Medium-chain Triglyceride Ketogenic Diet, An Effective Treatment for Drug-resistant Epilepsy and A Comparison with Other Ketogenic Diets

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The ketogenic diet (KD) is one of the most effective therapies for drug-resistant epilepsy. The efficacy of the medium-chain triglyceride KD (MCTKD) is as excellent as the classic KD (CKD), which has been documented in several subsequent retrospective, prospective, and randomized studies. MCT oil is more ketogenic than long-chain triglycerides. Therefore, the MCTKD allows more carbohydrate and protein food, which makes the diet more palatable than the CKD. The MCTKD is not based on diet ratios as is the CKD, but uses a percentage of calories from MCT oil to create ketones. There has also been literature which documents the associated gastrointestinal side effects from the MCTKD, such as diarrhea, vomiting, bloating, and cramps. Therefore, the MCTKD has been an underutilized diet therapy for intractable epilepsy among children.The author has used up to >70% MCTKD diet to maximize seizure control with gastrointestinal side effects optimally controlled. As long as health care professionals carefully manage MCTKD, many more patients with epilepsy who are not appropriate for CKD or modified Atkins diet or low glycemic index treatment will benefit from this treatment. A comparison between the MCTKD and other KDs is also discussed. *(Biomed J 2013;36:9-15)*

Key words: epilepsy, ketogenic diet, low glycemic index treatment, medium-chain triglyceride, modified Atkins diet

The ketogenic diet (KD), introduced by Wilder in 1921,[1] continues to be one of the most effective therapies for drug-resistant epilepsy in the pediatric population.[2,3] Due to severe restriction of the classic KD (CKD), the medium-chain triglyceride ketogenic diet (MCTKD) was introduced by Huttenlocher in 1971.[4] Medium-chain triglycerides (MCT, C6–C12) are more ketogenic than long-chain triglycerides (LCT) and because of this, Huttenlocher was able to introduce a more palatable KD than the CKD. The MCTKD is not based on diet ratios but uses a percentage of calories from MCT oil to create ketones. However, the literature frequently documents the associated gastrointestinal (GI) side effects from the MCTKD, such as diarrhea, vomiting, bloating, and cramps.[4-10] For this reason, the MCTKD has been an underutilized diet therapy for intractable epilepsy among children. In the past few years, two other dietary therapies have been developed for the treatment of epilepsy: The modified Atkins diet (MAD)[11-14] and low glycemic index treatment (LGIT).[15-17]

Efficacy

The efficacy of the MCTKD is excellent, as it is similar to that achieved by the CKD, which has been verified in several subsequent retrospective, prospective, and randomized studies. These studies have shown that more than 50% of the children had achieved >50% reduction in seizure control.[4-10,18] Schwartz directly compared MCTKD with CKD and found no difference in seizure control.[7] Liu and Sell also indicated similar efficacy between CKD and MCTKD.[8,9] Neal's randomized trial comparing CKD and MCTKD indicated there were no significant differences between these two diets.[10,18] Animal studies suggested both CKD and MCTKD have a positive effect in decreasing brain cerebral excitability in young animal,[19] and acute anticon-

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vulsant property of caprylic acid, the main constituent of the MCTKD, may benefit and add to the overall clinical efficacy for seizure control.[20] Due to lack of large systemic review or randomized study with MAD and LGIT, more studies are in progress to prove the effectiveness of MAD and LGIT.

Benefits and limitations of the MCTKD

The main benefit of the MCTKD is allowing more carbohydrate (CHO) than the CKD, with resultant increased palatability.[4] Food exchanges are used which allow more food choices and larger food portion sizes, especially fruits and vegetables, in the MCTKD.[9] As patients consume more varieties and larger quantities of food, children have better growth and require fewer micronutrient supplements compared to the CKD.[9] There are also fewer incidents of renal calculi, hypoglycemia, ketoacidosis, constipation, low bone density, and growth retardation.[9] With MCTKD, there is no acidosis[21] or reduction in serum alanine, as in the CKD.[7] In addition, there is a positive effect on lipid levels with a significantly lower total cholesterol/high density lipoprotein (HDL) ratios, compared to the CKD.[22]

There are limitations that need to be considered when initiating the MCTKD. Due to reports of liver failure when MCTKD and valproate are combined, any patients on valproate are not recommended to start the MCTKD.[9] MCTKD takes longer to achieve seizure control since MCT oil must be increased gradually to lower the risk of complications.[9] Other limitations include expenses and a lack of trained dietitians. MCT oil can be expensive and more dietitians need to be trained to use MCT therapy.[9]

