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Kinetics and Thermogenesis of Medium-Chain Monocarboxylic and Dicarboxylic Acids in Man: Sebacate and Medium-Chain Triglycerides

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ABSTRACT. The effects on oxygen consumption and carbon dioxide production of a constant intravenous infusion of 0.15 g of disodium sebacate (Sb), the sodic salt of a medium-chain dicarboxylic acid with 10 carbon atoms, per kilogram of body weight per hour over 5 hours and of a 50% mixture of medium- and long-chain triglycerides (MCT/LCT) were compared in 10 healthy men. Oxygen consumption and carbon dioxide production were measured by indirect calorimetry. Mean oxygen consumption was about 19% higher than the basal oxygen consumption at the end of MCT/LCT infusion but was only 5% higher than the basal oxygen consumption when Sb was infused. There was an eightfold increase in plasma β-hydroxybutyrate and acetoacetate concentrations and a threefold increase in serum insulin levels during MCT/LCT infusion, but no significant change in ketone bodies and insulin from basal values was observed during and after Sb infusion. Pharmacokinetic parameters were also computed, showing an average apparent volume of distribution of 167 mL/kg of body weight for MCTs and 112 mL/kg of body weight for Sb. The $t_{1/2}$ of MCTs was 50 minutes and that of Sb was 78 minutes. Urinary excretion of Sb and its β-oxidative by-product, suberic acid, globally accounted for 48% of the given amount of Sb. In spite of its urinary loss and slower tissue uptake compared with MCTs, Sb avoided ketone body formation or elevation in insulin levels and did not induce a significant increase in oxygen consumption. The Sb caloric equivalent was 6.643 kcal/g, and the remaining amount of Sb administered (approximately 5.2 g/h in a 70-kg subject) seemed to be energetically useful by furnishing 34.54 kcal/h, ie, 829 kcal over 24 hours. This caloric support is equivalent to or even higher than that usually given as MCTs; however, formation of ketone bodies and interference with glucose metabolism are avoided. (*Journal of Parenteral and Enteral Nutrition* **17**:257–264, 1993)

Medium-chain triglyceride (MCT) emulsions, with esterified monocarboxylic fatty acids containing mainly eight and 10 carbon atoms, have been shown to be a viable parenteral source of calories when administered in varying proportions combined with long-chain triglycerides (LCTs). Contrary to LCTs, MCTs do not require chylomicron formation and are transported directly to the liver by the portal system.[1,2] MCTs are characterized by prompt tissue availability, relevant oxidation in the liver to ketone bodies,[3,4] and stronger stimulation of thermogenesis than LCTs.[5–7].

In the area of parenteral nutrition, in particular in the treatment of the critically ill, the use of tailor-made lipid molecules may prove particularly useful in providing alternate and readily available energy sources. Concerning this, we have recently proposed the use of another family of medium-chain lipid-like substrates[8–12] in total parenteral nutrition. We are referring to the salts of dicarboxylic acids (DAs), which, being water-soluble, do not require emulsifying procedures and the administration of fluids containing large micelles. Furthermore, they are rapidly metabolized and their intramitochondrial transport is carnitine-independent.[13]

Sebacic acid (Sb) is a DA with 10 carbon atoms that exhibits neither toxic nor teratogenic effects in laboratory animals.[10] It is oxidized to water and carbon dioxide passing through acetyl coenzyme A (CoA) and succinyl-CoA formation.[11,12] Succinyl-CoA can also be used as a starting point in the gluconeogenetic pathway.[14,15] Sb provides more calories than carbohydrates[12] and it is inexpensive to prepare.

Sb is a straight-chain, medium-length acid that differs from the homologous medium-chain fatty acid (MCFA) with 10 carbon atoms, capric acid, only by having another terminal carboxyl group, which allows it to be stable as a simple salt solution instead of being esterified to give triglycerides. Because of this structural similarity, in this study we have examined energy expenditure behavior during continuous intravenous (IV) infusion of comparable amounts of Sb or MCTs (as a 50% mixture with LCTs, inasmuch as MCTs are not available alone for parenteral nutrition purposes) and computed the pharmacokinetic parameters of these two compounds.

MATERIALS AND METHODS

Patients and Experimental Design

The mean body mass index of the 10 male volunteers examined in this study was 23.43 ± 0.77 kg/m^2, and the ages ranged from 28 to 32 years. The study was approved by the Institutional Investigation Committee. All subjects were studied as in-patients at the Metabolic Disease Department of the Catholic University in Rome undergoing a continuous IV infusion of either Sb or MCTs over 5 hours. All patients were admitted to the hospital on

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the evening before the day of each experimental session.

Six subjects received IV Sb, and four others were infused with an MCT/LCT mixture (Lipofundin 20%, Braun Pharmaceuticals, Melsungen, Germany). Sb or MCT/LCT was continuously infused with use of a syringe infusion pump over a period of 5 hours at a constant rate of 0.15 g/kg of body weight per hour. Thus, the infusion rate of Sb was 2500 μg/kg of body weight per minute, whereas, because C8 and C10 accounted for 57.4% and 34.7% of MCT oil weight, respectively, we effectively infused 1435 μg of C8 per kilogram of body weight per minute and 857.5 μg of C10 per kilogram of body weight per minute. Blood samples were taken at 0, 30, 60, 120, 180, 240, and 300 minutes during infusion and at 30, 60, 120, 180, and 240 minutes after infusion.

