

Implementing a ketogenic diet based on medium-chain triglyceride oil in pediatric patients with cancer

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ABSTRACT

Traditionally, a ketogenic diet is given to drug-resistant children with epilepsy to improve seizure control. Inducing a ketogenic state in patients with cancer may be a useful adjunct to cancer treatment by affecting tumor glucose metabolism and growth while maintaining the patient's nutritional status. A ketogenic diet consisting of 60% medium-chain triglyceride (MCT) oil, 20% protein, 10% carbohydrate, and 10% other dietary fats was provided to a select group of pediatric patients with advanced-stage cancer to test the effects of dietary-induced ketosis on tumor glucose metabolism. Issues of tolerance and compliance for patients consuming an oral diet (consisting of normal table foods and daily MCT oil "shakes") and for patients receiving an enteral formula are reviewed. Preliminary use of the MCT oil-based diet suggests a potential in pediatric patients with cancer. *J Am Diet Assoc.* 1995; 95:693-697.

Certain tumors, particularly those that are poorly differentiated and slow growing and have a limited blood supply, are known to use glucose as the primary source of fuel (1-5). Shifting the prime substrate for energy metabolism in the host from glucose to ketone bodies by means of a ketogenic diet, thereby decreasing the availability of glucose to the tumor, could potentially inhibit tumor growth (6). A ketogenic diet based on medium-chain triglyceride (MCT) oil was administered to five adult patients with cancerous cachexia, and the results were promising (7). The ketogenic diet (14% protein, 16% carbohydrate, and 70% MCT oil supplemented with D-3-hydroxybutyrate at 4 mmol/kg per day) maintained these persons with cachexia in positive nitrogen balance and induced significant weight gain during a 2-week period. Whether implementation of the ketogenic diet in patients with cancer would affect tumor metabolism remained to be determined.

In a study we reported elsewhere (8,9), dietary-induced ketosis was established in select pediatric patients with cancer to determine whether a ketogenic state would decrease glucose availability to certain tumors, thereby impairing tumor metabolism without adversely affecting the patients' overall nutritional status. Pediatric patients with advanced-stage malignant astrocytoma tumors were monitored for 8 weeks during which ketosis was maintained by the administration of an MCT-oil-based diet (60% MCT oil, 20% protein, 10% carbohydrate, and 10% other dietary fats). Tumor glucose metabolism was assessed by positron emission tomography (PET), which compared [fluorine-18] 2-deoxy-2-fluoro-D-glucose uptake at the tumor site before and after the trial. Within 7 days of initiating the ketogenic diet, blood glucose levels declined to low-normal levels and blood ketones were elevated 20- to 30-fold. Body weights remained stable throughout the study. The PET scan data indicated a 21.8% average decline in glucose

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Table 1
Calculated medium-chain triglyceride (MCT) oil allowance per day

Total kcal/day ^a	Tbsp MCT oil/day
1,500	8.0
1,800	9.5
2,000	10.5
2,200	11.5
2,400	12.5

^aForty percent of total energy provided by foods; 60% of total energy provided by MCT oil.

Table 2
Dietary exchanges^a

Source ^b	Daily portion	Carbohydrate	Protein	Fat
		← g →		
MCT shake	1.5 c	21	26	2
Starch	1 c	14	3	...
Vegetable	1 c	6	2	...
Fruit	1 c	14
Protein	10 oz	...	70	30
Total		55	101	32

^aBased on a 2,200-kcal diet; 1,320 kcal from medium-chain triglyceride (MCT) oil =

11.5 Tbsp/day and 880 kcal from food = 55 g carbohydrate and 110 g protein.

^bPlus vitamin supplements.

uptake at the tumor site (9). This article summarizes the successful implementation strategy of the MCT oil-based ketogenic diet in a select pediatric population.

WHY WE SELECTED AN MCT OIL-BASED KETOGENIC DIET

A high-fat, low-carbohydrate ketogenic diet has been used since the 1920s as an effective method of controlling epileptic seizures in prepubescent children (10). Unfortunately, this type of diet is not without side effects — poor tolerance, hyperlipidemia, and elevated serum cholesterol and triglyceride levels (11). The diet, consisting predominantly of heavy cream and butter fat, is often quite unpalatable, and some patients complain of hunger between meals (11,12). Fluid restrictions are often required to maintain ketosis (12). Transient gastrointestinal disturbances such as nausea, vomiting, diarrhea, or constipation often occur if ketosis is initiated too quickly (12).