Comparison of other KD therapies

CKD, MCTKD, MAD, and LGIT are all limited in their carbohydrate intake, but loaded with large amounts of fat. Patients on all four diet therapies need medical supervision as medical complications can occur. For all four diet therapies, pre-diet and during-diet laboratory evaluations are essential to prevent nutrition deficiencies and medical complications. All four KDs' patients do not require fluid restriction. Maintenance fluid according to body weight should be prescribed as daily maximum fluid intake. Too much fluid can dilute ketones and may induce unnecessary recurrent seizure activities. Urine ketone level for CKD and MCTKD's patients can be up to 160 mg/dL (16 mmol/L), but for LGIT and MAD it can be low as 15 mg/dL (1.5 mmol/L). Patients usually start the CKD and MCKD in the hospital. MAD and LGIT can be started in an out-patients' clinic.

The CKD uses dietary ratio for diet prescription. Diet ratio represents the relationship between the grams of fat and the combined grams of protein and carbohydrate, i.e. "1800 kcal 4:1 ratio classic ketogenic diet" contains four times as many grams of fat for every 1 g of protein and CHO combined.[23] The 4:1 ratio diet contains 90% of daily calorie from fat.[23,24] The ratio of this diet can be adjusted to affect better seizure control and can also be liberalized for better tolerance. This diet is also considered a low glycemic therapy and results in steady glucose levels.[25] The MCTKD is not diet ratio related. This diet depends on the percentage of calorie from MCT oil to contribute major ketone resource, i.e. "1800 kcal 60% MCT ketogenic diet."[9] The percentage of MCT, long chain fat, carbohydrate, and protein can be adjusted to effect better seizure control and can also be liberalized for better tolerance. This diet is also considered a low glycemic therapy and results in steady glucose levels.[9] Dietitians/neurologist need to prescribe CKD and MCTKD. Caloric intake is calculated upon each individual's basal metabolic rate (BMR) plus activity/growth/stress factors. All foods have to be weighed by either gram or decimal gram scale. Meal plans and feeding schedules have to be planned by dietitians to help each individual approach their best ketone levels and to maximize their seizure control. Vitamin and mineral supplements are prescribed according to the difference between individual's intake and Daily Reference Intakes (DRI).[26]

The LGIT limits the percentage of CHO to 40–60 g/d, while protein contributes 20–30% and fat contributes 60% of daily calorie. All CHO foods' glycemic index are lower than 50.[15,16] This diet needs to be prescribed by a dietitian. Specific meal plans are not typically provided, but recommendations are made depending on food preferences and individual goals. Menu planning is discussed and a sample menu is provided. Foods do not need to be weighed; intake is based on portion size which is based on diabetic exchanges. Vitamins and minerals are supplemented to meet individual needs.[15,16] The balance of low glycemic CHO in combination with fat results in steady glucose levels.[15,16]

The MAD does not need diet prescription. Meal planning and food measurements are not required. CHO may be consumed at any time during the day as long as it is within limit. Patients can choose all the protein and fat without limitation. The only restriction is CHO intake. In children, the CHO are limited initially to 10 g/d and then increased after 1 month to 15 g/d. The CHO is then increased to 20–30 g/d as tolerated based on seizure control.[13] Adults are started at 15 g/d and can be increased to 20–30 g/d after 1 month. MAD does not count fiber as CHO, but sugar alcohols are not allowed.[13]

Comparison of all four KDs is given in Table 1.[24,25]

Appropriate candidates and contraindications

The international KD study group has recommended KD therapy should be considered as an early treatment for intractable epilepsy patients, especially for patients with glucose transporter protein 1 (GLUT-1) deficiency, pyruvate