All urine for 24 hours from the beginning of the infusion was collected in a container with 0.1% sodium azide to prevent bacterial growth. Monocarboxylic acids and DAs were measured in all urine samples.

Oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) were measured by using indirect calorimetry on the morning of the continuous infusion day after a 12-hour fast. Thirty minutes before the start of the infusion, $\dot{V}O_2$, $\dot{V}CO_2$, and nonprotein respiratory quotient were measured with a Deltatrac Monitoring System (Datex Instrumentation Corp, Helsinki, Finland).

The indirect calorimetry measurements ($\dot{V}O_2$ and $\dot{V}CO_2$) were performed each minute for 30 minutes every hour during a period of 8 hours corresponding to the 5 hours of continuous IV infusion and the 3-h postinfusion period. The thermic effect of the administered substrates was calculated as the difference between the $\dot{V}O_2$ measured at the fifth hour of infusion and the basal $\dot{V}O_2$.

Analytical Procedures

Ketone bodies and insulin analysis. Acetoacetic acid and β-hydroxybutyrate were measured enzymatically.[16] Plasma insulin concentrations were measured by radioimmunoassay.

DA extraction from urine samples. Urine samples (0.5 mL), with 100 μg of nonadioic (azelaic) acid added as an internal standard, were treated with cation-exchange resin (Dowex 50 W-X4, 100- to 200-μm mesh, H^+; Sigma Chemical Co, St. Louis, MO) to remove salts, concentrated under reduced pressure, and filtered through a Millipore HV (0.45-mm) filter (Millipore Corp, Bedford, MA). The samples were extracted three times with eight volumes of ethylacetate and evaporated under nitrogen.

Plasma MCT and Sb extraction and purification. Fifty micrograms of nonadioic (azelaic) or undecanoic acid as an internal standard was added to plasma samples from subjects infused with Sb or MCT/LCT. Proteins were then precipitated with ethanol, kept at −20°C overnight, and removed by centrifugation at 5000 rpm for 15 minutes. The pellet was washed three times with 0.6 mL of ethanol and the supernatants were collected together. The combined extracts were dried over anhydrous sodium sulfate and evaporated under nitrogen stream.

Plasma MCTs extracted with ethanol were purified from other lipid fractions by thin-layer chromatography with hexane–diethyl ether–acetic acid (70:30:1.8, vol/vol/vol) as the solvent system. A mixture of tricaprylin (1,2,3-trioctanoylglycerol) and tricaprin (1,2,3-tridecanoylglycerol) in chloroform-methanol (1:1, vol/vol) was used as a reference standard for MCTs, and a mixture of tripalmitin (1,2,3-trihexadecanoylglycerol) and triolein (1,2,3-tri[cis-9-octadecenoyl]glycerol) was used as a standard for LCTs. With use of the above solvent system, MCTs migrated immediately below the LCT spot, from which, however, they were well separated. MCTs were scraped off the plate and extracted with three volumes of ethanol. MCT hydrolysis was performed by adding 0.5 mL of 2 N potassium hydroxide in methanol to the above solution. The complete hydrolysis was achieved after 60 minutes at 60° to 65°C. At this temperature, no methyl esters were formed, as demonstrated by preliminary analysis performed by a 2330 Supelco capillary column (Supelco Inc, Bellafonte, PA) for standard free fatty acid analysis. The samples were acidified with 4 N hydrochloric acid to pH 1 to 2 and then extracted three times with peroxide-free diethyl ether. Ether solutions were evaporated under nitrogen and the residue was redissolved in a solution of methanol-acetonitrile (1:1, vol/vol) to perform p-bromophenacyl esters.

Derivatization procedure. The reaction of both MCFAs and DAs with *p*-bromophenacyl bromide with use of N,N-diisopropylethylamine as a catalyst quantitatively yields strongly absorbing *p*-bromophenacyl esters that can be determined by high-performance liquid chromatography (HPLC) with absorbance measured at 254 nm.

The extracted solutes, containing either MCFAs or DAs, were dissolved in 2 mL acetonitrile/methanol (1:1, vol/vol) and added to 6 mg of *p*-bromophenacyl bromide and 14 μL of N,N-diisopropylethylamine as a catalyst. The reaction was complete after approximately 30 minutes at 60°C. The solvent was evaporated under nitrogen down to a volume of 1 mL.

Recovery of standard MCFAs and standard MCTs. Ten to one hundred micrograms of C8, C10, C11, and C12 standard MCFAs in 100 μL of ethanol was added to 0.5 mL of plasma from five untreated subjects. MCFAs were extracted and analyzed by HPLC as described above.

Ten to two hundred micrograms of tricaprylin and tricaprin in chloroform-methanol (1:1, vol/vol) was added to 0.5 mL of plasma from five untreated subjects. MCTs were first extracted in ethanol and then saponified and analyzed by HPLC as described above.