Because of these limitations, alternative lipid sources were tried that would be well tolerated yet maintain a strong ketotic state (13). MCT oil (manufactured by Mead Johnson/Bristol-Myers Co, Evansville, Ind) was discovered to match these requirements ideally. The oil consists of fatty acids with molecular chain varying in length between 6 and 12 carbon atoms. MCTs are absorbed by intestinal cells in the form of medium-chain fatty acids and are carried directly to the liver by the portal vein, thus bypassing the lymphatic system. In the liver they are converted to carbon dioxide, acetate, ketones, and long-chain fatty acids (14). MCTs are hydrolyzed to fatty acids more rapidly than are long-chain triglycerides derived from dietary fats (15). Researchers think that MCTs produce ketosis as a result of this rapid intestinal absorption along with the prompt delivery to the liver where they are rapidly oxidized to ketone bodies (16).

The MCT oil-based diet is as effective in controlling seizures as the traditional ketogenic diet; in addition, fewer limitations and side effects are reported with the MCT oil-based diet (17-22). At 1,600 kcal, a traditional ketogenic diet with a fat to nonfat ratio of 3:1 contains 29 g protein, 23 g carbohydrate, and 156 g dietary fat, whereas the MCT diet with a fat to nonfat ratio of 3:1 contains 41 g protein, 74 g carbohydrate, 20 g dietary fat, and 116 g MCT (19). Thus, the MCT oil-based diet has larger allowances for protein and carbohydrates, which makes the MCT diet slightly more flexible, easier to prepare, and less lipogenic than the traditional ketogenic diet (19). Gradual introduction of the diet minimizes any potential gastric disturbance that could be caused by administering large amounts of the MCT oil too rapidly (20).

THE MCT OIL-BASED KETOGENIC DIET

The diet consists of 60% MCT oil, 20% protein, 10% carbohydrate, and 10% other dietary fats as percentage of total kilocalories (Tables 1 and 2). Other sources of dietary fats are included in the diet to prevent a deficiency in essential fatty acids. The percentages of carbohydrate, protein, and dietary fats may be modified slightly to satisfy patient preferences; however, they should not exceed 40% of total kilocalories to maintain ketosis (21,22).

The diet is designed to promote weight gain and ketosis in pediatric patients. Energy levels should be calculated at 120% of the Recommended Dietary Allowance (RDA) (23) for age to prevent possible weight loss. Weight loss has been documented during the introduction to the diet and is speculated to be caused by alterations in the patient's metabolism during this time (21,22). Energy estimates may be increased from 120% up to 150% of the RDA depending on the patient's individual need, or if the patient experiences hunger or weight loss while consuming the diet (22).

Normal table foods and beverages are used in combination with an MCT oil "shake," which is consumed four to five times per day with meals and snacks (Table 3). Shakes are made with a variety of flavorings (cocoa powder, sugar-free Kool-Aid [Kraft Foods, White Plains, NY], fruit), low-fat milk, water, and up to two thirds of the MCT oil allowance. Two or three tablespoons of Pro-Mod protein powder (Ross Laboratories, Columbus, Ohio) may be added to the shake to improve nutrient content and emulsion if desired (Figure). The remaining oil allotment is added into foods such as unsweetened applesauce, scrambled eggs, tuna fish, salads, or casseroles.

Because the ketogenic diet consists of small portions of food, it is deficient in B-complex vitamins, vitamin D, calcium, iron, and other minerals (20). Therefore, supplements of all vitamin and minerals known to be essential must be provided to meet the requirements for age and sex.

Potential side effects may include nausea, vomiting, bloating, and frequent, bulky bowel movements if the MCT oil is administered too rapidly into the diet. Most side effects generally occur during the introductory phase of the diet. Dividing the MCT oil allotment into five or more small feedings and providing food with the MCT oil reduces these effects (24).

