Effects of Carbohydrate (CHO) and Fat Supplementation on CHO Metabolism During Prolonged Exercise

Asker E. Jeukendrup, Wim H.M. Saris, Fred Brouns, David Halliday, and Anton J.M. Wagenmakers

The aim of the study was to examine carbohydrate (CHO) utilization in subjects receiving CHO or CHO + medium-chain triglycerides (MCT) supplements during 180 minutes of exercise at 50% maximal aerobic work rate (Wmax) 57% maximal oxygen consumption (VO2max). In a double-blind crossover design, nine trained athletes cycled four times. Subjects received a bolus of 4 mL · kg⁻¹ at the start and 2 mL · kg⁻¹ every 20 minutes during exercise of either a 150-g · L⁻¹ CHO solution (CHO trial), an equicaloric 70 energy% (en%) CHO–30 en% MCT suspension containing 29 g MCT (CHO + MCT trial), or a 150-g · L⁻¹ CHO (high-CHO [HCHO]) solution plus 29 g MCT (HCHO + MCT trial). A fourth trial consisted of a 13C-background control trial (CON). The four trials were randomized. Before and after the exercise bout, muscle biopsies were taken from the quadriceps muscle and muscle glycogen levels were determined. During exercise, breath samples were collected for estimation of exogenous and endogenous CHO oxidation. No significant differences were detected in glycogen breakdown among the trials (277 ± 14 14 mmol · kg dry weight⁻¹ CHO, 249 ± 20 CHO + MCT, and 240 ± 18 HCHO + MCT) or in the respiratory exchange ratio during exercise. Mean exogenous CHO oxidation rates during the final hour of exercise were 0.79, 0.63, and 0.73 g · min⁻¹, respectively. No differences were observed between the trials regarding exogenous or endogenous CHO oxidation. Plasma free fatty acid (FFA) concentrations were elevated during exercise to a level of approximately 500 µmol · L⁻¹ and were comparable in all trials, whereas plasma ketone concentrations significantly increased after MCT ingestion as compared with the CHO trial. It is concluded that 29 g MCT co-ingested with CHO during 180 minutes of exercise does not influence CHO utilization or glycogen breakdown.

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Oral ingestion of carbohydrate (CHO) during exercise has been shown to better maintain plasma glucose levels and high rates of plasma glucose oxidation, resulting in improved endurance capacity. Oxidation rates of orally ingested CHO have never been observed to be higher than 1.0 to 1.1 g · min⁻¹, which seems to be the maximum oxidation rate. Even ingestion rates of up to 2 g · min⁻¹ during exercise at 70% maximal oxygen consumption (VO2max) resulted in oral glucose oxidation rates of no more than 1 g · min⁻¹. To supply an additional exogenous energy source for the working muscle, substrates other than CHO might be ingested. One potential candidate for such an energy source could be medium-chain triglycerides (MCT). MCT have been shown to be rapidly hydrolyzed, absorbed, and subsequently oxidized. In addition, a preliminary study showed that MCT co-ingested with CHO do not inhibit gastric emptying. Moreover, it has been suggested that MCT ingestion may improve exercise performance by elevating plasma free fatty acid (FFA) levels and sparing muscle glycogen. Several studies have reported this relationship between increased availability of plasma FFA, reduced rate of muscle glycogen breakdown, and delayed onset of exhaustion.

However, increased supply and subsequent oxidation of FFA or ketone bodies have been shown to result in an inhibition of plasma glucose utilization as well as overall CHO utilization. From these observations, one might hypothesize that increasing the FFA availability by oral fat intake may also limit the utilization of the exogenously supplied CHO.

The aim of the present study therefore was to investigate the effects of MCT co-ingested with CHO on exogenous and endogenous CHO utilization during prolonged exercise, and to determine what effect this regimen had on muscle glycogen breakdown. The CHO + MCT mixture was based on the CHO + MCT suspension that emptied most rapidly from the stomach in a previous comparative study. The amount ingested was based on the maximal amount of MCT that could be ingested without causing gastrointestinal problems.

