Review paper

Medium chain triglycerides (MCT) formulas in paediatric and allergological practice

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Gastroenterology Rev 2016; 11 (4): 226–231
DOI: 10.5114/pg.2016.61374

Key words: fat, medium chain triglycerides, feeding, infant formula, allergy.

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Abstract

Fats constitute the most significant nutritional source of energy. Their proper use by the body conditions a number of complex mechanisms of digestion, absorption, distribution, and metabolism. These mechanisms are facilitated by fats made of medium chain fatty acids; therefore, they are an easy and quick source of energy. Thus, an increased supply of medium chain triglycerides (MCT) is particularly important in patients with disturbances of digestion and absorption such as disturbed bile secretion, classic coeliac disease, short bowel syndrome, inflammatory diseases of the intestines, disturbed outflow of lymph, some metabolic disease, and severe food allergies, as well as in prematurely born neonates. Use of preparations containing an additive of MCT is limited, especially if they are to be used for a longer period of time. With a large quantity of MCT in a diet, there is a risk of deficiency of necessary unsaturated fatty acids and some fat-soluble vitamins. The caloricity of MTC compared to long-chain triglycerides is lower, and formulas with MCT are characterised by higher osmolality. Medium chain triglycerides is not recommended as an additive to standard formulas for healthy children. The use of MCT should be limited to strictly specified medical indications.

Fats constitute the most significant nutritional source of energy. They provide approximately 9 kcal/g of energy, which is over two times more than carbohydrates and proteins. Fats originating from food not only provide us with energy, but are also a source of building substances and take part in the synthesis of important biological compounds such as prostaglandins, thromboxanes, leukotrienes, and prostacyclins. Particularly crucial is a proper supply of the necessary unsaturated fatty acids, which are a building material for cell membranes (especially in the nervous system and the retina of the eye). Among them, linoleic acid (LA: 18:2n-6) and linolenic acid (ALA: 18:3n-3) are exclusively exogenous. All the other acids (mainly arachidonic acid AA: C20:4n-6, docosahexaenoic acid DHA C22:6n-3, and eicosapentaenoic acid EPA: C20:5n-3) can theoretically be synthesised by the body from their precursors (i.e. LA and ALA). However, this synthesis is insufficient in most cases [1]. Cholesterol is a significant element of cell membranes and precursors of bile acids, some steroid hormones, and vitamin D_3. It also takes part in myelinisation of the brain and the central nervous system. Thus, it is particularly important during early development. Dietary fats are also a carrier of ADEK vitamins and flavour substances in food products [2].

Triglycerides (glycerol esters and three molecules of identical or different fatty acids) constitute the basic dietary fats (approximately 98%). Moreover, food contains free fatty acids, phospholipids, sphingolipids, glycolipids, sterols, waxes, carotenes, vitamins A and D, cholesterol, and many others. The structure of fats is diverse, both as regards their type (number of carbon atoms in the chain, presence or absence of unsaturated bonds and their number) and their position in the triglyceride molecule. Depending on the number of carbon atoms in a molecule, fatty acids are divided into short- (C4-6), medium- (C6-10), and long-chain variants (C12-26). If triglycerides contain long-chain acids, they make the so-called fats, i.e. long-chain triglycerides (LCT); if they contain medium chain acids, they make fats, i.e. medium-chain triglycerides (MCT) [3, 4]. The latter ones, in a natural form, occur in a very limited quantity, mainly in coconut oil [5]. Use of the coconut oil is however limited due to its high content of lauric and myristic acid, which have atherogenic properties [1].

Dietary fats are divided according to the source of origin. Saturated fatty acids are the most prevalent animal fats. Vegetable and fish fats mainly include mono- and polyunsaturated fatty acids. When feeding an infant one has to remember to provide it with fats of a proper composition. Thus, formulas fed to an artificially fed baby should be maximally similar to human milk. This is because there are some significant differences between human milk and cow's milk as regards the total content and proportions of mono- and polysaturated fatty acids, the proportion of long-chain polyunsaturated fatty acids (LC-PUFA – C > 20), cholesterol, and the stereoisometric structure of triglycerides [6, 7]. Fats contained in human milk provide 50% of energy. Long-chain fatty acids constitute about 95% of all fatty acids. Medium-chain triglycerides constitute up to 10% (usually about 2%) of the total fat. Among saturated fatty acids, as well as mono- and polyunsaturated fatty acids, palmitic, oleic, and linoleic acids are prevalent, respectively [1, 8]. Use of vegetable oils in particular proportions in modified milk formulas allows us to obtain a profile of fatty acids that is similar to natural human milk [1, 9].