Some protocols suggest that the patient should fast 24 to 48 hours before starting the diet to enhance the ketogenic state (12). Unfortunately, this period of fasting can prolong the introductory phase, because the diet is not introduced until urinary ketone levels are high (24). Extended fasting could also be contraindicated for a cancer patient. Alternatively, a step-by-step method of introduction has successfully reduced the period of transition to the diet to 3 or 4 days. After an overnight fast (usually 12 hours, with water ad libitum), 50% of the total required energy is provided to the patient. If no

Table 3
Sample menu of 2,200 kcal

Meal	Carbohydrate (g)
Breakfast	
MCT ^a oil shake (4 oz)	5.25
2 eggs scrambled + 1 tsp MCT oil	1
4 strips bacon	1
1/2 orange	7
1 slice low-carbohydrate bread	7
2 pats margarine	None
Lunch	
2 slices tomato	2
3 oz ground beef patty, cooked + 1 Tbsp MCT oil	None
1/2 c watermelon	5
3 dill pickle slices	None
MCT shake (4 oz)	5.25
Snack	
MCT oil shake (4 oz)	5.25
1 Tbsp peanut butter + 1 tsp MCT oil	3
1/4 c carrot sticks	2
Dinner	
3 oz baked chicken, no skin + 1 Tbsp MCT oil	None
1/4 c asparagus tips + margarine	4
1 c salad (lettuce, cucumber) + 1 Tbsp MCT oil + vinegar	2
Sugar-free beverage	None
Snack	
MCT oil shake (4 oz)	5.25
Sugarfree flavored gelatin	None
TOTAL	55

^aMCT = medium-chain triglyceride.

Ingredients

- 1.5 c low-fat milk
- 0.5 c water
- 4.0 Tbsp Pro-Mod protein powder (Ross Laboratories, Columbus, Ohio)
- 1.0 tsp cocoa powder
- 8.0 Tbsp MCT oil
- Artificial sweetener to taste

Directions

Combine the ingredients in a glass blender. Mix until smooth. Makes four 4-oz servings. Sip slowly with meals and snacks.

Recipe for a medium-chain triglyceride (MCT) shake. The shake provides 92 kcal/oz and is designed for a 2,200-kcal diet. At 11.5 Tbsp MCT oil, the shake provides 1,350 kcal from MCT oil or approximately 1,470 kcal for the 16-oz shake mix.

tolerance problems occur, the diet is advanced to 75% of the total energy on the second day. The patient should be advanced to 100% of total required energy by the third day. Dietary proportions (60% MCT oil, 20% protein, 10% carbohydrate, and 10% other dietary fat) should be maintained during the entire introductory period. Initiating the patient to the diet in this manner virtually eliminates most tolerance issues that have been reported (24). If symptoms of intolerance arise, however, the percentage of total required kilocalories may be reduced for a day, then incrementally increased back to desired levels as tolerance improves.

To be successful, a high degree of accuracy in planning and implementing a ketogenic diet is needed. Strong commitment

and cooperation from both the patient and family are also necessary if dietary-induced ketosis is to be maintained. All carbohydrate-containing medications, foods, or beverages should be included in the total daily carbohydrate allowance (19). Protein allowances are more liberal because they contain minimal amounts of carbohydrates per serving. Adding protein-rich foods such as beef, lamb, pork, poultry, or fish to diets helps reduce hunger and improves patient satisfaction without notably increasing the amount of carbohydrates consumed.

ENTERAL FORMULA

The MCT oil-based ketogenic diet may be provided as an enteral formula for tube feedings. The oil is blended with a variety of commercially available products to create formula of 60% MCT oil, 20% protein, 10% carbohydrate, and 10% other dietary fat. Suggested products include Portagen (Mead Johnson/Bristol-Myers Co, Evansville, Ind), Casec Protein powder (Mead Johnson/Bristol-Myers Co) and Pro-mod powder (Ross Laboratories, Columbus, Ohio). Liquid supplements containing MCT oil may also be used successfully in the diet. The products should mix well with MCT oil (via a blender) and remain in emulsion. Powdered components allow for greater composition flexibility should the diet need to be modified for any reason. As with any enteral formula, issues of sanitation and storage are key concerns. Detailed instruction as to proper handling, storage, and refrigeration procedures must be provided to the patient's primary caretaker. Nonplastic containers must be used to mix and store the formula because the MCT oil could soften plastic materials.

SUPPLEMENTS

Use of vitamin/mineral supplements is essential to maintain nutrient adequacy in the ketogenic diet. Generally, over-the-counter supplements are provided on a daily basis. Unfortunately, these products do not always provide recommended levels of certain minerals, especially trace minerals, for pediatric patients with cancer.