The linearity and reproducibility of the method for DAs together with data concerning the recovery of standards from plasma and urine samples have been previously reported.[8]

HPLC apparatus. The analysis was carried out by using a 1050 liquid chromatograph (Hewlett-Packard Co, Palo Alto, CA) equipped with a scanning spectrophotometer operating in the 190 to 600 nm wavelength range (light source: deuterium lamp). The HPLC includes an integrator, so that areas and times are given for each peak in the chromatogram. A reversed-phase LC-18 column (Supelco Inc), 25 cm × 4.6 mm internal diameter, particle size 5 μm, was used.

HPLC analysis. Mobile phase B was methanol-water (50:50, vol/vol); mobile phase A was acetonitrile. The

run started isocratically for 20 minutes with 15% mobile phase B; a first gradient elution was taken from 15% to 60% acetonitrile in 40 minutes, a second gradient was programmed from 60% to 100% acetonitrile in 80 minutes, and then the run was maintained isocratic. The detector used UV light (at 254 nm). The flow rate was 1 mL/min. The sensitivity was from 4.0 to 128.0 $\times 10^{-4}$ absorbance units per centimeter (depending on the amount of injected substances), and the chart speed was 0.2 cm/min.

With this mobile phase, the excess derivatizing reagent and its degradation products came immediately at the start of the run.

Pharmacokinetic Analysis

The pharmacokinetics and metabolic fate of LCTs were not taken into account in the present study.

Plasma concentrations *vs* time curves were analyzed for six subjects undergoing Sb infusion and four subjects undergoing MCT infusion. Two curves were obtained for each patient receiving MCTs, one for C8 and one for C10. Twelve to 14 points were obtained for each subject during the infusion and postinfusion phases.

To analyze the data points, a simple one-compartment model has been used, considering both MCT and Sb diffusion throughout their spaces to be very fast with respect to metabolism and urinary loss. This model assumes a first-order loss from the compartment (constant clearance); more complicated models have been found in this case to present a marked variability of the parameters and thus to be unacceptable. The composite linear infusion-postinfusion expression for the model is

$$dC/dt = (IR/V) - kC,\ C^0 = 0,$$

solved for the infusion phase as

$$C(t) = (IR/kV)\ (1 - e^{-kt})$$

and for the postinfusion phase as

$$C(t) = C_{300}{}^{-k(t\ -\ 300)}$$

with

$$C_{300} = IR/kV\ (1 - e^{-300\ k})$$

where IR is the infusion rate (micrograms per kilogram of body weight), V is the apparent volume of distribution (milliliters per kilogram of body weight), C is the concentration (micrograms per milliliter), t is the time (minutes), and k is the linear elimination rate constant (minutes^{-1}). The model was fitted separately on each subject by quasi-Newton nonlinear least squares, and the resulting parameter estimates were averaged (traditional two-stage procedure).

Statistical Procedures

Paired *t* tests between first and fifth hour values were performed to determine differences in metabolic parameters ($\dot{V}O_2$, $\dot{V}CO_2$) after infusion. All data are expressed as mean ± SD.

RESULTS

The HPLC method described above allowed a linearity of detection of each standard MCFA in a range from 50 μg to 1500 μg. The recovery of the single MCFA standards added to MCFA-free plasma was in the order of 85% to 95%.

Figure 1 shows the HPLC separation of a mixture of both saturated and unsaturated straight-chain fatty acids, ranging between eight and 18 carbon atoms, and of saturated medium-chain DAs from C7 (adipic acid) to C12 (dodecanedioic acid). The chromatograms of two plasma samples from two different subjects, the first infused with IV MCTs and the second infused with Sb, are shown in Figure 2*A* and *B*, respectively. The plasma concentrations of octanoic (C8) and decanoic (C10) acids from MCTs are plotted in Figure 3*A* and 3*B*, respectively, together with the fitted model curves. The apparent volume of distribution of C8 was estimated to be 173.40 ± 38.36 mL/kg of body weight and the constant of elimination from plasma was 0.0132 ± 0.00314 min^{-1} ($t_{1/2}$ of 52 minutes and plasma clearance of 2.3 mL/kg of body weight per minute). The values of the pharmacokinetic parameters for C10 gave results similar to those for C8. In fact, the volume of distribution was 160.75 ± 36.61 mL/kg of body weight and the constant of elimination from plasma was 0.0145 ± 0.00338 min^{-1}; consequently, $t_{1/2}$ was 48 minutes and plasma clearance was 2.33 mL/kg of body weight per minute. Neither monocarboxylic acids (C8, C10) nor DAs of the same or shorter chain length (β-oxidation products) were retrieved from the urine after MCT administration.

Figure 4 shows the Sb plasma concentrations in the subjects given Sb at an infusion rate of 0.15 g/kg of body weight per minute. The peak volume of plasma Sb was reached at the end of Sb infusion. The apparent volume of distribution of Sb was computed as 111.63 ± 10.43 mL/kg of body weight and the elimination constant was 0.00888 ± 0.000804 min^{-1}. The $t_{1/2}$ of Sb was 78 minutes and plasma clearance was 0.986 mL/kg of body weight per minute.

Because Sb and suberate, its β-oxidative by-product with eight carbon atoms, were eliminated with urine and because the urinary loss globally accounted for 48.08% of the administered dose, the value of Sb renal clearance was computed to be 0.474 mL/kg of body weight per minute and the constant of renal elimination was 0.00427 min^{-1}.

