Leucine metabolism in preterm infants receiving parenteral nutrition with medium-chain compared with long-chain triacylglycerol emulsions[1–3]

Jean-Michel Liet, Hugues Piloquet, Julio S Marchini, Pascale Maugère, Christine Bobin, Jean-Christophe Rozé, and Dominique Darmaun

ABSTRACT

Background: Although medium-chain triacylglycerols (MCTs) may be utilized more efficiently than long-chain triacylglycerols (LCTs), their effect on protein metabolism remains controversial.

Objective: The aim of the study was to compare the effects of mixed MCT-LCT and pure LCT emulsions on leucine metabolism in preterm infants.

Design: Fourteen preterm [gestational age: 30 ± 1 wk; birth weight: 1409 ± 78 g ($\bar{x}$ ± SE)] neonates were randomly assigned to receive, from the first day of life, either a 50:50 MCT-LCT (mixed MCT group; n = 7) or an LCT (LCT group; n = 7) lipid emulsion as part of an isonitrogenous, isoenergetic total parenteral nutrition program. On the fourth day, infants received intravenous feeding providing 3 g lipid, 15 g glucose, and 3 g amino acids $\cdot kg^{-1} \cdot d^{-1}$ and underwent *1*) indirect calorimetry and *2*) a primed, 2-h infusion of $H^{13}CO_3Na$ to assess the recovery of ^{13}C in breath, immediately followed by *3*) a 3-h infusion of L-[1-^{13}C]leucine.

Results: The respiratory quotient tended to be slightly but not significantly higher in the mixed MCT than in the LCT group (0.96 ± 0.06 compared with 0.93 ± 0.03). We did not detect a significant difference between the mixed MCT and LCT groups with regard to release of leucine from protein breakdown (*B*; 309 ± 40 compared with 257 ± 46 $\mu mol \cdot kg^{-1} \cdot h^{-1}$) and nonoxidative leucine disposal (NOLD; 296 ± 36 compared with 285 ± 49 $\mu mol \cdot kg^{-1} \cdot h^{-1}$). In contrast, leucine oxidation was greater in the mixed MCT than in the LCT group (113 ± 10 compared with 67 ± 10 $\mu mol \cdot kg^{-1} \cdot h^{-1}$; P = 0.007). Net leucine balance (NOLD − *B*) was less positive in the mixed MCT than in the LCT group (−14 ± 9 compared with 28 ± 10 $\mu mol \cdot kg^{-1} \cdot h^{-1}$; P = 0.011).

Conclusion: Mixed MCTs may not be as effective as LCT-containing emulsions in promoting protein accretion in parenterally fed preterm neonates. *Am J Clin Nutr* 1999;69:539–43.

KEY WORDS Parenteral nutrition, protein metabolism, preterm infants, [^{13}C]leucine, [^{13}C]bicarbonate, lipid emulsions, stable isotopes, energy substrates, medium-chain triacylglycerols, long-chain triacylglycerols

INTRODUCTION

Over the first few weeks of life, preterm infants are faced with the challenging task of doubling their body weight (1), at a time when they have a high risk of developing sepsis as well as other severe diseases associated with protein wasting. In that context of accelerated growth and intense stress, accretion of body protein is a major goal of nutrition. Because the gastrointestinal system of prteterm infants is immature, the bulk of nutrients must be supplied intravenously, at least for the first several weeks.

Because lipid emulsions are more energy dense and potentially as effective as glucose for protein accretion (2), intravenous lipid emulsions are increasingly used in preterm infants receiving total parenteral nutrition (TPN). Compared with the conventional long-chain triacylglycerols (LCTs), medium-chain triacylglycerols (MCTs) have potential benefits (3) because they may *1*) be more rapidly cleared from plasma, *2*) enter liver mitochondria without the need for carnitine-mediated transport, and *3*) preserve immune function better than do LCTs (4).

Studies performed in animals (5) and healthy adult humans (6), however, suggest that MCT emulsions may not be as effective as LCT emulsions in promoting protein deposition. The aim of this study was therefore to determine whether, when administered as part of an isonitrogenous, isoenergetic TPN regimen, MCTs have the same protein-sparing effect as LCT-containing emulsions in preterm neonates.

