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Medium-chain triglyceride (MCT) ketogenic therapy

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SUMMARY

The medium-chain triglyceride diet (MCTD) is a variant of the classic 4:1 ketogenic diet (KD) introduced in 1971 by Huttenlocher as an attempt to improve the palatability of the KD by allowing more carbohydrates yet preserving ketosis. Although initially found to be equally effective as the classic KD, use of the MCTD declined because of frequent gastrointestinal side effects such as cramps, diarrhea, and vomiting. Recently, we have used the MCTD in more than 50 patients. We have found excellent seizure control, similar to the classic KD, and with careful monitoring, we have encountered minimal side effects. The MCTD should remain a viable dietary option for children with refractory epilepsy who have large appetites, can tolerate more calories, or cannot accept the restrictions of the classic KD.

KEY WORDS: Medium-chain triglyceride, Ketogenic diet, Intractable epilepsy.

EFFICACY OF MCT KETOGENIC THERAPY

Because medium-chain triglycerides (MCT, C6-C12) are more ketogenic than long chain triglycerides (LCT) (Schön et al., 1959), Huttenlocher introduced a variant of the classic ketogenic diet (KD) to allow more carbohydrate (Huttenlocher et al., 1971). This medium-chain triglyceride diet (MCTD), with a ketogenic ratio of approximately 1.2:1, was thus more palatable than the classic 4:1 KD. Efficacy was excellent, with 58% of patients achieving >90% seizure reduction, a similar success rate to that achieved on the classic KD. One study that directly compared MCTD with a classic KD showed no difference in seizure control (Schwartz et al., 1989). The MCTD successfully suppressed a similar spectrum of seizures as the classic KD (e.g., minor motor, akinetic and myoclonic seizures). This excellent efficacy was verified in several subsequent studies (Table 1). However, the MCTD was frequently associated with gastrointestinal (GI) side effects including diarrhea, vomiting, bloating, and cramps (Table 1). For this reason, the MCTD has been underutilized for children with intractable epilepsy.

Recently, we have successfully employed the MCTD with minimal or controllable side effects and have achieved a similar degree of seizure control as with the classic KD (Sell et al., 2005). We are now in the process of studying 43 children with a mean age of 7.3 years (range: 2–16 years), on a MCTD consisting of 71% total fat, 19% carbohydrate, and 10% protein, a ratio of approximately 1.2:1. The children are divided into three groups: one group is receiving 40–55% MCT, another group is getting 60% MCT, and the third group is receiving a >60% MCT diet. At present, 21% of children are seizure free, 19% has a >90% seizure reduction, and another 42% has a 50–90% seizure reduction. In the past 3 years, with careful monitoring and management, we estimate 100% compliance; prior to 2005, about 7% of the cohort experienced gastrointestinal problems and discontinued the diet. Therefore, in our hands, the MCTD is providing superb efficacy and minimal side effects. The MCTD has been used with a variety of seizure types and underlying etiologies.

BENEFITS AND LIMITATIONS OF THE MCT DIET

The main benefit of the MCT diet is allowing more carbohydrate than the classic KD, with resultant increased palatability (Huttenlocher et al., 1971). The MCTD allows larger portion sizes and more fruits and vegetables. Food exchanges are used which allow more food choices. Patients consume more food, have better growth, and require fewer micronutrient supplements compared to the classic KD. There are fewer incidents of kidney stones, hypoglycemia, ketoacidosis, constipation, low bone density, and growth retardation (Liu et al., 2006). There is no acidosis (DeVivo et al., 1973) or reduction in serum alanine as in

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Table 1. Medium-chain triglyceride diet—clinical studies