Table 1: Comparison of diet therapies for pediatric epilepsy

Questions	Classic ketogenic diet	MCT ketogenic diet	Low glycemic index treatment	Modified Atkins
Is medical supervision required?	Yes	Yes	Yes	Yes
Is diet high in fat?	Yes	Yes	Yes	Yes
Is diet low in carbohydrate?	Yes	Yes	Yes	Yes
What is the ratio of fat to carbohydrate and protein?	4:1, 3.1, 2:1, 1:1	Not diet ratio related. Not able to convert to ratio of fat to carbohydrate and protein. It is because MCT produces more ketosis then LCT. Diet depends on % of calorie from MCT oil to contribute major ketone resource	Approximately 1:1	Approximately 1:1
How much carbohydrate intake per day is allowed on a 1000 kcal diet and a 2000 kcal diet?	1000 kcal diet: 8 g on a 4:1 16 g on a 3:1 30 g on a 2:1 40–60 g on a 1:1 2000 kcal diet: 7 g on a 4:1 22 g on a 3:1 48 g on a 2:1 110 g on a 1:1	1000 kcal diet: 48 g 2000 kcal diet: 95 g	1000 kcal diet and 2000 kcal diet: 40–60 g	1000 kcal diet and 2000 kcal diet: 10 g for the first month Then 20–30 g
How are foods measured?	Weighed	Weighed	Measured or estimated	Estimated
Are meal plans used?	Yes	Yes	Yes	Optional
Where is the diet started?	Hospital	Hospital	Home	Home
Are calories controlled?	Yes	Yes	Yes	No
Are vitamin and mineral supplements required?	Yes	Yes	Yes	Yes
Are fluids restricted?	No	No	No	No
Is pre-diet and during-diet laboratory evaluation required?	Yes	Yes	Yes	Yes
Can there be side effects?	Yes	Yes	Yes	Yes
Urine ketone level?	Can be high up to 160 mg/dL (16 mmol/L)	Can be high up to 160 mg/dL (16 mmol/L)	Can be low around 15 mg/dL (1.5 mmol/L)	Can be low around 15 mg/dL (1.5 mmol/L)
What is the overall difference in design of these diets?	This is an individualized and structured diet that provides specific meal plans. Foods have to be weighted accurately in gram or decimal gram. The ratio of this diet can be adjusted to affect better seizure control and also liberalized for better tolerance. This diet is also considered a low glycemic therapy and results in steady glucose levels	This is an individualized and structured diet that provides specific meal plans. Foods have to be weighted accurately in gram or decimal gram. It uses exchange lists for meal planning. The percentage of MCT oil, long-chain fat, carbohydrate, and protein can be adjusted to effect better seizure control and also liberalized for better tolerance. This diet is also considered a low glycemic therapy and results in steady glucose levels	This is an individualized but less-structured diet than the classic and MCT ketogenic diets. It uses exchange lists for planning meal and emphasizes complex carbohydrates. The balance of low glycemic carbohydrates in combination with fat result in steady glucose levels	This diet focuses on limiting the amount of carbohydrate while encouraging fat. Carbohydrate may be consumed at any time during the day as long as it is within limits. Standard meal plans are used as a guide. Protein is not limited

Abbreviations: Adapted from Liu *et al*.[24] and modified from Zupec-Kania[25]

dehydrogenase deficiency (PDHD), myoclonic-astatic epilepsy (Doose syndrome), tuberous sclerosis complex, Rett syndrome, severe myoclonic epilepsy of infancy (Dravet syndrome), and infantile spasms.[2] The KD is contraindicated in patients with specific disorders of fat metabolism, such as primary carnitine deficiency, carnitine palmitoyltransferase (CPT) I or II deficiency, carnitine translocase deficiency, β-oxidation defects, pyruvate carboxylase deficiency, and porphyria.[2]

The MCTKD is the appropriate choice for patients who are picky, incompatible with LGIT (LGIT not sufficient to treat their seizure), not able to follow the CKD or the

MAD, have large appetites, and like milk and starch and/or enjoy a variety of food choices. For these patients, the MCTKD allows them to follow a KD without the restrictions of the classic KD while working toward seizure control. Any patients with chronic vomiting or diarrhea prior to the diet are not candidates for the MCTKD treatment. It is not recommended to start patients on the MCTKD who take valproate, due to reports of liver failure when MCTKD and valproate are combined.

MCTKD intervention

Liu has used MCT from 40% up to >70% from daily caloric intake to maximize seizure control with estimated 100% compliance from 2005 to 2008; about 7% of the cohort experienced GI problems and discontinued the diet prior 2005.[9] This is a decrease in GI side effects, when compared with the previous studies.

The MCTKD intervention starts prior to hospital admission to ensure families/caregivers and patients are prepared.

Pre-diet initiation

Patients are instructed to stop all sweets 1 week prior to initiating the diet.[9] Dietitians explain the following to parents/caregivers: Fasting versus non-fasting, how to initiate the diet, and equipment needed for initiating the diet. Having a baseline biochemical index, EEG, ECG, bone density, and renal ultrasound is recommended.

