We investigated our ability to treat hyperlipidemias in children on the KD by altering the fat sources and the cholesterol content of the diet and whether seizure control was affected by this change. While maintaining the KD ratio, types of fats and cholesterol intake were manipulated, and changes in fasting lipid profiles were monitored.

The purpose of this study was to investigate the response in patients with hyperlipidemias induced by the KD to manipulation of the amount of saturated and unsaturated fats and total cholesterol intake, while remaining on the KD.

Methods

Permission to perform retrospective chart review was obtained from The Children's Hospital of Philadelphia Institutional Review Board, and children who had been diagnosed with hyperlipidemias on the KD were identified. Our treatment practices of hyperlipidemias were investigated. Demographic information, including family history of hyperlipidemia, early heart disease, and stroke, was collected.

Prior to initiating the KD, the children were assessed to determine tolerance of a daily high-fat intake (reflux, aspiration risk, gastrointestinal motility) and risk for hyperlipidemia. The dietary assessment included food preferences and a 3-day weighed dietary record.

A fasting lipid profile was obtained before beginning the KD and repeated every 3 months while the child was treated with the KD. Three-day weighed diet records were analyzed before KD and every 3 months thereafter. Records were analyzed using Food Processor for Windows, Nutrition and Fitness Software (Version 8.22). All food substance was analyzed completely for total calories, macronutrient composition, and micronutrient intake. Statistical analysis was descriptive and included means, standard deviations, and ranges.

Table 1.

Dietary Intake of Macronutrients for 6 Children With Refractory Epilepsy Treated With the Ketogenic Diet (KD) Before and After Dietary Intervention

	On KD	After Intervention
Ketogenic ratio[a]	4 ± 0.7:1	4 ± 0.3:1
Mean caloric intake, kcal/d	1337 ± 431	1379 ± 401
Protein, g/d	26 ± 14	25 ± 13
Carbohydrate, g/d	11 ± 6	10 ± 3
Fat, g/d	133 ± 47	135 ± 38
Percentage kcal from fat	88 ± 4.3	91 ± 1.0
Percentage kcal from saturated fat	46 ± 8.7	28 ± 11.9
Percentage kcal from unsaturated fat (poly- and monounsaturated)	39 ± 2.4	51 ± 14.8
Cholesterol, mg/d	419 ± 211	245 ± 129

[a]Weight (g) of ketogenic food to weight (g) of antiketogenic food.

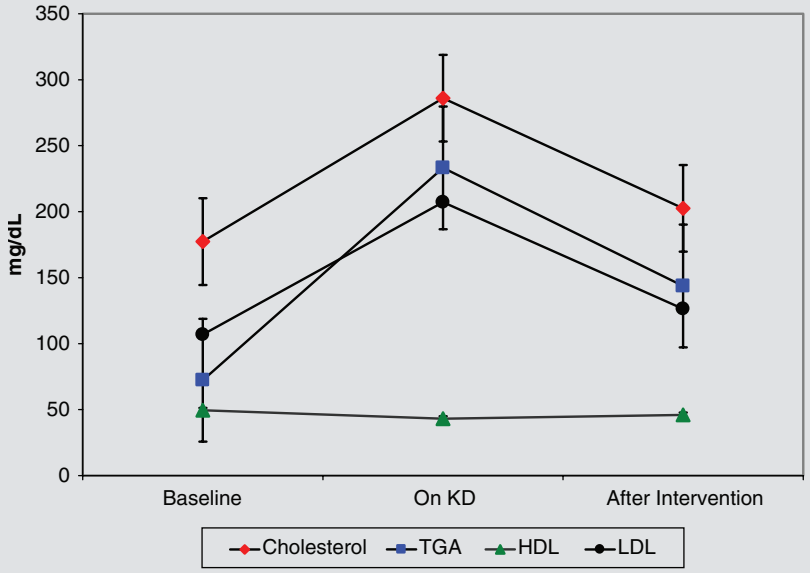
Results

Six children were identified who developed hypercholesterolemia and/or hypertriglyceridemia. Three were girls and 3 were boys. The average age was 5 ± 3.0 years at the start of the KD treatment. A family history of hyperlipidemia was present in 3 children.