SUBJECTS AND METHODS

Subjects

Nine male trained triathletes or cyclists aged (mean ± SEM) 26.0 ± 5.0 years with a weight of 75.7 ± 4.3 kg, height 185 ± 8 cm, maximal aerobic work rate (Wmax) 5.48 ± 0.24 W · kg⁻¹, VO2max 64.7 ± 2.3 mL · kg⁻¹, and maximal heart rate 194 ± 5.3 bpm participated in this study. The nature and the risks of the experimental procedures were explained to the subjects, and their written informed consent was obtained. The study was approved by the local medical ethics committee.

Pretrials

Wmax was measured on an electronically braked ergometer (Lode Excalibur, Groningen, The Netherlands) during an incremental exhaustive exercise test 1 week before the first experimental trial. The results of this initial test were used to determine 50% Wmax, which was later used in the experimental trials.

Experimental Trials

Nine subjects performed four trials, each separated by at least 7 days. A trial consisted of 180 minutes of cycling at 50% Wmax (57% ± 2% VO2max). Drinks were given in a randomized order.
and double-blind; all drinks were vanilla-flavored (Sandoz Nutrition, Berne, Switzerland). Subjects abstained from training and were instructed to consume a similar diet for the 3 days before each trial. In addition, they were instructed not to consume any products with a high natural abundance of $^{13}$C during the entire experimental period.

**Protocol**

Subjects reported to the laboratory at 8:00 AM after an overnight fast, and a standardized breakfast of two crackers with cheese was provided (14 g CHO, 4 g fat, and 6 g protein). A Teflon catheter (Baxter Quick Cath; Uden, The Netherlands) was inserted into an antecubital vein, and at 8:30 AM a resting blood sample was drawn. Also, a muscle biopsy was taken from the lateral part of the vastus lateralis. Resting breath gases were collected for measurement of oxygen consumption (2900 analyzer; SensorMedics, Anaheim, CA), and vacutainer tubes were filled directly from the mixing chamber in duplicate to determine the $^{13}$C/$^{12}$C ratio in expired CO$_2$. At 8:50 AM, subjects started cycling for 10 minutes at 100 W as a warm-up. At 9:00 AM, exercise intensity was increased to 50% Wmax for 180 minutes. Blood samples were drawn at 30-minute intervals until the end of exercise. Expiratory gases were collected every 15 minutes. Two subjects were tested on the same day, starting the protocol 10 minutes apart. Directly after the exercise bout, a second muscle biopsy was taken 2 cm proximal to the first biopsy.

**Drinks**

Subjects received a bolus of 4 mL · kg$^{-1}$ at the start (t = 0) and 2 mL · kg$^{-1}$ every 20 minutes during exercise of either a 15% CHO solution (CHO) or an equicaloric CHO + MCT suspension ([CHO + MCT]; 70 energy% [en%] as CHO [149 g/180 min] and 30 en% as MCT [29 g/180 min]). To study the effect of MCT added to the CHO instead of the equicaloric CHO + MCT suspension, a third trial (high-CHO [HCHO] + MCT) was included in which a differential amount of CHO. The CHO in these trials were known laboratory reference standard according to the formula, $\delta^{13}$C (per mil) = ([$^{13}$C/$^{12}$C sample] / [$^{13}$C/$^{12}$C standard] - 1) × 10$^3$. The $\delta^{13}$C was then related to the international standard, Pee Dee Bellemnitella (PDB-I). The amount of CHO oxidized was calculated according to the formula, exogenous CHO oxidation = VCO$_2$ · (6 ref - $\delta$ exp) / (6 ref - $\delta$ ing) · 1/k, in which $\delta$ ref is the $^{13}$C enrichment of expired air in the reference test CON (background), $\delta$ exp is the $^{13}$C enrichment of expired CO$_2$ during exercise with CHO (or MCT) ingestion at different time points, and $\delta$ ing is the $^{13}$C enrichment of the CHO in the ingested CHO + MCT suspension, and k is the amount of CO$_2$ (in liters) produced via oxidation of 1 gram glucose (k = 0.7466 L CO$_2$/g glucose).