The 8-hour average pattern of $\dot{V}O_2$ (mL/min, mean ± SD) during the 5 hours of MCT/LCT or Sb infusion and the 3 hours after the end of the infusion period are shown in Figure 5; all values have been normalized for the body surface area of the examined subject. The percentage increase of the value of $\dot{V}O_2$ at the fifth hour of Sb infusion over the basal $\dot{V}O_2$ was 5.41%; however, the difference between the $\dot{V}O_2$ values was not significant. The increase in $\dot{V}O_2$ at the end of MCT/LCT infusion (fifth hour) was 18.66% ($p < .0001$).

The decrease in nonprotein respiratory quotient during MCT/LCT administration was not statistically significant (Fig. 6*A*). Also, the nonprotein respiratory quotient (Fig. 6*B*) gradually but insignificantly decreased

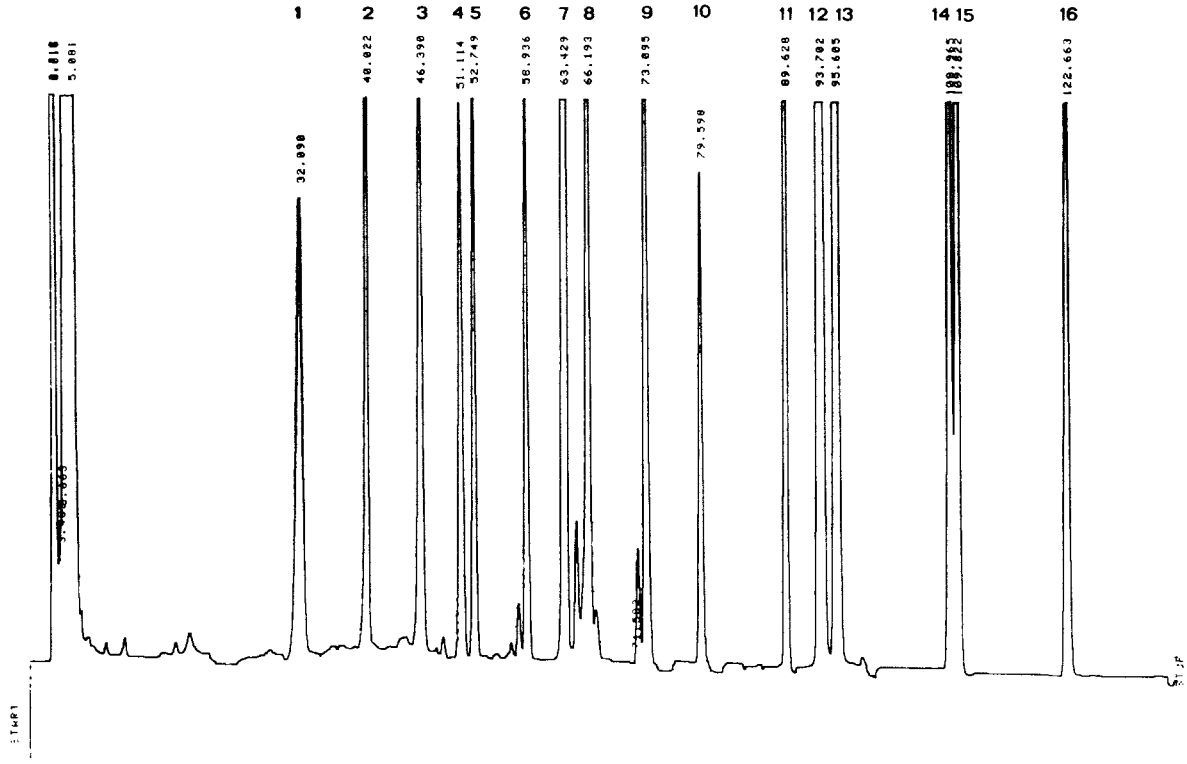

FIG. 1. HPLC separation of a synthetic mixture of monocarboxylic acids and DAs. Conditions are described in "Analytical Procedures." Amount injected was 1 μg of each standard. Peak identification: 1, heptanedioic (pimelic) acid; 2, octanedioic (suberic) acid; 3, octanoic (caprylic) acid; 4, nonanedioic (azelaic) acid; 5, nonanoic acid; 6, decanoic (capric) acid; 7, decanedioic (sebacic) acid; 8, undecanoic acid; 9, dodecanedioic acid; 10, dodecanoic (lauric) acid; 11, tetradecanoic (myristic) acid; 12, *cis*-9-hexadecenoic (palmitoleic) acid; 13, *cis*-9,*cis*-12-octadecadienoic (linoleic) acid; 14, hexadecanoic (palmitic) acid; 15, *cis*-9-octadecenoic (oleic) acid; and 16, octadecanoic (stearic) acid.

from the initial value (0.81 ± 0.041 to 0.79 ± 0.032) during Sb administration, then remained quite constant during the entire period of observation (p = not significant). No change in urea nitrogen excretion in the urine computed according to Long et al[17] was observed in either group of subjects examined. Preliminary studies have shown that no change is produced by the infusion of SB at these rates in the arterial acid-base equilibrium parameters.

