Comparison of the effect of medium-chain and long-chain triacylglycerols on calcium absorption in healthy subjects\(^1\)-\(^3\)

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ABSTRACT

**Background:** The absorption efficiency of calcium in humans is low. Some studies in infants have shown that calcium absorption can be increased by adding medium-chain triacylglycerols to the formula diet.

**Objective:** The effect of medium- and long-chain triacylglycerols on calcium absorption was studied in 18 healthy, young men. The results were compared with data obtained from calcium ingestion of a protein-carbohydrate formula devoid of triacylglycerols.

**Design:** Calcium absorption was measured by using a double-isotope technique and the kinetic parameters were obtained by using a deconvolution method.

**Results:** The total fractional calcium absorption measured in the presence of medium-chain triacylglycerols (0.236 ± 0.016) or from a protein-carbohydrate formula without triacylglycerols (0.235 ± 0.012) was not significantly different. The same result was observed with long-chain triacylglycerols (0.309 ± 0.026) and the protein-carbohydrate formula (0.275 ± 0.012). No kinetic parameters were significantly different regardless of the diet (protein-carbohydrate, medium-chain triacylglycerol, or long-chain triacylglycerol). This suggests that the same mechanism for calcium absorption was operative.

**Conclusions:** Triacylglycerols had no direct effect on calcium absorption from a protein-carbohydrate formula in healthy subjects. These data do not support the use of medium-chain triacylglycerols as adjuvants to increase the absorption of calcium in healthy adults. *Am J Clin Nutr* 1999;69:1237–42.

KEY WORDS Calcium, calcium absorption, medium-chain triacylglycerols, long-chain triacylglycerols, osteoporosis, men

INTRODUCTION

Osteoporosis is a major public health problem, affecting 24 million persons in the United States and contributing to more than 1 million fractures annually. The risk of osteoporotic fracture increases with age such that >40% of women in the Western world experience one or more osteoporotic fractures by the time they reach 70 y of age.

Despite a lack of consensus among different authors, many experts support a relation between calcium deficiency and osteoporosis (1–7) and acknowledge the important role of a positive calcium balance, as well as adequate vitamin D status, in maintaining good bone health. Calcium intake and vitamin D status may also play a role in hypertension, colon cancer, and breast cancer (8). Chapuy et al (9) and Dawson-Hughes (10) noted the relation between life-long calcium intake and the prevention of bone fragility in the aged. However, it has been established that it is not the absolute content of calcium in supplements and foodstuffs (ie, intake) that influences retention but rather the bioavailability (fraction absorbable) that ultimately determines calcium status in the body (11). Unfortunately, the absorption efficiency of calcium in humans is relatively low (25–30%), with some calcium salts such as calcium citrate malate exhibiting the best bioavailability (12). Attempts to increase the amount of body calcium through increased consumption of calcium-containing foods or through use of an increased dose of supplements have not always been successful and often lead to problems of non-compliance in addition to the increased cost associated with supplement use. Therefore, it is apparent that an increase in the absorption efficiency of the normal dose of calcium ingested daily in foodstuffs would not only make it easier for the elderly to fulfill their daily requirements but also improve compliance.

The literature indicates that lactose and glucose (13, 14), medium-chain triacylglycerols (MCTs) (15–17), and other agents (18) can enhance the intestinal absorption of calcium. MCTs were introduced for the treatment of disorders of lipid metabolism in which fat malabsorption and defective calcium absorption occur regularly (19). Indeed, the replacement of a certain proportion of LCTs by MCTs in the diet of preterm infants resulted in a better absorption of fats (17). In addition, MCTs have been used in the...
treatment of a variety of malabsorption syndromes, in which they have successfully reduced fecal fat loss (20). As an explanation of this favorable action, it has been postulated that in the presence of steatorrhea, calcium malabsorption may be due to the formation of insoluble calcium soaps, loss of vitamin D in the stool, or both. However, the effects of dietary addition of MCTs on calcium absorption have been somewhat conflicting, with some studies showing an enhancement of absorption (15–17) and others (21) finding no effect. Despite the potential of MCTs to increase calcium absorption, their role in this regard has not been evaluated systematically. In fact, the test solutions used in previous studies were often mixtures of long-chain triacylglycerols (LCTs) and MCTs, making it difficult to evaluate precisely the specific effect of MCTs on calcium absorption. The goal of this study was therefore to clarify the effects of MCTs by comparing the effects of MCTs and LCTs on calcium absorption in healthy, young men.