In the present study and in previous studies from our laboratory, it was shown that instructing the subjects not to eat any products of high natural $^{13}$C abundance during the experimental period was effective in reducing the background shift (change in $^{13}$C) from endogenous substrate stores.

**Calculations**

CHO and fat oxidation rates were calculated from VCO$_2$ and VO$_2$ using the nonprotein respiratory quotient$^{20}$. CHO oxidation = 4.585VCO$_2$ - 3.226VO$_2$, and fat oxidation = 1.695VCO$_2$ - 1.701VO$_2$. In the present study and in previous studies from our laboratory, it was shown that instructing the subjects not to eat any products of high natural $^{13}$C abundance during the experimental period was effective in reducing the background shift (change in $^{13}$C) from endogenous substrate stores.

**Analysis**

Blood (10 mL) was collected into EDTA-containing tubes and centrifuged for 4 minutes. Aliquots of plasma were frozen immediately in liquid nitrogen and stored at $-40^\circ$C until analyses of glucose (Uni Kit III, 0710970; La Roche, Basel, Switzerland), lactate,$^{17}$ hydroxybutyrate,$^{18}$ FFA (Wako FFA-C test kit; Wako Chemicals, Neuss, Germany), and glyceral (GPO-trinder 337; Sigma, St Louis, MO), which were performed with the COBAS BIO analyzer (La Roche). Muscle biopsies were freeze-dried, and glycogen content was assayed spectrophotometrically after hydrolysis with HCl.$^{19}$ Glycogen concentration was expressed as millimoles of glucose units per kilogram dry weight of tissue. Total energy expenditure and oxidation rates of total fat, total CHO, and exogenous MCT were calculated from indirect calorimetry (respiratory quotient and VO$_2$) and stable-isotope measurements ($^{13}$CO$_2$/ $^{12}$CO$_2$) (GC continuous-flow IRMS; Finnigan MAT 252, Bremen, Germany). Enrichments of the substrates (in drinks) were measured with an elemental analyzer-IRMS combination (Carlo-Erba on-line [EA 1108CHN; Fisons, Milan, Italy] connected to the Finnigan MAT 252).

**Table 1. VO$_2$ and Respiratory Exchange Ratio (mean ± SEM) During 3 Hours of Cycling Exercise at 57% VO$_2$max with ingestion of CHO, CHO + MCT, or HCHO + MCT**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>2.78 ± 0.08</td>
<td>2.79 ± 0.10</td>
<td>2.79 ± 0.10</td>
<td>2.77 ± 0.10</td>
<td>2.80 ± 0.08</td>
<td>2.75 ± 0.10</td>
</tr>
<tr>
<td>CHO + MCT</td>
<td>2.76 ± 0.08</td>
<td>2.76 ± 0.09</td>
<td>2.79 ± 0.07</td>
<td>2.76 ± 0.08</td>
<td>2.77 ± 0.09</td>
<td>2.73 ± 0.09</td>
</tr>
<tr>
<td>HCHO + MCT</td>
<td>2.77 ± 0.07</td>
<td>2.80 ± 0.07</td>
<td>2.80 ± 0.08</td>
<td>2.84 ± 0.09</td>
<td>2.73 ± 0.08</td>
<td>2.80 ± 0.09</td>
</tr>
<tr>
<td>Respiratory exchange ratio</td>
<td>0.89 ± 0.01</td>
<td>0.86 ± 0.01</td>
<td>0.87 ± 0.01</td>
<td>0.88 ± 0.01</td>
<td>0.87 ± 0.01</td>
<td>0.87 ± 0.01</td>
</tr>
</tbody>
</table>

NOTE. No significant differences were observed among the trials or over time.
CARBOHYDRATE AND MCT INGESTION DURING EXERCISE

Fig 1. Breath $^{13}$CO$_2$ enrichment during exercise in (O) CHO, (D) CHO + MCT, and (A) HCHO + MCT trials and during the (I) CON trial used for background correction (mean ± SEM, n = 6).