At the initiation of the KD, all had either normal or mildly elevated lipid profile results (see Figure 1). The normal reference ranges used were total cholesterol, 109 to 189 mg/dL; triglycerides, 32 to 116 mg/dL; high-density lipoprotein (HDL), 35 to 82 mg/dL; and low-density lipoprotein (LDL), 0 to 99 mg/dL. LDL data were available for all intervals for 5 of the 6 children. The elevated lipid levels were detected after an average of 7 ± 4.3 months on KD treatment. On average, the total cholesterol was increased to 286 ± 25 mg/dL, triglyceride was 233 ± 204 mg/dL, and LDL was 207 ± 17 mg/dL HDL remained within reference range at 43 ± 15 mg/dL. An abnormal cholesterol level was an indication to reevaluate the child's dietary intake. Four children were on the 4:1 ratio KD treatment, which provided 90% to 92% of their total daily caloric intake as fat. The other 2 children were on the 3:1 and the 3.5:1 ratio KD treatment, which provided 87.0% and 88.7% of their total daily caloric intake, respectively. Evaluation of food intake at the time of hyperlipidemia, via 3-day weighed diet records, showed that, on average, 46% ± 9% of the total dietary fat intake was saturated fats, whereas 39% ± 2% was mono/polyunsaturated fat. The average daily cholesterol intake was 419 ± 211 mg (see Table 1). Heavy cream (40% butterfat) constituted 50% of the fat source, with the rest of the fat calories provided as butter, mayonnaise, margarines, and oils. Protein sources were high in saturated fats, with bacon, hotdogs, and eggs being some of the favorite protein sources of all 6 children.

Figure 1.

Lipid profiles at baseline, on the ketogenic diet and after dietary intervention for 6 children, expressed as means and standard error. KD, ketogenic diet; TGA, triglycerides; HDL, high-density lipoprotein; LD, low-density lipoprotein.



The families were counseled on the dietary sources of saturated fat and cholesterol and were asked to increase the use of polyunsaturated fats. They were encouraged to reduce or discontinue the use of butter, heavy cream, high-fat processed meats, cheese, and egg yolks. They were also encouraged to increase the use of oils, margarines not containing trans fats, nuts and nut butters, fish, poultry, and egg whites. The follow-up fasting lipid profile was obtained 5 ± 2.3 months later and showed improvement in all 6 children (see Figure 1). Average cholesterol and triglycerides were reduced to 203 ± 35 mg/dL and 144 ± 60 mg/dL, respectively. The average HDL increased to 46 ± 11 mg/dL. For the 5 children who had LDL levels available, the average was reduced to 126 ± 35 mg/dL. Reevaluation of the 3-day diet record after the dietary intervention also showed a decreased percentage of saturated fats (28% ± 12% of total fat), increased percentage of poly and monounsaturated fats (51% ± 15% of total fat), and reduced cholesterol intake (245 ± 129 mg/d). At this time, the KD ratio had been increased to 4:1 for all 6 children, with 91% ± 1% of total daily caloric intake provided as fat (see Table 1). Seizure control was unaffected in all 6 children by the change in fat source.

Discussion

The KD is an effective therapy for intractable seizures but is not without side effects. One of these is hyperlipidemia, which in the general population can lead to serious health concerns such as coronary heart disease. Some studies report hypercholesterolemia, hypertriglyceridemia, and decreased HDL, whereas others report no change in total cholesterol levels after 6 months on the KD.[2-4] In the Kwiterovich et al[2] study of 141 children, 6 months of treatment with KD significantly increased the mean plasma levels of total cholesterol, LDL cholesterol, and triglycerides while significantly decreasing HDL cholesterol. In the Kang et al[3] study of 129 patients, the incidence of hyperlipidemia was noted within 4 weeks of initiating the KD. In this early phase of their study, 14.7% had hypercholesterolemia, 27.1% had hypertriglyceridemia, and 3.9% developed HDL hypocholesterolemia. However, Couch et al[4] reported no significant change in total cholesterol levels of 26 children treated with the KD for 6 months.