SUBJECTS AND METHODS

Materials

Purchased lots of L-[1-^{13}C]leucine and $H^{13}CO_3Na$ (both 99% ^{13}C; from Tracer Technologies, Somerville, MA, and Cambridge Isotope Laboratories, Woburn, MA, respectively) were tested for chemical, isotopic, and optical purity by gas chromatography–mass

[1] From the Division of Neonatology, Hôpital Mère-Enfant, CHU de Nantes, and Centre de Recherche en Nutrition Humaine, Nantes, France.

[2] Supported in part by grants from Baxter/Clintec; the Fondation pour la Recherche Médicale, Paris; the Conseil Général de Loire-Atlantique; the City of Nantes; and the Région des Pays-de-la-Loire.

[3] Address reprint requests to D Darmaun, Centre de Recherche en Nutrition Humaine, Hotel-Dieu Hospital, 44093 Nantes cedex 1, France. E-mail: ddarmaun@nantes.inserm.fr.

Received June 19, 1998.

Accepted for publication August 26, 1998.

spectrometry (GC-MS) or GC–isotope ratio MS (GC-IRMS). Tracer solutions were prepared in sterile, 0.45%-saline solution under a laminar flow hood and verified to be sterile (plate culture) and pyrogen free (*Limulus* lysate assay). Infusates were passed through a 0.22-μm Millipore filter (Bedford, MA) and stored in sterile containers at 4 °C for <24 h until used.

Subjects

Written, informed consent was obtained from the parents of 14 neonates before enrollment and after the purpose and potential risks of the study had been fully explained to them, according to procedures approved by the Ethical Committee of the University Hospital of Nantes, France (CCPPRB no. 2, Région des Pays-de-Loire). Subjects were recruited from the neonatal intensive care unit at Hôpital Mère-Enfant, Nantes. Patients were excluded if they had major surgery, were considered to be near death, required an inspired air oxygen fraction (FiO_2) >50% or had an elevated C-reactive protein concentration or other evidence of infection, a decreased platelet count, or bilirubin concentration >150 mg/L.

Nutritional regimen

In both groups, parenteral nutrition was started on the first day of life. Glucose was started at ≈5 $mg \cdot kg^{-1} \cdot min^{-1}$ (≈7 $g \cdot kg^{-1} \cdot d^{-1}$), and rapidly increased as tolerated up to ≈15 $g \cdot kg^{-1} \cdot d^{-1}$. Parenteral amino acids (Primène-10%; Baxter/Clintec, Maurepas, France) were started on day 1 (≈1 $g \cdot kg^{-1} \cdot d^{-1}$) and increased by 1 $g \cdot kg^{-1} \cdot d^{-1}$ to reach 3 $g \cdot kg^{-1} \cdot d^{-1}$ by day 3. Parenteral lipids were started on day 2 at ≈1 $g \cdot kg^{-1} \cdot d^{-1}$. In a double-blind fashion, patients were randomly assigned to receive either an LCT emulsion (LCT group: Ivelip-20%; Baxter/Clintec) or a 50:50 MCT-LCT emulsion (mixed MCT group: Médialipide-20%; Braun, Boulogne, France). Lipids were increased at a rate of 1 $g \cdot kg^{-1} \cdot d^{-1}$ to reach 3 $g \cdot kg^{-1} \cdot d^{-1}$ by day 3. None of the infants received any enteral nutrition until after completion of the isotope infusion study on day 4 of life.

Protocol for isotope infusion

The isotopic study was performed on day 4 of life in a total of 13 infants in the fed state (6 in the mixed MCT group, 7 in the LCT group) while infants were receiving continuous intravenous nutrition through a central venous catheter. Amino acids and glucose were administered as a mixture through a single syringe pump, whereas the lipid solution was administered through a separate pump. Because some of the babies studied had received ventilatory assistance, they had an arterial line in place as well. In the babies who did not have an arterial line in place at the time of the study, a butterfly needle was inserted in a hand vein to sample arterialized venous blood.