Fig 2. Exogenous MCT oxidation rates over 180 minutes of exercise (mean ± SEM, n = 6). Symbols are as in Fig 1.

Fig 3. ([ ]) Preexercise and ([ ]) postexercise glycogen concentrations and (I) glycogen breakdown (decrease) for the CHO, CHO + MCT, and HCHO + MCT trials. No significant differences were observed among the trials (mean ± SEM, n = 6).

Table 2. Oxidation of Endogenous and Exogenous Substrates (in grams) Over the 60- to 120-minute and 120- to 180-Minute Periods (mean ± SEM)

<table>
<thead>
<tr>
<th>Interval</th>
<th>CHO</th>
<th>CHO + MCT</th>
<th>HCHO + MCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-120</td>
<td>132.2 ± 11.4</td>
<td>122.5 ± 10.3</td>
<td>127.3 ± 10.3</td>
</tr>
<tr>
<td>Exogenous</td>
<td>44.2 ± 3.7</td>
<td>34.2 ± 3.7</td>
<td>38.6 ± 5.0</td>
</tr>
<tr>
<td>Endogenous</td>
<td>88.0 ± 8.3</td>
<td>88.3 ± 7.3</td>
<td>88.7 ± 9.3</td>
</tr>
<tr>
<td>Fat</td>
<td>34.3 ± 3.7</td>
<td>37.5 ± 3.7</td>
<td>36.7 ± 3.2</td>
</tr>
<tr>
<td>120-180</td>
<td>124.1 ± 12.8</td>
<td>119.6 ± 9.8</td>
<td>130.8 ± 9.9</td>
</tr>
<tr>
<td>Exogenous</td>
<td>50.3 ± 3.2</td>
<td>41.5 ± 5.0</td>
<td>48.5 ± 4.8</td>
</tr>
<tr>
<td>Endogenous</td>
<td>73.8 ± 9.9</td>
<td>78.1 ± 6.5</td>
<td>82.3 ± 9.3</td>
</tr>
<tr>
<td>Fat</td>
<td>33.8 ± 4.2</td>
<td>38.7 ± 3.0</td>
<td>35.1 ± 3.1</td>
</tr>
</tbody>
</table>

NOTE. No significant differences in substrate utilization were observed among the trials or time periods.

Another methodological consideration when using $^{13}$CO$_2$ in expired gases to calculate exogenous substrate oxidation is the trapping of exogenous $^{13}$CO$_2$ in the bicarbonate pool, a very large and slowly exchanging pool in which some CO$_2$ arising from decarboxylation of energy substrates is temporarily trapped. However, during exercise, CO$_2$ production increases several-fold so that a physiological steady-state situation will occur and $^{13}$CO$_2$ in expired air will be rapidly equilibrated with the $^{13}$CO$_2$/H$^{13}$CO$_3^-$ pool. The dilution of $^{13}$CO$_2$ becomes negligible and recovery of $^{13}$CO$_2$ approaches 100% after 60 minutes of exercise. Therefore, in the present study, data from the initial 60 minutes were not used for calculation of exogenous MCT oxidation.

Gastrointestinal Discomfort

A questionnaire assessing gastrointestinal discomfort was provided after each exercise test. Subjects had to score the following items on a scale from 1 to 5 (1 = not at all to 5 = very severe): nausea, intestinal cramps, belching, vomiting, diarrhea, flatulence, stomach ache, abdominal pressure, and eructation.

Statistics

ANOVA for repeated measures was used to compare differences in substrate utilization and in blood-related parameters and slow-moving pool in which some CO$_2$ arising from decarboxylation of energy substrates is temporarily trapped. However, during exercise, CO$_2$ production increases several-fold so that a physiological steady-state situation will occur and $^{13}$CO$_2$ in expired air will be rapidly equilibrated with the $^{13}$CO$_2$/H$^{13}$CO$_3^-$ pool. The dilution of $^{13}$CO$_2$ becomes negligible and recovery of $^{13}$CO$_2$ approaches 100% after 60 minutes of exercise. Therefore, in the present study, data from the initial 60 minutes were not used for calculation of exogenous MCT oxidation.