The diversity of lipid structures is associated with the multitude of their biological and biophysical features, such as easiness of lipolysis, way of absorption, metabolism, and biological functions. Absorption of the larger part of lipids (LCT) requires special processing in the digestive tract, i.e. emulsification with bile. This process is aimed at obtaining maximum surface for digestion (lipolysis with breakage of ester bonds of triglycerides and with release of monoglycerides, free fatty acids, and glycerol). Fats of short carbon chains and unsaturated bonds are digested more easily than the saturated long-chain fatty acids [3, 10]. The process of digestion of fats mainly takes place in the duodenum and the initial segment of the jejunum. Lipases are found in the pancreatic juice and the brush border. At infantile age gastric lipase is also significant. This is because the activity of the pancreatic lipase in children during the first few months of life is low.

The degree of absorption of a given fatty acid depends on its location in the molecule [11]. Fatty acids located in the central position are easily absorbed because lipases are very efficient at breaking the bond between glycerol and the residue of a fatty acid. This is why butter is an easily absorbed dietary fat, in which 80% of the saturated fatty acids bound with glycerol are in the central position. In ripening and blue cheeses, on the other hand, fatty acids are located in the first and third position and are therefore more difficult to absorb. The chemical structure of triglycerides in human milk provides better absorption than in the case of cow's milk. This is because these triglycerides have optimal assimilability, which is provided by a species-specific esterification of the palmitic acid (in the second position of glycerol) [2, 8, 11].

Once they are absorbed into an enterocyte, fatty acids and monoglycerides undergo resynthesis to triglycerides, in the presence of ligase, co-enzyme A, and ATP. Chylomicrons are formed. They get to the lymph and only then can they be transported to blood and destination organs [10, 12]. Thus, shortly after a fatty meal, a significant increase in the quantity of chylomicrons is observed in blood (lipaemia). The peak of this phenomenon is observed 2–4 h after a meal and may last for up to 36 h. Release of fats from chylomicrons requires the presence of plasmatic lipases, and only then can they be metabolised or stored as a reserve in the fatty tissue [12].

Hydrolysis of MCT (which is faster than LCT hydrolysis anyway) does not require bile and lipase. Without hydrolysis, they may also be absorbed by the enterocytes and they do not require re-esterification [4, 8]. From enterocytes they are directly absorbed into the portal vein and then transported mainly to the liver. Thus, absorption of MCT is faster than that of LCTs. Their metabolism is facilitated as well because they are metabolised by the liver almost completely (only when the liver's metabolic abilities are exceeded the process is taken over by peripheral tissues) with energy release, regardless of the presence of carnitine (which is necessary for the transport of long-chain fatty acids through the mitochondrial membrane). Thanks to this the availability of medium-chain fatty acids for mitochondrial oxidation is better [12]. This means that MCT are an easy and quick source of energy [3, 10]. However, it should be borne in mind that quantities of MCT exceeding the abilities of the liver are metabolised peripherally in a carnitine-dependent mechanism, which can increase the demand for it. On the other hand, it has been observed that on the enterohormonal pathway (an important element of which is a MCT-induced increase of the YY peptide concentration and a decrease in cholecystokinin release) MCT cause a decrease of appetite and consequently a decrease in energy intake [3, 13]. They also interfere with the metabolism of the fatty tissue, by hindering the creation of a deposit from long chain acids [12]. It has been proven that an MCT-enriched diet modulates metabolism of fats, which is manifested as a decrease in the concentration of triglycerides and cholesterol [14].

The properties of fats contained in food, include the length of fatty acids, modulate the motor function of the digestive tract, secretion of enterohormones, and even the mesenteric flow [15–17]. Unlike LCT, MCT do not affect the release of cholecystokinin or the emptying of the gallbladder and they do not increase the secretion of pancreatic enzymes [13, 18]. They can speed up the intestinal passage by affecting the release of the YY peptide, but only in the distal sections of the intestine [13]. Moreover, it has been found that MCT facilitate absorption of calcium [10, 19, 20].