At 0800 on the isotope study day, measurement of respiratory gas exchanges was started and continued throughout the study until 1600 by using an indirect calorimeter as described previously (7, 8). At 1030 a baseline arterial blood sample (0.5 mL) was obtained for measurement of background isotopic enrichment in plasma α-ketoisocaproate (KIC). Three 1-min collections of expired air were obtained for determination of background $^{13}CO_2$. For babies who were receiving ventilatory assistance, expired air was collected from the exhaust of the ventilator into a 10-L Douglas bag. For babies who were breathing spontaneously under a hood, expired air was collected from the outlet of the ventilated canopy. Triplicate aliquots of expired air from each sampling time point were then immediately transferred with a syringe into evacuated tubes for later analysis.

Two stable-isotope infusions were carried out consecutively on the same day in each infant. First, a primed, continuous 2-h infusion (7.5 μmol/kg and 5 $\mu mol \cdot kg^{-1} \cdot h^{-1}$) of $H^{13}CO_3Na$ was performed from 1100 to 1300, ie, from time 0 to 120 min. The purpose of the first isotope infusion was to estimate the rate of total carbon dioxide production and the rate of recovery of ^{13}C in breath from the appearance of ^{13}C in expired air carbon dioxide. The labeled bicarbonate infusion was immediately followed by a primed, continuous 3-h infusion (15 μmol/kg and 15 $\mu mol \cdot kg^{-1} \cdot d^{-1}$) of L-[1-^{13}C]leucine from 1300 to 1600 (ie, from 120 min to 300 min), designed to assess leucine kinetics.

Blood samples (0.5 mL) were drawn from the arterial catheter to determine plasma concentrations and enrichments of KIC at 1500, 1530, and 1600, ie, at 240, 270, and 300 min. The total volume of blood sampled was therefore ≈2 mL, which is <5% of blood volume in a 1000-g infant. Expired air samples were obtained at 15-min intervals between 1200 and 1300 and between 1500 and 1600, ie, during the last hour of labeled bicarbonate and labeled leucine infusion, respectively.

Analytic methods

Known amounts of α-ketocaproate were added to each 100-μL aliquot of plasma to serve as an internal standard for measurement of KIC concentration by reverse isotope dilution. KIC was isolated from 100 μL plasma by passing the acidified plasma sample over an AG50 cation exchange column (Bio-Rad; Richmond, CA). To each KIC-containing fraction, 3 drops of 10 mol NaOH/L and 200 μL 0.36 mol hydroxylamine HCl/L were then added and samples were incubated at 60 °C for 30 min to produce an oxime derivative. Samples were then cooled immediately on ice, acidified with 2 mol HCl/L, and mixed with 1 mL supersaturated ammonium sulfate. KIC was extracted twice by shaking after adding 8 mL ethylacetate. The supernate was then dried under nitrogen gas. Fifty microliters *N*-methyl-*N*-(*t*-butyldimethylsilyl)-trifluoroacetamide was added to each dry sample and incubated for 24–36 h at room temperature to obtain an oxime-*t*-butyldimethylsilyl (oxime-TBDMS) KIC derivative. This modified method enhanced the sensitivity of the KIC assay, allowing us to use smaller volumes of plasma than for the previously described TBDMS derivative (9).

Isotopic enrichments in plasma KIC were determined by selected ion monitoring GC-MS (MSD 5970; Hewlett-Packard, Palo Alto, CA). Ions at mass-to-charge ratios of 316 and 317, representing the prominent ions of natural KIC and [^{13}C]KIC, respectively, were selectively monitored.

Expired air $^{13}CO_2$ enrichment was measured by GC-IRMS using a PoraPLOT-Q capillary column (Chrompack, Middelburg, Netherlands) in a Hewlett-Packard (model 5890) gas chromatograph connected online to a Finnigan Delta-S (Finnigan-MAT, Bremen, Germany) isotope ratio mass spectrometer.