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Statistics

ANOVA for repeated measures was used to compare differences in substrate utilization and in blood-related parameters
among the CHO, CHO + MCT, and HCHO + MCT trials. A Scheffé post hoc test was used in the event of a significant ($P < .05$) F ratio. All results are expressed as the mean ± SEM.

**RESULTS**

*Breath Analysis*

Oxygen consumption (Table 1) during exercise was relatively constant, with exercise intensity of the subjects maintained at close to 57% $\text{VO}_2\text{max}$ and not significantly different among the trials. The respiratory exchange ratio also was not significantly different among the trials.

The mean $^{13}\text{C}$ enrichment of the resting breath samples was $-26.36 \pm 0.25$ δ per mil versus PDB ($0.0109410^{13}\text{C}/^{12}\text{C}$ ratio). Changes in the isotopic composition of expired CO$_2$ in response to exercise are depicted in Fig 1. During CON (with ingestion of CHO of low $^{13}\text{C}$ natural abundance), there was a small nonsignificant increase of $^{13}\text{C}$ in the expired air (0.2 to 0.5 δ per mil v PDB). In the CHO(+ MCT) trials, the increase in $^{13}\text{C}$ was significant, reaching a difference of 3 to 4 δ per mil versus PDB toward the end of 180 minutes' exercise (compared with resting breath sample; Fig 1). Exogenous CHO oxidation increased during the first hour and leveled off during the final 90 minutes (Fig 2). At the end of the exercise bout, exogenous CHO oxidation
rates were 0.89, 0.73, and 0.91 g·min⁻¹ for CHO, CHO + MCT, and HCHO + MCT, respectively. Mean oxidation rates over the 60- to 180-minute period were 0.79, 0.63, and 0.73 g·min⁻¹, respectively. Exogenous CHO oxidation tended to be slightly lower in the CHO + MCT trial than in the CHO trial. However, this difference did not reach statistical significance. It was estimated that during the 60- to 180-minute period in the CHO trial, 94.5 g exogenous CHO was oxidized, versus 75.7 g in CHO + MCT and 87.1 g in HCHO + MCT. The amounts of CHO (exogenous and endogenous) and fat oxidation during the second and third hour of exercise are presented in Table 2. Energy expenditure was comparable in all trials.

Muscle Glycogen

Preexercise muscle glycogen concentrations were comparable among the trials: 516 ± 32, 518 ± 30, and 505 ± 26 mmol glucose·kg dry weight (dw)⁻¹ for CHO, CHO + MCT, and HCHO + MCT, respectively. Muscle glycogen levels decreased significantly in the three trials: 277 ± 14 mmol glucose·kg dw⁻¹ for CHO, 249 ± 20 for CHO + MCT, and 240 ± 18 for HCHO + MCT. Glycogen breakdown was not significantly different among the three trials (Fig 3).

Plasma Variables

Compared with rest, plasma FFA levels were decreased after 30 minutes of exercise and were significantly elevated during the final 30 minutes of exercise (Fig 4A). No differences in plasma FFA levels were observed among the trials. There was a significant increase in plasma glycerol levels after 30 minutes in all trials, but no differences were observed among the three trials (Fig 4B). Plasma β-hydroxybutyrate concentrations increased to approximately 500 μmol·L⁻¹ during the first 30 minutes in the CHO + MCT and HCHO + MCT trials; thereafter, concentrations remained stable (Fig 4C). In the CHO trial, no changes in β-hydroxybutyrate were observed throughout exercise. Plasma glucose levels were maintained during exercise (Fig 5A), whereas plasma lactate concentrations tended to decrease as compared with the resting value (Fig 5B). No differences were observed in plasma glucose or lactate concentrations between the trials.