SUBJECTS AND METHODS

Subjects

Eighteen white men participated in the study. Each subject was given a thorough explanation of the experiment and provided his written consent for participation. The protocol was approved by the ethics committee of the Department of Medicine of the University Hospital of Geneva. The subjects were aged 22–28 y and weighed 65–80 kg. All were in good health, were taking no drugs, and had no history of milk intolerance. Serum calcium, creatinine, phosphorus, protein, and alkaline phosphatase values were within normal limits. Subjects were also required to have normal lactase activity as determined by a breath-hydrogen test (22). In the test, hydrogen concentrations were measured before and then at 60-min intervals for 4 h after ingestion of 50 g lactose dissolved in 450 mL water. A maximum increase of 0.88 mmol/L above the fasting hydrogen concentration was considered indicative of normal lactase activity. Only subjects with a hydrogen concentration increase < 0.88 mmol/L were required to have normal lactase activity as determined by a breath-hydrogen test (22). In the test, hydrogen concentrations were measured before and then at 60-min intervals for 4 h after ingestion of 50 g lactose dissolved in 450 mL water. A maximum increase of 0.88 mmol/L above the fasting hydrogen concentration was considered indicative of normal lactase activity. Only subjects with a hydrogen concentration increase < 0.88 mmol/L participated in the study.

Procedures

The calcium absorption study was performed as described previously (14). Subjects were ambulatory and maintained their usual diets and activities throughout the study. A supplement of 0.5 g Ca (as gluconolactobionate and carbonate of calcium, Calcium-Sandoz; Sandoz SA, Bâle, Switzerland) was given by mouth twice daily for 7 d before each calcium absorption test to decrease individual variation in calcium intake.

The calcium test drink was prepared by dissolving 38 g of a protein-carbohydrate powder (Build-Up; Nestlé Ltd, Croydon, United Kingdom; Table 1) in 285 mL distilled water; 740 kBq 45 Ca (Medipro AG, Teufen, Switzerland) was then added and the solution was left to equilibrate for 15 ± 1 h at 4°C before administration (protein-carbohydrate formula). For the MCT formula, 6.68 g MCTs [232.6 kJ (55.6 kcal), Miglyol 812; Dynamit-Nobel Aktiengesellschaft GB, Troisdorf, Germany] was homogenized with a shaker and added to the protein-carbohydrate formula; for the LCT formula, 5.85 g LCTs [232.6 kJ (55.6 kcal), Soya oil; Morgia AG, Lyss, Switzerland] was homogenized with a shaker and added to the protein-carbohydrate formula. The fatty acid composition of the MCT and LCT formulas is shown in Table 2. The total Ca2+ content of each formula was 0.5 g; the total energy content of each equilibrated nutritional drink was 824.2 kJ (197 kcal), with 29.0% as fat, 53.0% as carbohydrate, and 17.6% as protein.

After an overnight fast, each subject consumed the test drink orally within 5 min. At the time of the first swallow, 410 kBq sterile 47 Ca (Riso National Laboratory, Rosilide, Denmark) was injected intravenously. The total body irradiation for each test was < 1.4 mSv (< 140 mrem), which is about the same irradiation received during liver or bone scintigraphy. No food was allowed for 4 h after the start of the test, after which a lunch low in calcium (2 ham sandwiches) was given. After 8 h, subjects were permitted to resume their normal eating habits. Blood samples were collected from an indwelling venous catheter into heparin-treated tubes 26 times during the first 8 h and again at 24 and 32 h to measure concentrations of 45 Ca and 47 Ca. To minimize exposure to radiation, each subject underwent only 2 tests of calcium absorption at 6–10-wk intervals in random order.

Radioactivity measurement

Blood 47 Ca radioactivity was determined from 3.0-mL plasma samples by using a well-type gamma counter. After 8 wk of storage, 1.5 mL plasma was mixed with 15 mL Instagel (Packard Instruments International SA, Zurich, Switzerland) and 47 Ca radioactivity was counted in a liquid scintillation spectrometer. All counts were corrected for quenching and for 45 Ca contamination by the intravenous 47 Ca preparation. The oral and intravenous radioactivity concentrations were expressed as a percentage of the total dose per liter plasma.