The average values of 3-hydroxybutyrate and acetoacetate and those of insulin for both Sb- and MCT/LCT-treated subjects are reported in Figures 7 through 9. Although ketone bodies and insulin did not show any significant increase during or after Sb infusion, MCT/LCT administration caused a significant increase in ketone bodies and insulin.

DISCUSSION

The goal of the present study was to investigate the possible similarities or differences of kinetic and thermogenetic behavior between medium-chain monocarboxylic acids and DAs in humans. We also described a new method for the simultaneous separation and quantification of monocarboxylic and dicarboxylic MCFAs.

The HPLC method for separation and quantification of fatty acids with both medium and long chain length and of medium-chain DAs described in the present paper allows a very good resolution of the different peaks, permitting the simultaneous analysis of free fatty acids and DAs.

Because the pharmaceutical products currently available for nutritional purposes are mixtures of both LCTs and MCTs, it is very important to use a method that permits the analysis of long-chain fatty acids and MCFAs at the same time. In this way, it is possible to perform accurate studies of pharmacokinetics and follow plasma concentrations of MCFAs and long-chain fatty acids over time and, thus, to study their metabolic fate. In the present study, we did not take into account the fate of LCTs, which has been studied extensively elsewhere in the literature.

The purpose of the simple pharmacokinetic model used in the present study is to allow a general comparison to be made between the distribution and metabolic characteristics of the two substrates. It was observed that MCTs and Sb have similar volumes of distribution (approximately 167 *vs* 112 mL/kg of body weight). These volumes of distribution, for a 70-kg man, come out to be about 8 L for Sb and 12 L for MCTs. Although these volumes are substantially greater than that of plasma water, they are also smaller than the whole of plasma water plus interstitial water. Interstitial fluid can be thought of as being composed of several fractions with different exchange rates with plasma, and the time frame of our experiment may not be sufficient to explore the slow interstitial compartments. A simple model like the

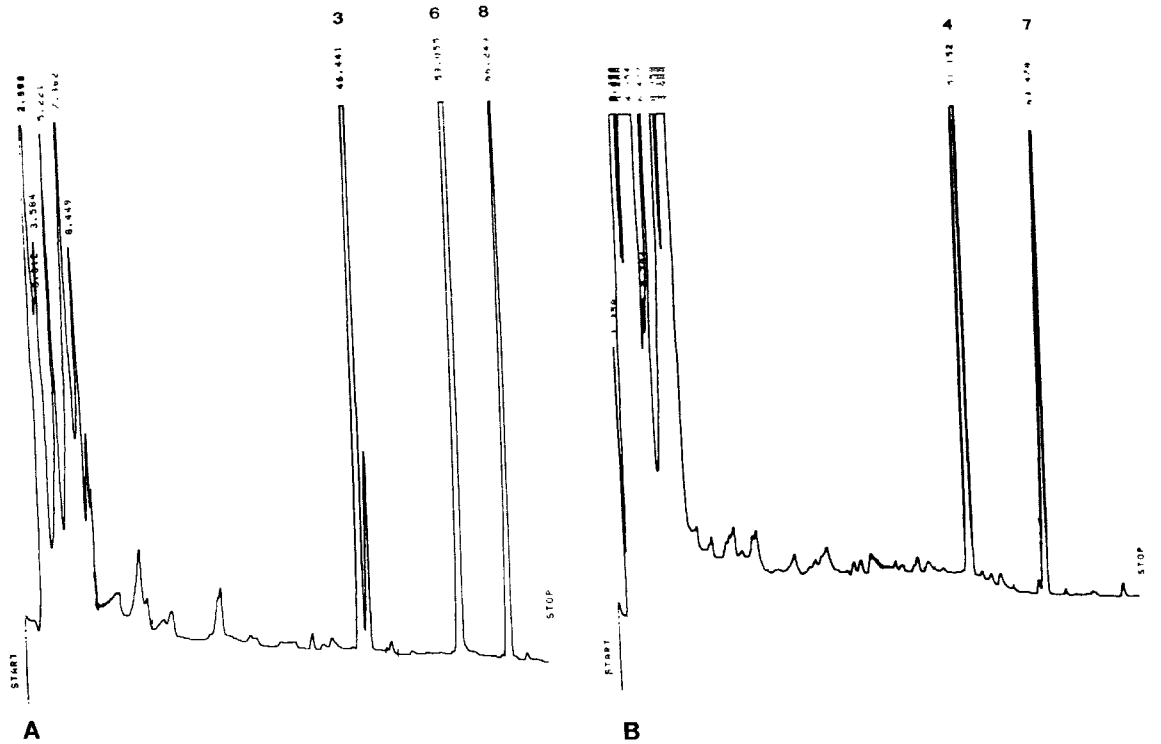

FIG. 2. *A*, HPLC separation of MCFAs from a plasma sample of a volunteer infused with MCT/LCT emulsion. Undecanoic acid was used as an internal standard. For peak identification, see Figure 1. *B*, HPLC separation of medium-chain DAs from a plasma sample of a volunteer infused with Sb solution. Azelaic acid was used as an internal standard. For peak identification, see Figure 1.

one proposed serves to highlight macroscopic differences of behavior between compounds. The $t_{1/2}$ of Sb (78 minutes) is greater than that of either C8 (48 minutes) or C10 (52 minutes). Because MCTs are not directly hydrosoluble, their urinary loss as such is practically absent. On the other hand, the mean urinary loss of Sb during the present regimen of IV infusion was about 48%. Preliminary data have shown that the elimination of Sb in the urine is virtually complete by 6 hours after the end of the administration. It must be surmised that the disposition rate constant associated with Sb is the sum of two components, a urinary loss component (k_e) and another component (k_m) depending on both tissue uptake and intracellular metabolism, so that the urinary loss rate constant is approximately 48% of the global disposition rate constant. In this case, k_m of Sb would equal 0.0045 min^{-1}, or about one third that of MCTs.