Gastrointestinal Discomfort

Subjects reported some gastrointestinal discomfort in all tests. The occurrence and severity (mean score, 2.8) of the complaints were not different among the trials. Most frequently reported were intestinal cramps, nausea, and belching.

DISCUSSION

Muscle Glycogen and Plasma FFA

It has been reported in several studies that increased availability of plasma FFA resulted in muscle glycogen sparing⁹,¹³,²⁴ and hence increased performance.¹⁰ In humans, plasma FFA levels have been elevated by injecting heparin, which stimulates lipoprotein lipase activity, after feeding subjects a high-fat meal (long-chain fatty acids) or infusing a triglyceride emulsion (Intralipid).⁹,¹³,²⁴ In these studies, a glycogen-sparing effect was observed when FFA availability was high. Although the infusion of fats and consumption of triglycerides in combination with an injection of heparin are interesting approaches to test the
interaction between CHO and fat metabolism during exercise, this method has little practical value. It has therefore been suggested that ingestion of MCT will increase FFA availability. In the present study, MCT ingestion did not affect plasma FFA levels. Hence, no effect on muscle glycogen utilization was observed. This is in agreement with the only other available study in which muscle glycogen concentrations were determined after MCT ingestion. In it, MCT were ingested 1 hour before exercise and did not result in glycogen-sparing during 1 hour of exercise at 60% VO2max. It may be that the amount of MCT provided was too small to influence plasma FFA concentrations, or that medium-chain fatty acids are oxidized rapidly in the liver and/or in skeletal muscle so that plasma FFA concentration remains the same.

Plasma Glycerol and Ketone Bodies

Increased plasma levels of glycerol and ketone bodies have been frequently observed after MCT feeding. In the present study, glycerol concentrations were not significantly elevated after MCT ingestion. Plasma β-hydroxybutyrate was elevated to moderate levels (400 to 500 mmol·L⁻¹) after MCT ingestion. This may indicate that part of the MCT are metabolized in the liver, resulting in the production of ketone bodies, while the glycerol from hydrolysis of MCT is rapidly utilized for gluconeogenesis.

Substrate Utilization

We found that MCT ingestion did not affect total CHO or fat utilization. Peak oxidation rates of the oral ingested long-chain glucose polymer were 0.80 to 0.94 g·min⁻¹, which is in line with previous studies. Peak oxidation rates of glucose, glucose polymers, and starch have been found to be between 0.8 and 1.0 g·min⁻¹ with comparable ingestion rate, feeding schedule, and exercise intensity. The oxidation rate of orally ingested CHO seemed to be slightly lower (although not significantly) in the CHO + MCT trial as compared with CHO and HCHO + MCT. The reason for this small difference may be that the amount of CHO ingested was lower (149 v 214 g). As shown previously, the oxidation rate of orally ingested CHO did not increase to the same magnitude as the amount of CHO ingested. The rate of exogenous CHO oxidation seems to be limited by a yet-undetermined factor. The ingested CHO contributed 15% to 25% to energy expenditure during the 120- to 180-minute period. The contribution of MCT to energy expenditure has been shown to be approximately 7% during the same period (120 to 180 minutes) with similar experimental conditions.

However, according to the literature, the amount of MCT ingested in the present study (29 g) is reported to be the maximal amount of MCT that can be ingested without causing gastrointestinal problems.

Gastrointestinal Discomfort

The MCT (29 g) seemed to have no influence on palatability of the beverages. However, since in all tests some such discomfort was reported, this may be attributed to the long-chain glucose polymers that were co-ingested with the MCT. Ivy et al reported that administration of 30 g MCT in combination with cereal caused some minor distress in 10% of the subjects. In summary, 29 g MCT co-ingested with CHO during 180 minutes of exercise at 57% VO2max does not influence exogenous or endogenous CHO utilization or muscle glycogen breakdown.

REFERENCES

CARBOHYDRATE AND MCT INGESTION DURING EXERCISE


