A Cross-Over Study of the Effect of a Single Oral Feeding of Medium Chain Triglyceride Oil vs. Canola Oil on Post-Ingestion Plasma Triglyceride Levels in Healthy Men

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Abstract

Due to its unique absorption and metabolism characteristics, medium chain triglyceride (MCT) oil, consisting of fatty acids with 8-12 carbons, has been used therapeutically since the 1950s in the treatment of fat malabsorption, cystic fibrosis, epilepsy, weight control, and to increase exercise performance. Medium chain triglycerides are easily hydrolyzed in the intestines and the fatty acids are transported directly to the liver via the portal venous system, in contrast to long-chain fatty acids (LCFAs), which are incorporated into chylomicrons for transport through the lymphatic system or peripheral circulation. Medium chain fatty acids (MCFAs) do not require carnitine to cross the double mitochondrial membrane of the hepatocyte, thus they quickly enter the mitochondria and undergo rapid beta-oxidation, whereas most LCFAs are packaged into triglycerides in the hepatocyte. In this single-blind, randomized, cross-over study, 20 healthy men ingested a single dose of either 71 g of MCT oil or canola oil. Blood samples were taken at baseline and at hours one through five post-ingestion to compare the effect of a single oral dosing of MCT oil versus canola oil on post-ingestion plasma triglyceride levels. Mean triglyceride values after canola oil increased 47 percent above baseline ($p < 0.001$), while mean triglyceride values after MCT oil decreased 15 percent from baseline ($p < 0.001$), which is consistent with several other studies involving short- and longer-term feeding with MCT oil. The effect of long-term usage of MCT oil on triglycerides is yet to be established.

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Introduction

Medium chain triglyceride (MCT) oil is manufactured from coconut and palm kernel oil, and contains fatty acids with 8-12 carbons. It was first introduced in the 1950s as a well-absorbed, calorically-dense nutrient used to treat patients suffering from impaired absorption of traditional long-chain fats. MCT oil has since been used as a major component of enteral and parenteral nutritional support, in the treatment of cystic fibrosis and fat-induced hyperlipidemia, as part of a ketogenic diet in the treatment of epilepsy, to enhance exercise performance, and to aid in increasing the metabolism for weight control.[1,2] MCT oil has also been found to be useful in controlling diarrhea and fat malabsorption in HIV-positive patients,[3,4] and may have potential as part of a ketogenic diet in slowing tumor growth.[5] Although MCT oil is being used for a variety of clinical conditions and is becoming increasingly popular, questions still remain about the nutritional advantages of this product. Specifically, the scientific literature is not yet conclusive regarding the effect of MCT oil on plasma triglyceride levels.

Several studies conducted on human subjects with normal intestinal absorption have shown a hypertriglyceridemic effect in response to MCT feeding.[6-9] Children with malabsorption syndromes[10] or cystic fibrosis[11] experienced slight elevations in triglyceride levels associated with MCT feeding. Patients with acute[12] or chronic renal failure[13] experienced similar changes in triglycerides with MCT- or LCT-containing lipid infusions. MCT oil has been shown to markedly lower triglyceride levels in patients with hyperchylomicronemia.[14,15] Healthy male subjects who were given a single oral load of MCT oil (1 g/kg of body weight) or 48 g of MCT oil in a test meal did not experience significant changes in triglyceride levels.[16,17]

The purpose of this single-blind, randomized, cross-over study was to examine and further clarify the blood lipid responses associated with MCT feeding. The primary aim of the study was to compare the effect of a single oral feeding of MCT oil with the effect of a single oral feeding of canola oil on the post-ingestion plasma triglyceride levels in healthy men.

Table 1. Mean Triglyceride Levels and Mean Difference Between Canola and MCT Levels at Each Hour

	Baseline	1	2	3	4	5
Can Mean (mg/dL)	79.7 ± 37.1	78.9 ± 37.3	97.7 ± 43.5	114.5 ± 51.9	117.2 ± 53.0	112.0 ± 60.7
MCT Mean (mg/dL)	80.4 ± 34	77.5 ± 32.5	72.6 ± 33.8	68.6 ± 33.3	69.5 ± 31.3	69.6 ± 31.4
Can - MCT (mg/dL)	-0.7 ± 21.0	1.6 ± 18.7	24.6 ± 28.4	45.4 ± 40.1	46.6 ± 44.2	42.05 ± 51.4
t value*	-0.15	0.38	3.88	5.07	4.72	3.66
p - value*	0.883	0.706	0.001	<0.001	<0.001	0.001
95% C.I.	(-12.1, 10.7)	(-8.6, 11.8)	(9.2, 40.0)	(23.6, 67.1)	(22.6, 70.6)	(14.1, 70.1)

Methods

Participants: The Institutional Review Board at Bastyr University approved the research plan. Twenty healthy men were recruited for the study, and informed consent was obtained from each participant. Potential participants were screened for the following exclusionary criteria: obesity; cardiovascular disease; liver disease; hypoglycemia; hyperlipidemia; pancreatic disease; thyroid dysfunction; current use of prescription drugs, illegal drugs, and/or tobacco; and history of alcohol and/or drug abuse. Participants had normal fasting plasma triglyceride levels (40-160 mg/dL), reasonably prominent veins, and no known sensitivity to canola, palm, or MCT oil. Each participant was asked to maintain his current level of exercise and alcohol consumption, and to abstain from recreational drug use during the course of the study, beginning one week prior to the first test day. The mean age of the participants was 26 years, with a range of 22-31 years. Mean weight and height were 74.9 kg and 179 cm, respectively. On the final testing day, each subject was given an exit questionnaire to complete and return.