From the metabolic point of view, the present study shows an average 19% increase above the basal $\dot{V}O_2$ after 5 hours of MCT/LCT infusion ($p < .005$). In contrast, Sb produced a very small increase in $\dot{V}O_2$—approximately 5% (not significant). In this study, no independent estimate of Sb oxidation rate could be obtained and the formulas generally used to compute the metabolic rate from $\dot{V}CO_2$ and $\dot{V}O_2$ were not strictly applicable. For this reason, all results have simply been espressed in terms of $\dot{V}O_2$.

Seaton et al[5] observed a 12% increase in $\dot{V}O_2$ after oral ingestion of 48 g of MCT oil and a 4% increase after ingestion of an equicaloric amount of LCT oil. Hill et al[7] also found a significant thermic response to food after oral administration of MCTs. Weissman et al[6] demonstrated that a continuous IV infusion of an MCT-enriched mixture containing 56% MCTs and 44% LCTs causes a significant (12%) increase in $\dot{V}O_2$ similar to that obtained with an oral bolus.

Our data on $\dot{V}O_2$ modifications after MCT/LCT IV infusion thus agree with those reported in the literature, although we found a greater increase in $\dot{V}O_2$ than other authors,[5-7] probably because of the larger amounts of MCTs we administered. Sb administration, in contrast, did not produce a significant elevation of $\dot{V}O_2$, in agreement with the theoretical estimates of the obligatory thermic effect of this compound computed at about 3% of the calories introduced.[18]

As expected, MCT/LCT infusion caused a relevant increase in serum ketone bodies, which remained elevated up to the last sampling point. Sb did not produce any alteration in the blood level of ketones.

The increase in serum insulin concentration after MCT/LCT infusion was of the same order of magnitude as that reported after MCT ingestion.[5,19] Again, Sb infusion did not modify either plasma insulin or glucose levels, suggesting that its metabolism is insulin-independent.

It is well known that IV MCT-containing lipid emulsions, like oral MCTs, increase serum ketones and insulin levels.[4,7,20] The only data available in the literature concerning IV administration of pure MCT emulsion are those of Guisard and Debry,[7] who infused 0.12 g of 100%

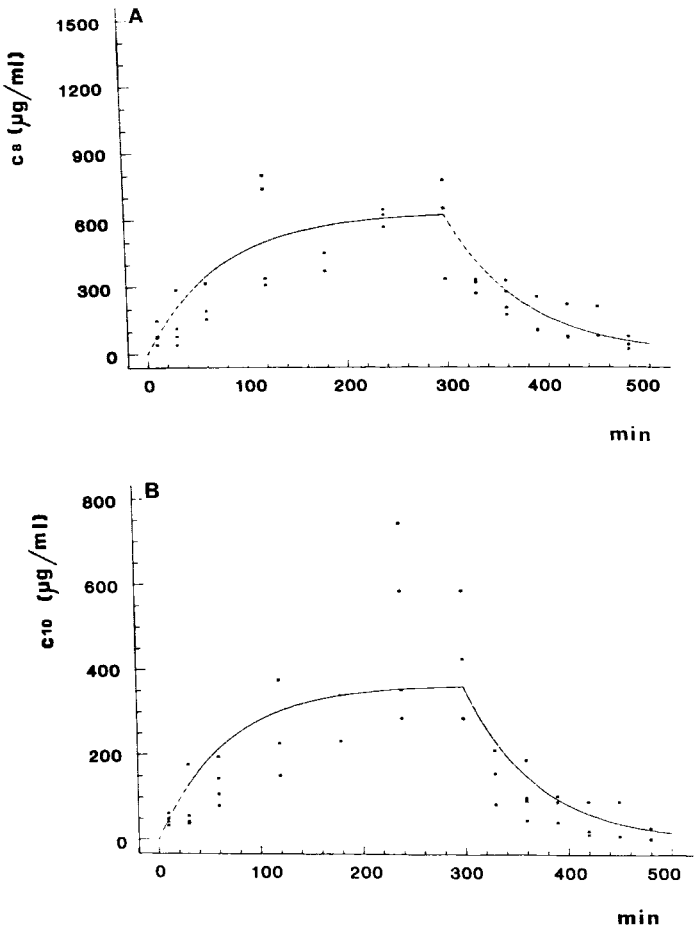

FIG. 3. Computer best fit (line) of experimental concentration values (micrograms per milliliter, squares) of octanoic (C8) (*A*) and decanoic (C10) acid (*B*) obtained by hydrolysis of plasma MCTs *vs* time.