Studies	N	Age (year)	Diet formulation					Efficacy (% seizure reduction)			GI side effects and/or noncompliance (%)
			Duration	MCT (%)	CHO (%)	Protein (%)	LCT (%)	100	>90	50–90	
Huttenlocher et al., 1971	12	2.5–16	2.5–13 months	60	19	10	11	50	8	8	41
Trauner, 1985	17	1–13	2 months–5years	60	15	15	10	29	–	29	30
Sills et al., 1986	50	2–15	9 months–2 years	60	–	–	–	18	9	23	12
				50–58							
				45							
Schwartz et al., 1989	59	<5–54	6 months–4 year	30	19	10	41	–	41	25	
				60	19	10	11		37	41	60
				KD 4:1	*	*	*		46	46	
Sell et al., 2005	36	3–17	3 months–5 years	50–67	10	19	21–4	17	23	27	6

*The KD 4:1 consisted of 36 cal from fat, 4 cal from protein and carbohydrate; 75 cal/kg BW; 1 g protein/kg BW.

the classic KD (Schwartz et al., 1989). We found a positive effect on lipid levels with a significantly lower total cholesterol/high density lipoprotein (HDL) ratios compared to the classic KD (Liu et al., 2003).

Some limitations need to be considered when initiating the MCTD. First, we do not start patients on the MCTD who take valproate, due to reports of liver failure when MCTD and valproate are combined. Second, MCT oil is expensive. Third, it takes longer to achieve seizure control since MCT oil must be increased gradually to lower the risk of complications. Finally, few dietitians have been trained to use MCT therapy.

Practical Design and Implementation of a MCT Treatment Program

Preadmission preparation

It is essential to have a thorough preadmission assessment and education about the MCTD to patients and caregivers to help them understand the in-depth involvement and commitment to the diet. A questionnaire includes diagnosis, seizure types/frequency; medications and methods of administration; family history, that is, epilepsy, hyperlipidemia, kidney stones; financial concerns; social background; growth/nutrition status; complete diet history; GI concerns, swallowing and chewing ability; and likelihood of compliance on the diet. Ideally, candidates do not have chronic diarrhea, are not G-tube fed, do not aspirate, and are over 1 year old. The MCTD accommodates those with large appetites, picky eaters, and teenagers/adults with the same efficacy as the classic diet and it is more nutritionally balanced. Patients/care givers and the ketogenic team make a joint decision for candidacy for the MCTD. After the first visit, families are instructed how to prepare the diet. Families must purchase all supplies (i.e., decimal gram scale, glucometer, ketostix) prior to starting the diet. There is ongoing phone or e-mail communication with families to help them eliminate highly concentrated carbohydrates and correct any nutritional concerns before initiating the diet. The preadmission biochemical index is completed, which includes BUN, creatinine, uric acid, alkaline phosphatase, aspartate transaminase (AST), alanine transaminase (ALT), complete blood count (CBC) with differential, fasting blood glucose, calcium, phosphorous, magnesium, fasting lipid profile, electrolytes, total protein, albumin, antiepileptic drug (AED) levels, ferritin, red blood cells (RBC) folate, vitamin E, 25-hydroxy vitamin D, zinc, selenium, and total/free carnitine. Patients are instructed to stop all sweets 1 week before admission. On the days before and of the admission, patients do not eat sweets, fruits, juices, or starches; after 6 p.m., only water is allowed.

Hospital admission

Upon admission, growth data (height, weight, anthropometrics) are recorded. The dietitian calculates the diet and maintenance fluid. Patients are started on a 1/3 ketogenic shake which contains cow, soy, or goat milk mixed with MCT, LCT and sugar/polycose or egg/protein powder. The 1/3 shake is fed every 2–3 h. They progress to a 2/3 ketogenic shake for six feeds, then to full solid foods as long as the diet is tolerated. The dietitian provides instruction to families during the 4- to 5-day admission, including identifying and treating complications; dealing with sick days and special occasions; understanding basic nutrition and nutrient composition; learning how to plan menus, use food exchange lists, and calculate portion sizes of each food into a meal; knowing how to incorporate MCT oil safely; selecting foods appropriate for the diet and identifying methods of making meals more appetizing; reading and understanding food labels; weighing foods and liquids on a decimal gram scale; and knowing how to find support after discharge. The nurses teach how to measure blood glucose and urine ketones.