Diet initiation

Centers usually admit patients to hospital to initiate the diet. Fasting may be appropriate when a quicker time to response is desired, but it is not necessary for long-term efficacy, and may have more immediate side effects such as hypoglycemia and acidosis.[2] Whether fasting or not, for patients admitted to the hospital, the meals are typically advanced daily in one-third caloric intervals of 6 feeds until full calorie meals are tolerated, while keeping the percentage of the MCT oil consistent.[9,24] The initial energy level is calculated at 80–100% of the Recommended Dietary Allowance. The diet prescription is dependent on the percentage of the MCT oil. The diet is initially calculated at 50% MCT, 19% CHO, 10% protein, and 21% LCT. Therefore, the MCTKD prescription is the number of calories and the percentage of the MCT oil. For example, the MCTKD prescription can be 1500 kcal 50% MCT KD, from which the patient would receive daily 90.4 g of MCT oil, 71.2 g of CHO, 37.5 g of protein, and 35 g of LCT. The MCTKD is divided into three meals plus three snacks as well as CHO-free or minimal CHO-containing multivitamins and minerals.

The meal plan is more flexible than the CKD. The CHO is usually higher than in the other three KDs. Dietitians prescribe patients' individualized daily calorie, CHO, protein, LCT, and MCT intake according to patient's age, sex, activities, and stress factor. Foods are divided into starch, fruits/vegetables, protein, milk, and fat food groups. The MCT oil is separated from food groups. Patients/parents/caregivers and dietitians can decide how many servings are allowed from each food group to meet the individual's CHO, protein, fat, and MCT prescription. MCT oil should be distributed equally into the 6 feeds per day. In this way, patients are not taking too much MCT oil in one feed, which prevents GI side effects. Patients/parents/caregivers are able to choose foods they prefer under the prescribed serving sizes. For patients with large appetites, patients are able to choose larger servings of food, such as 95 g of cooked mushroom plus 115 g of asparagus for 1 serving of vegetable/fruit instead of 70 g of cooked green peas or 45 g of banana.

The vitamin and mineral supplements are adjusted from baseline biochemical indices to meet dietary reference intakes (DRI) from each individual patient's food intake.[9] Baseline serum carnitine level is used to determine supplemental carnitine requirements at 50–100 mg/kg body weight (BW). In order to initiate the vitamin and mineral supplements safely, one supplement is started on a weekly basis after the diet is initiated to monitor for possible allergy or intolerance.[9]

If diarrhea or vomiting occurs, the MCT oil is lowered by 10% for the following meal. Patients are discharged once they tolerate the MCTKD without vomiting/diarrhea and patients/caretakers are confident in handling the diet.[9]

During diet initiation, dietitians provide intensive teaching to parents/caregivers/patients on the following topics: identifying foods that are appropriate for the diet, how to calculate the diet, how the diet prescription is made, how to weigh foods/formula, label reading, vitamin/mineral supplementation, how to deal with complications and potential problems, and sick day management. Nurses teach parents/caregivers/patients how to measure blood glucose, urine ketone, and/or specific gravity.

Fine-tuning and follow-up

After patients are discharged from the hospital, they are followed via phone or e-mail plus monthly clinic visits for the first few months, and then visits for every 3–6 months.[9] If a patient's seizure control requires optimizing, MCT oil can be gradually increased by 0.1–1.0 g per feed per day or 6 feeds per day every 1–3 days according to each individual's tolerance. During the fine-tuning stage, the dietitian monitors the patient's progress and modifies the diet to achieve improved seizure control. Nutritional assessments and nutrient adjustments are also essential to assure best growth and optimal nutritional status for each individual.[24]

Dietitians continue to provide education to parents/

caregivers on any questions and problems that may arise, as well as when diet and vitamin/mineral supplements need to be changed and how to wean the diet.[24]

The MCTKD allows a larger intake of CHO and protein, but is still limited to approximately 29% of energy.[9] Without nutrition supplementation, nutritional risk from the diet can occur. A prospective study of 25 children on the CKD and MCTKD, including daily multivitamin and mineral supplements, met or exceeded the DRI for all nutrients except for phosphorus and folate.[22] Both diets would have been inadequate in most micronutrients (including vitamin A, vitamin B1, vitamin B2, vitamin B3, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, folate, calcium, phosphate, magnesium, iron, zinc, and selenium) without the addition of vitamin and mineral supplements.[22]

Continuous monitoring of the patients' growth, renal ultrasound, bone density, lipid, carnitine, selenium levels, and ECG is significant in the correction or prevention of renal calculi, osteoporosis, hyperlipdemia, carnitine deficiency, and cardiomyopathy.