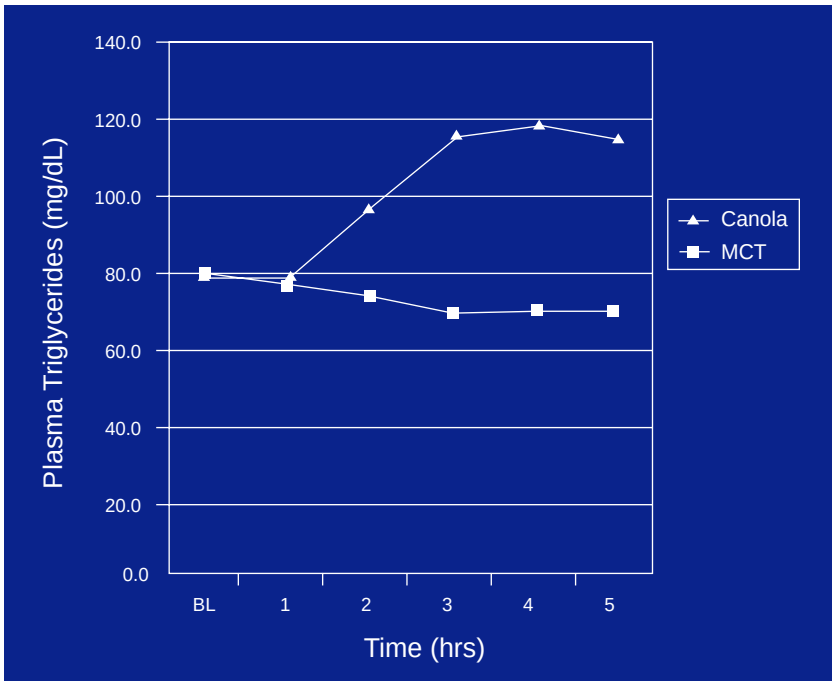
Materials and procedures: The oils used in the study were Sound Nutrition™ MCT oil and HAIN™ canola oil, and were purchased at a local supermarket. Each bottle of MCT oil and each bottle of canola oil had the same lot number. In a cross-over design, participants were randomly assigned (by coin toss) to receive either canola or MCT oil first, with ten subjects receiving canola and ten subjects receiving MCT. After a fasting blood draw, participants ingested 71 g (2.5 oz) of either canola or MCT oil, a dose equivalent to the amount of oil found in a meal consisting of a large order of French fries, a salad with oil-based dressing, and a cookie. Blood samples for determination of plasma triglyceride levels were taken at hours one, two, three, four, and five. Blood samples were collected in tubes containing EDTA, centrifuged on site, and refrigerated until testing was completed for the day. The samples were delivered to LabCorp in Seattle, WA, where Chem-23 screens were performed on each sample. Two weeks later, the procedure was repeated with the oil assignments reversed.

Statistical Analysis: Data was entered into a spreadsheet program (Microsoft Excel 7, Microsoft, Inc., Redmond, WA) and exported into SPSS (SPSS Inc., Chicago, IL) for analysis. Statistical analyses consisted of parametric comparison of means tests (t-tests) for triglyceride levels under MCT or canola oil at baseline and up to five hours after breaking fast. Paired comparisons were made to assess individual responses to treatment. Data exploration showed the hypotheses of normally distributed triglyceride levels and equal variances between treatment groups (at

Table 2. Mean Change from Baseline at Each Hour

	1	2	3	4	5
Can - BL (mg/dL)	-0.7 ± 9.5	17.9 ± 20.5	34.8 ± 32.8	37.5 ± 40.4	33.0 ± 48.6
Can p - value	0.712	<0.001	<0.001	<0.001	<0.009
MCT - BL (mg/dL)	-2.9 ± 10.7	-7.8 ± 14.1	-11.8 ± 14.6	-10.9 ± 12.8	-10.8 ± 12.4
MCT p - value	0.241	0.023	0.001	<0.001	<0.001

Figure 1. Mean absolute triglycerides



*t-values and significance statistics refer to mean differences between canola and MCT values

different triglyceride levels) could not be rejected, thus justifying the use of parametric tests.

Results : The two fasting samples provided by each participant (one on each test day) were not significantly different. Baseline triglycerides (TG) were not related to final TG levels, i.e., relatively high or low TG levels at baseline did not affect the response to MCT or canola oil. Neither age nor body mass index was related to baseline TG levels.