<table>
<thead>
<tr>
<th>Component</th>
<th>LCT formula</th>
<th>MCT formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprylic acid (8:0)</td>
<td>—</td>
<td>57</td>
</tr>
<tr>
<td>Capric acid (10:0)</td>
<td>—</td>
<td>42</td>
</tr>
<tr>
<td>Lauric acid (12:0)</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Myristic acid (14:0)</td>
<td>0.1</td>
<td>—</td>
</tr>
<tr>
<td>Palmitic acid (16:0)</td>
<td>11.0</td>
<td>—</td>
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<tr>
<td>Palmitoleic acid  (16:1)</td>
<td>0.1</td>
<td>—</td>
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<tr>
<td>Stearic acid (18:0)</td>
<td>4.0</td>
<td>—</td>
</tr>
<tr>
<td>Oleic acid (18:1)</td>
<td>23.4</td>
<td>—</td>
</tr>
<tr>
<td>Linoleic acid (18:2)</td>
<td>53.2</td>
<td>—</td>
</tr>
<tr>
<td>Linolenic acid (18:3)</td>
<td>7.8</td>
<td>—</td>
</tr>
<tr>
<td>Arachidic acid (20:0)</td>
<td>0.3</td>
<td>—</td>
</tr>
<tr>
<td>Behenic acid (22:0)</td>
<td>0.1</td>
<td>—</td>
</tr>
</tbody>
</table>

TABLE 1

Composition of the protein-carbohydrate formula (per 38 g)

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (g)</td>
<td>8.51</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>25.5*</td>
</tr>
<tr>
<td>Lipids (g)</td>
<td>0.19</td>
</tr>
<tr>
<td>Minerals (g)</td>
<td>1.92</td>
</tr>
<tr>
<td>Water (g)</td>
<td>1.52</td>
</tr>
</tbody>
</table>

*13.5 g lactose.
2380 mg Ca2+.
Mathematical method

The method involved a consideration of the time course of the 2 tracers: $^{45}$Ca given orally, which moves from the gastrointestinal tract into the plasma, and $^{45}$Ca given intravenously, which is distributed along with $^{45}$Ca from the plasma to the other tissues. The rate of disappearance of the intravenously administered calcium can be represented by a sum of exponentials. The calcium given orally disappears from the plasma at the same rate, but is continuously replaced by new radioactive calcium entering the plasma from the intestinal tract. The amount of $^{45}$Ca in the plasma from the oral dose is obtained from the convolution of the fractional $^{45}$Ca absorbed by disappearance curve of $^{47}$Ca. The mathematical problem involved inverting this convolution to obtain fractional $^{45}$Ca absorbed as a function of time.

Values for calcium absorption and the kinetic parameters were obtained by using the SAAM 30 program of Berman (23) and by a deconvolution method described previously (24). From fractional calcium absorption $A(t)$, the following 2 parameters were derived:

\[
\text{Mean transit time} = \int_{0}^{440} A(t) \, dt \\
\text{Mean absorption rate} = \int_{0}^{440} \frac{A(t)}{t} \, dt
\]

Statistical analysis of data

Results are expressed as means ± SEMs. The data were analyzed by using the model of 3 treatments in a 2-period crossover design with no carryover effects as proposed by Koch et al (25). Given the data structure, we could use the standard crossover analysis for each 2-treatment combination, using only 3 subjects per group, or apply the more powerful procedure of Koch et al, performing a multiple regression with all 18 subjects. Both analyses were done. Analysis of variance and unpaired $t$ tests were used to compare the effects of MCTs and LCTs. A $P$ value < 0.05 was considered statistically significant.

RESULTS

Intestinal calcium absorption

The addition of LCTs or MCTs to the protein-carbohydrate formula in 6 young men did not significantly change total fractional calcium absorption (Table 3). Mean total fractional calcium absorption was slightly higher from the LCT formula (0.287 ± 0.016) than from the MCT formula (0.245 ± 0.014), but this difference was not significant ($P > 0.05, n = 12$) as shown in Figure 1.