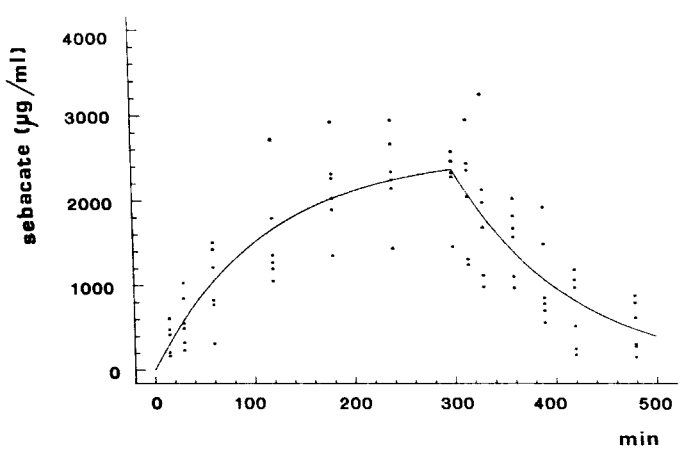

FIG. 4. Modal prediction of Sb plasma concentration *vs* time (line) and experimental data of Sb plasma concentration (squares).

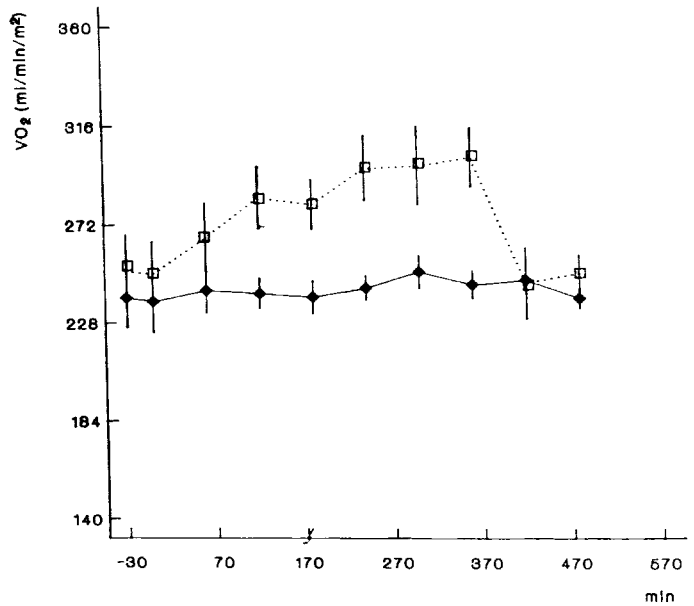

FIG. 5. $\dot{V}O_2$ values (milliliters per minute) are shown before MCT/LCT (dotted line) or Sb (solid line) administration, during the 5-hour constant infusion and during the 3 hours after the end of the infusion. Each point represents the mean ± SD of the values measured each minute for 30 minutes every hour.

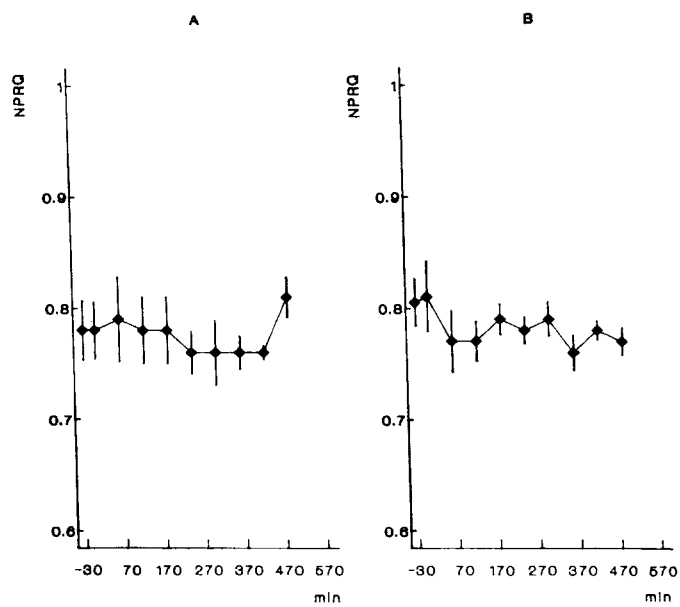

FIG. 6. Nonprotein respiratory quotient (NPRQ; mean ± SD) before, during, and after MCT/LCT (*A*) or Sb (*B*) infusion. As for $\dot{V}O_2$, each point represents the mean value of the measurements obtained each minute for 30 minutes every hour during the study period.

MCTs per kilogram over 1 hour; this study also showed a large increase in ketone bodies associated with the related clinical status.

It is therefore conceivable that the changes in blood ketone body concentration and serum insulin levels that we found are caused by the MCT component of the infusion and not by LCTs.