Controlling GI side effects when using the MCTKD treatment

As previously stated, Liu has used from 40% up to >70% MCTKD diet to maximize seizure control with GI side effects optimally controlled.[9] Careful monitoring and management of the MCTKD is the key to prevent the GI side effects[9] which are documented in previous studies.[4-10] Slow progression of the MCT oil dosage is important during the implementation of the MCTKD treatment.

During diet initiation, patients are required to come in for a hospital admission to ensure any complications can be corrected immediately under the close supervision from health care professionals. In addition, patients/parents/caregivers learn about lowering the MCT dosage immediately when GI discomfort appears to prevent further complications. Patients are started on a 1/3 ketogenic shake divided into 6 feeds made from cow, soy, or goat milk mixed with 1/3 daily dosage of MCT, LCT, and other ingredients such as sugar/polycose or egg/protein powder to make 1/3 daily nutrient content of MCT, LCT, CHO, and protein. The 1/3 shake is fed every 2–3 h. They progress to a 2/3 ketogenic shake for 6 feeds and then to a full 6 feeds per day from solid foods as long as the diet is tolerated. The diet is initially calculated at 50% MCT, 21% LCT, 19% CHO, and 10% protein. During the diet initiation, if diarrhea or vomiting occurs, the MCT is lowered by 10% and LCT is increased by 10% for the next feed until the patient is able to tolerate the diet. Vomiting is treated with a dimenhydrinate 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.[9]

During the fine-tuning stage, patients' GI tolerances have to be closely monitored by parents/caregivers. Health care providers keep in close contact with parents/caregivers through e-mail, phone, and patients' clinic visits. According to each individual's tolerance, dietitians/neurologists gradually increase MCT to achieve seizure control as long as there are no side effects and urine ketones are equal to or lower than 160 mg/dL (16 mmol/L). Dietitians/neurologists can also increase MCT oil in the morning, afternoon, or bedtime feed(s) only to improve seizure control based on the timing of the seizures and urine ketone levels.[9]

Foods recommended

When using the MCTKD, all foods are allowed except foods rich in CHO, including sugar and all sugar containing foods.[24]

Food exchanges are used to calculate the MCT diet. Food is divided into six food groups as follows: starch/grain, dairy (skim milk/nonfat yogurt), meat/egg/poultry/seafood, vegetables/fruits, fat, and MCT oil. MCTKD is divided into three meals plus three snacks per day. One gram of MCT oil is equal to 8.3 kcal. MCT oil can be mixed with milk or made into a salad dressing as it has no taste or smell. MCT oil cannot be used for frying at high temperature and should be stored in a dark glass container to maintain its biochemical properties.

Sample menus

Sample menus for a 1500 kcal 60% MCT, 11% LCT, 19% CHO, and 10% protein KD (daily nutrient intake: 108.5 g MCT, 18.4 g LCT, 71.2 g CHO, and 37.5 g protein) are presented in Tables 2 and 3.

Weaning from the KD

The timing and actual method of weaning from the KD is often individualized based on patient response to the diet.[2] Most parents are counseled to continue the KD for at least 3 months.[27] The international KD study group agreed that the KD should be used for at least a mean of 3.5 months before considering discontinuation.[2] In children with >50% seizure response, the KD is often discontinued after approximately 2 years; however, in children in whom seizure control is nearly complete (>90% seizure reduction) and side effects are low, the diet has been reported to be helpful for as long as 6–12 years.[28] This 2-year period is traditionally based on a similar time period used for anticonvulsant drugs, which are often discontinued after that time in children who become seizure free.[2] Children with GLUT-1 deficiency, PDHD, or tuberous sclerosis complex may require a longer KD duration than those with other conditions.[2] Of those who have