**TABLE 3**

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Fraction of dose administered</th>
<th>Mean absorption rate</th>
<th>Mean transit time</th>
<th>Median time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$^{45}$CaA</td>
<td>fraction/min $\times 10^{-3}$</td>
<td>min</td>
<td>min</td>
</tr>
<tr>
<td>Group 1 ($n = 6$)</td>
<td>P</td>
<td>0.235 ± 0.012</td>
<td>1.08 ± 0.12</td>
<td>119.8 ± 8.2</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>0.236 ± 0.016</td>
<td>0.94 ± 0.10</td>
<td>127.5 ± 5.9</td>
</tr>
<tr>
<td>Group 2 ($n = 6$)</td>
<td>P</td>
<td>0.275 ± 0.012</td>
<td>1.18 ± 0.09</td>
<td>117.6 ± 4.8</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.309 ± 0.026</td>
<td>1.28 ± 0.11</td>
<td>117.6 ± 4.8</td>
</tr>
<tr>
<td>Group 3 ($n = 6$)</td>
<td>L</td>
<td>0.266 ± 0.011</td>
<td>1.17 ± 0.14</td>
<td>117.3 ± 9.6</td>
</tr>
</tbody>
</table>

$\text{Table 3}$

Total fractional calcium absorption ($^{45}$CaA) and effects on absorption kinetics of a protein-carbohydrate solution and 2 solutions containing triacylglycerols. $^{1}$

$^{1}$ $\bar{x} \pm$ SEM. The mean absorption rate is the total amount of calcium absorbed during the first 440 min, independently of when absorption took place; mean transit time is the mean residence time necessary for transit through the body; and median time is the time it takes to absorb 50% of the total dose. P, protein-carbohydrate formula alone; M, protein-carbohydrate formula plus medium-chain triacylglycerols; L, protein-carbohydrate formula plus long-chain triacylglycerols. There were no significant differences between formulas.

DISCUSSION

We showed that in young, healthy men, calcium is absorbed from an MCT-enriched formula in short-term experiments as efficiently as from a formula containing LCTs. Moreover, the presence of fat in the formula seemed to have no significant influence on the time dependence or amount of intestinal calcium absorption.

In this study, total fractional calcium absorption was not significantly different between the 3 formulas. However, this does not necessarily imply that MCTs and LCTs have the same effect on calcium absorption. The kinetic parameters did not suggest a differing pattern for the absorption of calcium from the LCT and MCT formulas because neither the mean absorption rate nor the mean transit time was significantly different between formulas. Moreover, the shape of the curve describing the calcium absorption rate showed no significant differences between the 3 formulas that would suggest a change in gastric
FIGURE 1. Comparison of the effects of a protein-carbohydrate formula containing long-chain triacylglycerols (L) or medium-chain triacylglycerols (M) on total fractional calcium absorption (TFCaA) and the kinetic parameters of absorption. The mean absorption rate is the total amount of calcium absorbed during the first 440 min, independently of when absorption took place \( \int_{0}^{440} A(t) \, dt \); mean transit time is the mean residence time necessary for transit through the body \( \int_{0}^{440} t \, A(t) \, dt / \int_{0}^{440} A(t) \, dt \); and median time is the time it takes to absorb 50% of the total dose. No significant differences were observed.

FIGURE 2. Rate of initial calcium entry from the intestine into the vascular system; 2 transit curves were obtained in each of 3 subjects. M, protein-carbohydrate formula plus medium-chain triacylglycerols; P, protein-carbohydrate formula alone; L, protein-carbohydrate formula plus long-chain triacylglycerols.
emptying rate. The time to attain the plateau concentration was similar for the 3 formulas. It can therefore be concluded that the gastric emptying of calcium was not significantly different after the ingestion of the homogenized fat formulas, as also shown by Cortot et al (26).

It has been clearly shown in perfusion studies of human and rat jejunum that the absorption rate of calcium is related to the intralumenal calcium concentration (27, 28). Thus, the effect of MCTs and LCTs on the intralumenal solubilization of calcium in the present study appears to have been insignificant. Moreover, the MCTs did not seem to favor an increase in calcium transport. This is supported by the fact that a similar mean rate of calcium absorption was observed for the 3 formulas, suggesting that the luminal concentration of bioavailable calcium was comparable. In addition, our subjects did absorb the LCTs; therefore, sufficient quantities of bile acids would likely have been present for the formation of micelles and the solubilization of calcium.

In conclusion, our data indicate that there is no direct effect of MCTs on calcium absorption and do not support the use of MCTs as an adjuvant to increase calcium absorption. The beneficial effect of MCTs observed by other investigators was probably secondary to a better absorption of fats and an improvement in vitamin D absorption. The use of MCTs may therefore be appropriate in cases of lipid malabsorption and this hypothesis appears worthy of further testing.

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REFERENCES