Ketone bodies affect the insulin-glucose balance by increasing insulin delivery. Baba et al[22] suggested that MCT-induced hyperketonemia may stimulate brown adipose tissue activity. This is in accordance with the fact that acetoacetate stimulates high respiratory rates in brown adipose tissue.[23] Thus, Berry et al[24] suggested that the elevated thermogenesis found after MCT administration could be explained by an energy consumption proc-

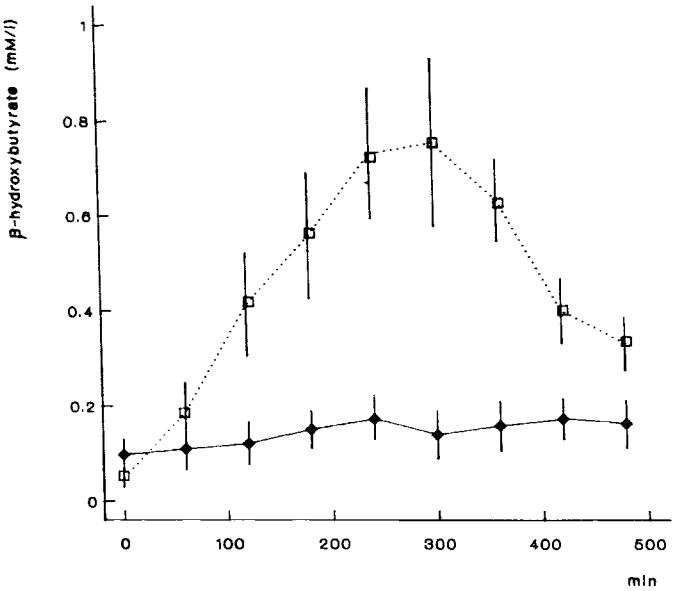

FIG. 7. Mean ± SD of plasma β-hydroxybutyrate (millimoles per liter) in 10 volunteers infused with MCT/LCT (dotted line) or Sb (solid line).

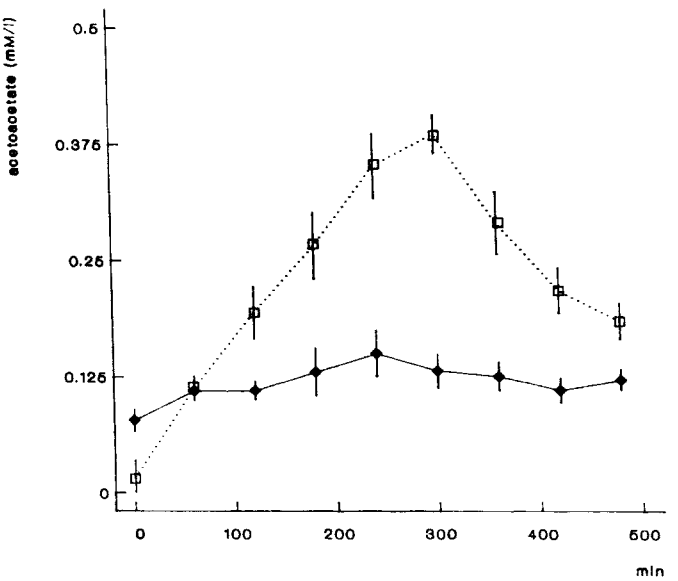

FIG. 8. Mean ± SD of plasma acetoacetate (millimoles per liter) in 10 volunteers infused with MCT/LCT (dotted line) or Sb (solid line).

ess, uncoupled with adenosine triphosphate synthesis in the presence of hyperketonemia.

Inasmuch as volumes of distribution are similar between MCTs and Sb, the main difference between monocarboxylic acids and DAs seems to be the high urinary loss of the latter. Moreover, it has been shown that both monocarboxylic acids and DAs undergo intramitochondrial and peroxysomal oxidation at comparable rates.[13–15] In previous work, we observed the urinary loss of azelate (dicarboxylic with nine carbon atoms) to be approximately 70% of the administered dose. With Sb, urinary loss decreased to 48%. Preliminary data suggest that dodecanedioic acid (dicarboxylic with 12 carbon

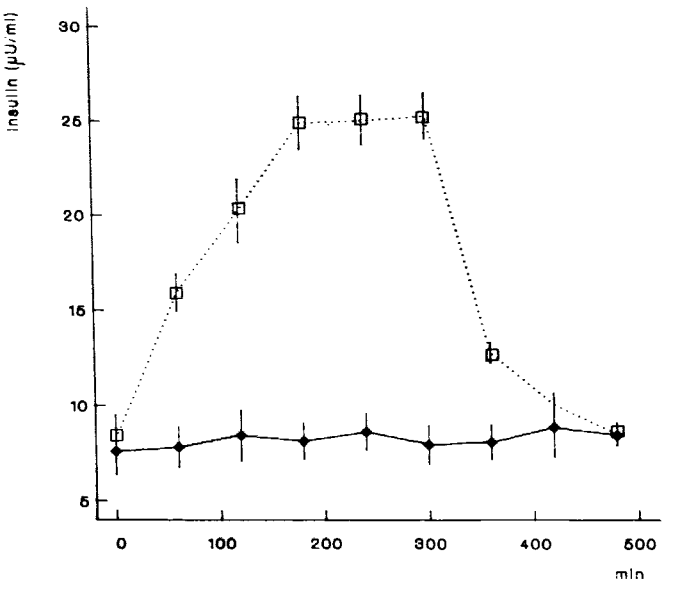

FIG. 9. Mean ± SD of serum insulin (microunits per milliliter) in 10 volunteers infused with MCT/LCT (dotted line) or Sb (solid line).

atoms) has a urinary loss as low as 5% in humans. It is therefore conceivable that either simple DAs or some chemically modified form thereof might in the near future be of interest for the nutrition support of the metabolically impaired patient.

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