Table 2: Sample menus for patients with large appetites

Meals	Breakfast	Lunch	Dinner
Starch foods	30 g brown rice	30 g brown rice	37 g cooked noodle
Fruit/vegetable	130 g cantaloupe	31 g lettuce, 46 g sliced cucumber, 26 g sliced tomatoes, 35 g alfalfa sprouts	35 g tomato sauce, 63 g lettuce, 26 g raw tomato slices, 70 g watermelon
Protein	55 g scrambled egg	30 g grilled chicken	30 g cooked ground lean beef
Milk	62.5 g skim milk	62.5 g skim milk	62.5 g skim milk
Fat	5 g canola oil	3 g canola oil	5 g canola oil
MCT oil (g)	18.1 (mix with milk)	18.1 (mix with milk)	18.1 (mix with milk)
Snacks	**Morning snack**	**Afternoon snack**	**Evening snack**
Starch foods	5 g soda crackers	5 g air-popped popcorn	
Fruit/vegetable			
Protein			
Milk	62.5 g skim milk	62.5 g skim milk	62.5 g skim milk
Fat			
MCT oil (g)	18.1 (mix with milk)	18.1 (mix with milk)	18.1 (mix with milk)

Table 3: Sample menus for patients with smaller appetites

Meals	Breakfast	Lunch	Dinner
Starch foods	15 g toast	25 g noodle	15 g whole wheat bread
Fruit/vegetable	45 g banana	35 g green peas	70 g pear
Protein	30 g sliced ham	30 g sliced roast beef	30 g sliced pork
Milk	62.5 g skim milk	62.5 g skim milk	62.5 g skim milk
Fat	5 g canola oil	3 g canola oil	5 g canola oil
MCT oil (g)	18.1	18.1	18.1
Snacks	**Morning snack**	**Afternoon snack**	**Evening snack**
Starch foods	5 g melba toast	5 g digestive biscuit	
Fruit/vegetable			
Protein			
Milk	62.5 g skim milk	62.5 g skim milk	62.5 g skim milk
Fat			
MCT oil (g)	18.1	18.1	18.1

become seizure free with the diet, 80% will remain seizure free after the diet has been discontinued.[28]

Although the diet can be discontinued abruptly in an emergency, typically in an intensive care unit, it is more often tapered slowly.[2] The MCTKD is weaned slowly by decreasing the MCT oil by 10% every 1–3 months to prevent seizure recurrence. The CHO percentage is gradually increased while the MCT percentage is gradually decreased. A low concentrated CHO diet without MCT oil is introduced after the 30% MCT diet.[9]

Once urinary ketosis is lost, higher concentrated CHO foods can be gradually reintroduced. This recommendation is based on traditional practice, and mimics the several weeks of gradual weaning of antiepileptics.[27] During this time period, nutritional supplementation needs to be continued.[2] If seizures worsen, the KD can be increased to the previously effective formulation.[2] In the majority (58%) of these cases, seizure control can once again be attained with earlier KD or anticonvulsants.[29]

Conclusions

MCTKD is an effective but underutilized epilepsy treatment. As long as health care professionals carefully manage MCTKD, many more patients with epilepsy who are not appropriate for CKD will benefit from this treatment.

REFERENCES

1. Wilder RM. The effects of ketonemia on the course of epilepsy. Mayo Clin Proc 1921;2:307-8.
2. Kossoff EH, Zupec-Kania BA, Amark PE, Ballaban-Gil KR, Bergqvist AG, Blackford R, *et al.* and the Charlie Foundation, and the Practice Committee of the Child Neurology Society. Optimal clinical management of children receiving the ketogenic diet: Recommendations of the international ketogenic diet study group. Epilepsia 2009;50:304-17.
3. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, *et al*. The ketogenic diet for the treatment of childhood epilepsy: A randomized controlled trial. Lancet Neurol 2008;7:500-6.
4. Huttenlocher PR, Wilbourn AJ, Signore JM. Medium-chain triglycerides as a therapy for intractable childhood epilepsy. Neurology 1971;21:1097-103.
5. Trauner DA. Medium-chain triglyceride (MCT) diet in intractable seizure disorders. Neurology 1985;35:237-8.
6. Sills MA, Forsythe WI, Haidukewych D, MacDonald A, Robinson M. The medium-chain triglyceride diet and intractable epilepsy. Arch Dis Child 1986;61(Suppl. 8):1168-72.
7. Schwartz RH, Eaton J, Bower BD, Aynsley-Green A. Ketogenic diets in the treatment of epilepsy: Short-term clinical effects. Dev Med Child Neurol 1989;31:145-51.
8. Sell E, Liu YMC, Donner E, Curtis R. The medium-chain triglyceride ketogenic diet for the treatment of refractory lesional epilepsy in children. Epilepsia 2005;46:234.
9. Liu YM. Medium-chain triglyceride (MCT) ketogenic therapy. Epilepsia 2008;49 Suppl. 8:33-6.
10. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, *et al*. A randomized trial of classical and medium-chain triglyceride ketogenic diets in the treatment of childhood epilepsy. Epilepsia 2009;50:1109-17.