Nutrients such as vitamin E, beta carotene, selenium, and zinc inactivate certain enzymes involved in carcinogen metabolism or decrease enzyme activities that play a role in the metabolic activation of chemical carcinogens (25). These antioxidants aid the body in preventing and repairing oxidative damage to cellular membranes. Such activities enhance cell capabilities for cancer prevention or repair from damage sustained by cytotoxic treatments (26). Therefore, inclusion of supplements that contain the RDAs for trace minerals is considered essential for patients consuming the ketogenic diet.

Pediatric supplements that include trace minerals in recommended safe and adequate ranges are not widely available. To provide optimal nutrient coverage, multiple supplements would be required. Tolerance and compliance issues are raised if four to five different supplements are needed daily. Multiple pill combinations are also proportionately more expensive. We found that chewable, broad-spectrum supplements work best (eg, Animal Friends Chewable for Children, Twin Laboratories, Ronkonkoma, NY, and Os-Cal Chewable 500-mg Calcium, Marion Laboratories, Kansas City, Mo).

A liquid vitamin/mineral supplement would be necessary for patients who are receiving the enteral formula. We conducted an extensive survey of products available with and without prescription (data not shown). Most products did not contain adequate levels of minerals and trace minerals. Most pediatric liquid vitamins are designed for use by infants and provide select nutrients (iron, B vitamins, vitamin C) but not broad-spectrum coverage. Adult formulations of liquid vitamin/mineral supplements provided at reduced dose to meet the needs

of the pediatric patient may be the best option (eg, Vita-Quick and Mini-Quick, Twin Laboratories, Ronkonkoma, NY).

TOLERANCE AND COMPLIANCE ISSUES

Tolerance to the diet may be established with minimal difficulty if the diet is introduced to the patient in a gradual manner. Periods of illness may require slight modifications in the composition of the diet. Certain medications or a common cold may alter the patient's tolerance. Depending on the situation, total energy requirements may be reduced to 75% for 24 to 48 hours to allow the episode to resolve. Sugar-free liquids and flavored gelatin can be provided as desired to sustain hydration during this time.

Dietary compliance is essential to maintain ketosis. Children are the best candidates because of their adaptability to the diet and the level of family support available. Extensive education must be provided to the patient and family caretaker to administer the diet correctly at home. Ideally, adherence to the diet should be made as easy as possible.

We designed a ketogenic diet manual to assist in food selection and compliance. The manual contains extensive food exchange lists and a variety of recipes that were developed and tested for this project. An exchange pattern is tailored to the patient's dietary requirements (Table 2). Sample menus for home use, based on the child's food preferences and the recommended exchange pattern, are provided to increase dietary compliance (Table 3). The primary caretaker and/or patient are taught how to read food labels and count grams of carbohydrates based on the food exchange lists provided within the manual. Successful adherence is normally achieved if the patient follows the recommended exchange pattern and does not exceed the grams of carbohydrate allowed.

Urinary ketone levels can be monitored by the patient at home to track the level of ketosis and, thus, dietary compliance. Blood lipid and ketone levels can be analyzed routinely by medical staff during clinic visits to monitor the patient's compliance and tolerance to the diet as well. Thus, compliance problems can be addressed at an early stage before the ketotic state is broken.

Pediatric patients with cancer have unique dietary needs and tolerance issues related to antineoplastic treatments. The diet described here is not recommended for patients who are receiving initial induction radiation or chemotherapy treatment, who have uncontrollable nausea or vomiting, who have extensive food aversions or intolerance, who have compromised liver or kidney function, or who have a nonsupportive home environment.

APPLICATIONS

This article describes the successful implementation of an MCT oil-based ketogenic diet in a select pediatric population. The oral or enteral form of the diet, combined with use of broad-spectrum supplements, is designed to meet the overall energy and nutrient needs of pediatric patients with cancer without compromising nutritional status. Tolerance issues are minimal when implementation is done carefully and gradually. Minor adjustments in dietary composition can be made to improve a child's tolerance without compromising the ketotic state. Therefore, an MCT oil-based diet may be a noninvasive option for medically stable patients. The results of preliminary use of this ketogenic diet in pediatric patients with cancer suggest a potential for clinical application. ■

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