Due to these features, increased supply of MCT is particularly important in patients with disturbances of digestion and absorption, who suffer from energy deficiency and disturbed absorption of fats [21]. These are patients with disturbed bile secretion (cholestasis, disturbances in hepatic-intestinal circulation of bile acids, intestinal dysbacteriosis), or pancreatic lipase secretion (for example, in pancreatic failure in the course of cystic fibrosis), since MCT do not have to be emulsified in the digestive tract or undergo the process of lipolysis [21–23]. Preparations containing MCT are also used in patients with disturbed absorption and energy deficiencies associated with, for example, classical coeliac disease, short bowel syndrome, or status post bowel transplantation [24–26].

A supply of MCT is also recommended in aggravated Crohn's disease [27]. What is more, studies conducted on animals showed that a diet based on elementary formula containing MCT (unlike LCTs) has an anti-inflammatory effect in inflammatory diseases of the intestines [28]. Medium-chain triglycerides are also recommended in Fabry disease (disturbances in resynthesis of triglycerides in enterocytes) and in disturbances of lymph outflow (for example after cardiosurgical surgeries or due to intestinal lymphangiectasia) [29, 30]. Some metabolic conditions, including (but not only) the ones associated with disturbances of mitochondrial β-oxidation of fatty acids, can also be treated with an MCT-enriched diet [31, 32], and early application of an MCT formula is usually significantly beneficial for the treatment.

Supply of MCT is indicated in enteropathy in the course of food allergy, including severe symptoms of allergy to cow's milk protein in infants [33–37]. Alterations in the structure of intestinal villi can take place. Clinical signs include chronic diarrhoea, disturbed growth, and poor appetite. Impaired digestion and absorption, whose symptoms are dominant in the clinical picture of the disease, lead to anaemia, hypoalbuminaemia, and other deficiencies [36–38]. Frequently, symptoms do not subside after application of potent hydrolysates of a non-modified composition of fats [39]. In such a situation, the hydrolysate or an elementary MCT formula, as well as, for example, a lactose-free or low-lactose formula applied at the initial stage of treatment, can determine effective dietetic therapy [40]. The time period between the beginning of the diet and the subsidence of symptoms is longer in the case of enteropathy (up to approximately 6 weeks) [41].

Iacono *et al.* [39] treated 9 infants with severe symptoms of food polyallergy, which did not subside after treatment with hydrolysates and soya-based formula. After a short period of parenteral nutrition, they applied donkey's milk with an additive of MCT (40 ml/l of milk), which lead to good tolerance of this food and an increase in the infants' body mass. However, taking other studies into consideration, it seems that it is not the addition of MCT that was crucial, but rather the type of the protein used. Verwimp *et al.* [42] compared the use of two elimination formulas in 79 young (below the age of 3 months) babies with allergy to cow's milk protein. Whey hydrolysate was used, which contained a standard composition of fats and lactose or a lactose-free whey hydrolysate containing 50% of MCT. After 10 weeks it was found that in both groups the diet turned out to be an effective means of treatment in 80% of cases.

Medium-chain triglycerides are also used in nutrition of prematurely born infants, due to the immaturity of their digestive tract and high demand for energy [3, 5, 19, 43–45]. It has been shown that the activity of gastric lipase in premature infants is insufficient, which negatively affects the hydrolysis of fats [46]. However, it has also been found that stimulation of the activity of gastric lipase is higher for the LCT formula, compared to the MCT formula [47].

Therapeutic formulas contain such proportions of fats that 48% of the energy is obtained from the fat, out of which 55% is obtained from MCT, which allows for appropriate proportion of EFA [21]. However, in the nutrition of patients requiring significant elimination of long-chain fatty acids, pure MCT oil constitutes the main source of fat. Milk formulas for premature infants are also enriched with MCT, but the quantity of MCT should not exceed 40% of total fat content [1]. High content of MCT increases the osmolality of the preparation, which should also be taken into account.

The use of preparations containing an additive of MCT has its limitations, especially if they are to be used for a longer period of time. It should be borne in mind that necessary unsaturated fatty acids belong to the LCT fraction, which means that we may be dealing with a risk of their deficiency when the content of MCT in a diet is too high [10, 48]. It is recommended that preparations with a high proportion of MCT should be used for a maximum time of several weeks and that patients should be provided with supplementation of essential unsaturated fatty acids [21].