Although adverse health outcomes such as hyperlipidemia have been reported in studies where classic KD was used for the treatment of intractable epilepsy, low-ratio KD has also been used in the treatment of obesity with improved health outcomes. Dashti et al,[5,6] in their 12-week and 56-week studies with obese participants on a ketogenic diet, reported significantly decreased levels of total cholesterol and LDL cholesterol and significantly increased levels of HDL cholesterol. Similarly, Yancy et al,[7] in their 24-week randomized controlled trial of 120 participants with obesity, showed that a low-carbohydrate KD resulted in greater weight loss, greater decrease in serum triglyceride level, and greater increase in HDL level compared to a low-fat diet regimen.

Similar to our study, other reports have investigated the use of different types of fats and their effects on serum lipid levels in the classic KD epilepsy population. Liu et al[8] showed that compared to the classic 3.5 to 4.3:1 ratio KD, a KD where 40% to 60% of total calories are provided as medium-chain triglycerides appears to reduce cardiac risks by reducing LDL levels and the ratio of total cholesterol to HDL. Although not statistically significant, their study showed that the classic 3.5 to 4.3:1 ratio KD showed the opposite effect, where LDL levels and total cholesterol to HDL ratio were both increased. It has not been reported whether the type of long-chain triglycerides (saturated vs unsaturated) used in the KD affects the lipid levels. In their prospective study of 25 children on the KD, Dahlin et al[9] started extra supplementation of omega-3 fatty acids in the form of fish oil at 1 month of treatment. They reported that the mean serum levels of cholesterol and triglycerides were at maximal levels at 1 month of KD treatment but then slightly decreased and remained relatively stable during the remainder of their 12-month study. Dahlin et al[9] also noted relatively high polyunsaturated fatty acid (PUFA) intake in their KD regimen, along with a decreased omega-6 to omega-3 fatty

acid ratio during their treatment period, which they state may be of cardiovascular benefit. According to Dahlin et al,[9] such possible cardiovascular benefit may be achieved by a KD regimen that is rich in PUFAs with emphasis on omega-3 intake. Similarly, our study showed that while maintaining the traditional high-fat composition of the KD, the percentage of saturated fat intake can be decreased, the percentage of poly- and monounsaturated fats can be increased, and total cholesterol intake can be successfully reduced, all of which could lead to cardiovascular benefits for patients treated with the KD.

Traditionally, fat sources used in the KD have included saturated fats such as heavy cream and butter as they are easier to incorporate into meals in larger quantities because of their taste and consistency. Unsaturated fats such as canola and olive oils are not easily incorporated into meals in large quantities as they separate out of mixtures. In addition, high-fat processed meats such as sausage and hot dogs are consumed frequently by patients on the KD, as a way to reduce the amount of additional fat with the meals. Our case series indicates that by minimizing the intake of saturated fats while maintaining the high ketogenic ratio, patients can improve their lipid profiles. By reducing the amount of heavy cream and butter and using canola oil as the primary source of dietary fat, eliminating egg yolks, cutting back on high-fat processed meats, and incorporating more poultry, fish, and nuts into the diet, we were able to reduce the overall saturated fat and cholesterol intake of our KD patients. At the same time, we were also able to increase their overall mono- and polyunsaturated fat intakes. Our experience has been that patients' families are open to experimenting with different recipes and cooking methods, as well as introducing a variety of new foods into their child's diet, in an effort to help reduce the hyperlipidemia. We have also observed that the KD patients adapted easily to drinking oil without much difficulty in cases where the quantity of oil could not be completely incorporated into the foods.

Limitations

Our report is a small retrospective case series. A greater number of participants and prospective trials are needed. For future studies, evaluation of trans fatty acid intake would be recommended.

Conclusion

For patients on the KD, dietary intake should be periodically analyzed to maintain healthy lipid profiles. In conjunction, fasting levels of cholesterol, HDL, LDL, and triglycerides should be monitored on a regular basis. When hyperlipidemias occur, changing food choices to reduce the saturated fat and cholesterol content of the KD may be all that is needed to normalize the lipid levels. Using more polyunsaturated fats did not decrease the palatability of the KD. Seizure control was unaffected by the change in fat source. Discontinuing the KD because of hyperlipidemia may not be necessary. Prospective clinical trials are necessary to prove the full effect of this type of intervention in children treated with the ketogenic diet. ■

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