Mean TG levels with each oil and the mean differences between canola and MCT levels at each hour are listed in Table 1. Table 2 lists the mean change from baseline at each hour after the ingestion of either oil. Figure 1 shows the curve of mean TG levels at each hour. Mean canola TG values peaked at hour four (117.2±53.0 mg/dL), with a mean difference from baseline of 37.5±40.4 mg/dL ($p < 0.001$). This represents a 47-percent elevation over baseline TG levels. Mean MCT TG levels were below baseline at each hour, and reached the lowest level at hour three (68.6±33.3 mg/dL), with a mean difference from baseline of –11.8±14.6 mg/dL ($p = 0.001$). This represents a 15-percent decline in plasma triglycerides from baseline TG levels. The mean difference between canola and MCT plasma triglycerides was greatest at hour four (46.6±44.16 mg/dL, $p < 0.001$), but also statistically significant at hours two ($p = 0.001$), three ($p < 0.001$), and five ($p = 0.001$). At hour three following the ingestion of canola oil, 80 percent of the participants experienced an increase in triglycerides compared to baseline. At hour three following the ingestion of MCT oil, 75 percent of the participants experienced a decrease in triglycerides compared to baseline.

Fifteen exit questionnaires were returned from 20 participants. Fourteen participants reported significant gastrointestinal side-effects, including cramping and diarrhea, associated with ingestion of oil. Thirteen participants experienced diarrhea after ingestion of MCT oil and four participants experienced diarrhea with canola oil ingestion. Three participants experienced diarrhea with ingestion of both oils.

Discussion

Due to its unique metabolism, medium chain triglyceride oil has proven to be an important source of energy in a variety of clinical conditions. The purpose of this study was to compare the effect of a single oral feeding of MCT oil with the effect of a single oral feeding of canola oil on the post-ingestion plasma triglyceride levels in healthy men. The results of this study are consistent with several previous studies involving short- and longer-term feeding with MCT oil, and further confirm a hypothesized metabolism of MCT oil.[14-17] The action of pancreatic lipase in the small intestine is enhanced by the relatively

small molecular weight of MCTs, resulting in rapid and near complete hydrolysis of the fatty acids. Unlike long chain fatty acids (LCFA), free medium chain fatty acids (MCFA) are not incorporated into chylomicrons for transport through the lymphatic system or peripheral circulation, but are transported directly to the liver via the portal venous system. MCFAs do not require carnitine or the activity of the regulated enzyme carnitine palmitoyltransferase I to cross the double mitochondrial membrane of the hepatocyte. As a result, the fatty acids quickly enter the mitochondria and undergo rapid beta-oxidation. Whereas, most LCFAs are packaged into triglycerides in the hepatocyte, the liver retains most of the MCFAs it receives for energy production. The rapid oxidation of MCFAs results in an excess of acetyl-CoA that can be used in a number of different biochemical pathways, including the Kreb's cycle, ketogenesis, elongation of fatty acids, and synthesis of fatty acids and cholesterol.[1,18] Because long-chain fatty acids from canola oil are incorporated preferentially into triglycerides and transported into the plasma via chylomicrons, an increase in triglyceride levels with canola oil feeding relative to MCT oil is not unexpected.

Two studies reporting a hypertriglyceridemic effect associated with MCT feeding support an alternative hypothesis that excess acetyl-CoA resulting from the rapid oxidation of MCFAs in the liver is used for fatty acid synthesis or elongation. It has also been suggested MCTs stimulate the release of fatty acids from adipose tissue.[8,9] This potential for increased fatty acid production and/or the release of fatty acids from adipose tissue may explain the increase in plasma triglyceride levels seen in these studies.

Therapeutic use of MCT oil has been limited due to the occasional occurrence of mild gastrointestinal (GI) symptoms, including borborygmi, crampy abdominal pain, nausea, and diarrhea,[19,20] which was confirmed in this study and at least two previous clinical trials.[17,21] According to Ledeboer et al, MCT oil significantly accelerates small-bowel transit time compared with that seen in control subjects.[19] This acceleration in small-bowel transit time can cause GI side-effects, especially diarrhea. Reportedly, these symptoms can be ameliorated with proper administration of MCT oil. The oil should be introduced in small amounts, heated to room temperature, diluted with an equal volume of water or fruit juice, and taken slowly. It is recommended that no more than 15-20 ml of MCT oil be taken at one time, with a maximum of 100 ml administered in a 24-hour period.[20,22]

In conclusion, this study shows a single oral feeding of MCT oil has a different effect than a single oral feeding of canola oil on post-ingestion plasma triglyceride levels in healthy men. Plasma TG levels were elevated 47 percent four hours after ingestion of 71 g of canola oil, while plasma TG levels were 15 percent below baseline three hours after ingestion of MCT oil. The effect of long-term feeding with canola and MCT oil on plasma triglycerides is still to be determined.

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