The MCTD is divided into three meals plus three snacks per day, plus multivitamins and minerals according to the dietary recommended intake (DRI). The diet is initially calculated at 50% MCT, 21% LCT, 19% carbohydrate (CHO), and 10% protein. The food exchange list is used to divide the food into milk, starch, vegetables/fruits, protein, fats and MCT oil groups, following the macronutrients content from Bowes and Church's Food Values book (Pennington & Douglass, 2004). The daily calories are calculated with basal metabolic rate (BMR) for age/sex × activity/stress factor × 75–100%. Protein is calculated with DRI for age/sex, set at 10% calorie from protein with a minimum of 0.8–1.2 g protein/kg body weight (BW). We use the fluid maintenance equation to determine fluid requirement. Vitamin and mineral supplements are adjusted from baseline biochemical indices to meet DRI from the difference in food intake. Baseline serum carnitine level is used to determine supplemental carnitine requirements at 50–100 mg/kg BW. One vitamin or mineral supplement is started each week after discharge.

If diarrhea or vomiting occurs, the MCT is lowered by 10% for the next feed until the patient is able to tolerate the diet. Vomiting is treated immediately with a diphenhydramine suppository. If vomiting recurs within 6 h, oral fluids are discontinued and hydration proceeds with IV normal saline; feedings are continued at a 10% lower MCT dose. Oral fluids are reintroduced as tolerated. Patients are discharged when they tolerate the MCTD and caretakers are confident in handling the diet.

Fine-tuning

After patients are discharged from hospital, they are followed via phone or e-mail plus clinic visits every month for 3 months, then every 3–6 months. MCT oil is gradually increased by 10% to achieve seizure control as long as there are no side effects and urine ketones are lower than 16 mmol/L. According to each individual's tolerance, we increase MCT at 0.1–1.0 g per feed every 1–3 days. We also increase MCT oil only at the morning, afternoon, or bedtime feed(s) to improve seizure control based on the timing of the seizures and urine ketone levels. We continue monitoring nutritional status by changing diet, carnitine, vitamin, and mineral supplements as needed after assessing anthropometric, clinical, and biochemical data (Liu et al., 2003). Any percentage of MCT oil can be used, based on tolerance and seizure control, just as the classic diet can be adjusted with different diet ratios, that is, 4:1, 3:1, etc.

Switching from the classic KD to the MCTD

Patients can be switched to the MCT diet if they require more variety or quantity of food to improve their quality of life. For patients with good seizure control and either constipation or normal bowel habits, we switch their diet to 50–60% MCT, 19% carbohydrate, 10% protein, and 71% total fat. MCT can then be gradually increased to achieve maximum seizure control. If seizures are only partially controlled, we use 50–60% MCT, but a lower percentage of carbohydrate and a higher percentage of protein and total fat. For patients with GI problems, we use 1/3 MCT diet plus 2/3 classic KD and gradually increase the MCT diet until they tolerate the full MCTD. For patients with a lower BW when reaching height growth, we gradually increase MCT oil to their classic KD.

Weaning the diet

The diet is weaned slowly by decreasing the MCT oil by 10% every 1–3 months to prevent seizure recurrence. Patients who have been on the diet longer will be weaned more slowly. The carbohydrate percentage is gradually increased while the MCT percentage is gradually decreased. A low concentrated carbohydrate diet without MCT oil is then introduced after the 30% MCT diet which continues for 6 months. We recommend avoiding sweets and "junk food" even when a regular diet is resumed. If seizures recur during weaning, an anticonvulsant is added or the MCTD is restarted.

Conclusions

The MCTD allows more carbohydrates and greater food choice for patients with large or finicky appetites. The efficacy of seizure control of the MCTD is the same as the classic KD. The MCT diet can vary by MCT oil percentage just as the classic diet does by ketogenic ratio. Careful management can avoid intolerance and complications. Using the MCTD, we have been able to manage epilepsy in children with such complicated disorders as glucose transport type 1 deficiency and Mowat Wilson syndrome with Hirschprung disease and short bowel syndrome.

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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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