11. Kossoff EH, Mcgrogan JR, Bluml RM, Pillas DJ, Rubenstein JE, Vining EP. A modified Atkins diet is effective for the treatment of intractable pediatric epilepsy. Epilepsia 2006;47:1-4.
12. Kang HC, Lee HS, You SJ, Kang DC, Ko TS. Use of a modified Atkins diet in intractable childhood epilepsy. Epilepsia 2007;48:182-6.
13. Kossoff EH. The modified Atkins diet. Epilepsia 2008;49 Suppl 8:37-41.
14. Kossoff EH, Dorward JL, Turner Z, Pyzik PL. Prospective study of the modified Atkins diet in combination with a ketogenic liquid supplement during the initial month. J Child Neurol 2011;26:147-51.
15. Pfeifer HH, Thiele EA. Low-glycemic-index treatment: A liberalized ketogenic diet for treatment of intractable epilepsy. Neurology 2005;65:1810-2.
16. Pfeifer HH, Lyczkowski DA, Thiele EA. Low glycemic index treatment: implementation and new insights into efficacy. Epilepsia 2008;49 Suppl 8:42-5.
17. Muzykewicz DA, Lyczkowski DA, Memon N, Conant KD, Pfeifer HH, Thiele EA. Efficacy, safety, and tolerability of the low glycemic index treatment in pediatric epilepsy. Epilepsia 2009;50:1118-26.
18. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, *et al*. The ketogenic diet for the treatment of childhood epilepsy: A randomized controlled trial. Lancet Neurol 2008;7:500-6.
19. de Almeida RO, da Rocha AT, de Oliveira SL, de Melo LA, de Lira CE, Soares AA, *et al*. Effects of short-term and long-term treatment with medium- and long-chain triglycerides ketogenic diet on cortical spreading depression in young rats. Neurosci Lett 2008;434:66-70.
20. Wla P, Socala K, Nieoczym D, Luszczki JJ, Zarnowska I, Zarnowski T, *et al*. Anticonvulsant profile of caprylic acid, a main constituent of the medium-chain triglyceride (MCT) ketogenic diet, in mice. Neuropharmacology 2012;62:1882-9.
21. DeVivo DC, Pagliara AS, Prensky AL. Ketotic hypoglycemia and the ketogenic diet. Neurology 1973;23:640-9.
22. Liu YM, Williams S, Basualdo-Hammond C, Stephens D, Curtis R. A prospective study: Growth and nutritional status of children treated with the ketogenic diet. J Am Diet Assoc 2003;103:707-12.
23. Zupec-Kania B, Spellman E. An overview of the ketogenic diet for pediatric epilepsy. Nutr Clin Pract 2008;23:589-96.
24. Liu YM. Dietary Management/Epilepsy. Pediatric Nutrition Care Manual®. American Dietetic Association 2011. Available from: http://www.ncm.portalxm.com [Last accessed on 2011 Sept 14].
25. Zupec-Kania B. The Charlie Foundation Position Statement on the Diet Therapies for Epilepsy, 2009. Available from: http://www.charliefoundation.org. [Last accessed on 2011 Sept 14].
26. Dietary Reference Intakes (DRIs), Food and Nutrition Board, Institute of Medicine, National Academy of Science, 2011. Available from: http://www.iom.edu/Activities/Nutrition/Summary [Last accessed on 2011 Sept 14].
27. Freeman JM, Kossoff EH, Freeman JB, Kelly MT. The ketogenic diet: A treatment for children and others with epilepsy. 4th ed. New York, NY: Demos; 2007.
28. Groesbeck DK. Bluml RM, Kossoff EH. Long-term use of the ketogenic diet in the treatment of epilepsy. Dev Med Child Neurol 2006;48:978-81.
29. Martinez CC, Pyzik PL, Kossoff EH. Discontinuing the ketogenic diet in seizure-free children: recurrence and risk factors. Epilepsia 2007;48:187-90.