In studies conducted on infants with cholestasis, deficiencies of essential unsaturated fatty acids were found in the group fed with a preparation in which the content of MCT was 87% of total fat and the content of linoleic acid was 3.4% of energy, while in the group fed with a preparation with the content of MCT of 40% (the content of linoleic acid – 7% of energy) no such deficiencies were detected [49].

The proportion of MCT is undoubtedly crucial for potential deficiencies. It has been shown that in infants fed with a MCT formula (40% of total fat), oxidation of long-chain unsaturated fatty acids was lower than in prematurely born infants fed with a standard formula. Rodriguez *et al.* [5] studied prematurely born infants fed with MCT or standard formulas. They administered marked linolenic acid and tested the concentration of marked CO_2 in the exhaled air and the concentration of polyunsaturated fatty acids in serum. They found lower concentration of marked CO_2 and even higher concentration of fatty acids.

In the case of formulas containing MCT a decrease in the concentration of some fat-soluble vitamins was observed (especially vitamin E) [48, 50].

We should also take into account the lower caloricity of MCT, compared to LCT (approximately 8.3 kcal/g and 9.1 kcal/g, respectively). It has been suggested in studies conducted on adult patients that the supply of MCT increases energy expenditure and the burning of fatty tissue, and consequently reduces body mass [15, 51]. Observations of the increase of body mass in prematurely born infants fed with MCT formulas do not explicitly confirm improvement of increase in body mass, compared to infants fed with formulas of a standard fat content [43, 45, 47]. There have been no differences detected in the increase of body mass between children fed with formulas containing different proportions of MCT [45].

However, other observations indicate that there is a positive effect of MCT formulas on the growth of prematurely born children with low body mass. Another study examined the potential effect of MCT on hindering appetite and decreasing fat deposition as fatty tissue in prematurely born infants (which had been suggested in studies conducted on adults). Telliez *et al.* [3] gave their patients a formula containing 37% of MCT or a formula containing 100% of LCT, for 3 days. Then they found that absorption of food and energy in the group fed with MCT formula was higher compared to the group fed with a formula containing LCT only. Children from this group also presented with higher use of oxygen, higher temperature, and longer sleep. It has been found that feeding prematurely born infants with MCT formulas is more beneficial, also due to its effect on temperature regulation, compared to feeding with standard formulas. Sulkers *et al.* [52] showed that in prematurely born infants fed with a formula with increased content of MCT the increase of body mass was higher (which was associated with deposition of fatty tissue), compared to prematurely born infants fed with a formula of only a small quantity of MCT (38% vs. 6%). Improvement in the increase of body mass and increase of the skin fold thickness in infants born with low body mass, induced by MCT formula, was observed by Vaidya *et al.* [53].

Even though no significant benefits for the course of disease was found in infants with allergy to cow's milk protein compared to hydrolysed formula of traditional fat composition, no negative effect on the increase of body mass was found during 10 weeks of observation [42].

Higher osmolality of the formulas containing MCT should not be underestimated, since it is associated with higher risk of osmotic diarrhoea. Therefore, the dose of MCT should be increased gradually and the osmolality of the preparation should not exceed 400 mOsm/kg [54].

Other adverse effects of formulas containing high proportion of MCT described in literature include deficiency of carnitine resulting in damage of the liver and kidneys due to long-lasting feeding of a prematurely born infant (24 Hbd) with extremely low body mass [55]. It has also been found that MCT can engage carnitine in the course of their metabolism and carnitine reserves in infants are low. Therefore, in such cases supplementation with carnitine should be considered.

Interesting observations were recently described by Li *et al.* [56], who carried out a study on mice and showed that dietary MCT can promote allergy to food allergens simultaneously eaten with it, by hindering absorption of the allergen into blood and increasing its absorption in Peyer's patches, where stimulation of Th2 response takes place. Medium-chain triglycerides can also cause an increase in allergic response after an oral attempt at food provocation. The study was not conducted on a human population; however, it clearly indicates that MCT should be used sensibly.

Medium-chain triglycerides are therefore not recommended as an additive to standard formulas for healthy children. Their use should be limited to strictly specified medical indications [9].

Conflict of interest

The authors declare no conflict of interest.

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Received: 24.04.2015
Accepted: 10.07.2015