Calculations

The fractional recovery of bicarbonate in breath ($FRCO_2$) was calculated on the basis of the excretion of $^{13}CO_2$ in expired air over the course of the intravenous infusion of $H^{13}CO_3Na$ as follows:

$$FRCO_2 = \dot{V}CO_2 \times E_{bicarb}CO_2/i_{bicarb} \quad (1)$$

TABLE 1
Infants' characteristics and total parenteral nutrition (TPN) intake on the day of study[1]

Study group	Gestational age	Birth weight	Ventilatory status[2]	TPN glucose	TPN lipid	TPN amino acids
	wk	*g*		$g \cdot kg^{-1} \cdot d^{-1}$	$g \cdot kg^{-1} \cdot d^{-1}$	$g \cdot kg^{-1} \cdot d^{-1}$
Mixed MCT (n = 7)	29 ± 0.7	1283 ± 99	MV: 2 SO: 1 RA: 4	15 ± 0.4	3.0 ± 0.1	2.9 ± 0.1
LCT (n = 7)	31 ± 0.4	1432 ± 91	MV: 5 SO : 0 RA: 2	16 ± 0.4	3.1 ± 0.1	3.0 ± 0.1

[1] $\bar{x}$ ± SE. MCT, medium-chain triaclyglycerol emulsion; LCT, long-chain triacylglycerol emulsion.
[2] MV, mechanical ventilation; SO, supplemental oxygen (expired air oxygen fraction of 32% in one patient); RA, room air with no supplemental support.

where $\dot{V}CO_2$ ($\mu mol \cdot kg^{-1} \cdot h^{-1}$) is the total rate of carbon dioxide production (measured by indirect calorimetry), $E_{bicarb}CO_2$ is the steady state enrichment in expired air of $^{13}CO_2$ during the last hour (1000–1100) of the $H^{13}CO_3Na$ infusion and i_{bicarb} ($\mu mol \cdot kg^{-1} \cdot h^{-1}$) is the rate of $H^{13}CO_3Na$ infusion. The concentration of labeled bicarbonate (i_{bicarb}) in the infusate was determined in a fresh aliquot of the infusate by reverse isotope dilution with GC-IRMS using unlabeled sodium carbonate as an internal standard, as described previously (10).

^{13}C-Labeled bicarbonate infusion can be used to estimate $\dot{V}CO_2$ by isotope dilution as well. The appearance rate of carbon dioxide (R_aCO_2) was calculated as follows:

$$R_aCO_2 = i_{bicarb}CO_2 [(ECO_2/E_{bicarb}CO_2) - 1] \quad (2)$$

as shown by us (10) and others (3), and

$$R_aCO_2 = \dot{V}CO_2/FRCO_2 \quad (3)$$

where $FRCO_2$ is the fractional recovery of $^{13}CO_2$ in breath. When labeled bicarbonate is infused, the recovery of ^{13}C in expired air is usually < 100%. R_aCO_2 therefore usually exceeds $\dot{V}CO_2$ determined by indirect calorimetry.

Leucine appearance

R_a ($\mu mol \cdot kg^{-1} \cdot h^{-1}$) into the plasma compartment was calculated as

$$R_a = i_{Leu} [(E_i/E_p) - 1] \quad (4)$$

where i_{Leu} is the rate of [^{13}C]leucine infusion ($\mu mol \cdot kg^{-1} \cdot h^{-1}$) and E_i and E_p are the ^{13}C enrichments (mol % excess) in the infusate leucine and in plasma KIC, respectively.

Because leucine kinetics was measured under fed conditions, both exogenous (leucine from parenteral nutrition; PN_{Leu}) and endogenous leucine contributed to leucine R_a (flux). Because leucine is an essential amino acid, release from protein breakdown (B) is the only endogenous source of leucine; it was therefore calculated by subtracting PN_{Leu} intake from total leucine R_a: $B = R_a - PN_{Leu}$. Leucine oxidation (Ox, $\mu mol \cdot kg^{-1} \cdot h^{-1}$) was calculated as

$$Ox = \dot{V}CO_2 \times E_{Leu}CO_2 \times [(1/E_p) - (1/E_i)]/FRCO_2 \quad (5)$$

where $E_{Leu}CO_2$ is $^{13}CO_2$ enrichment in expired air over the last hour of L-[1-^{13}C]leucine infusion (1500–1600).

Nonoxidative leucine disposal (NOLD), an index of whole-body protein synthesis, was calculated as NOLD = R_a − Ox. Finally, net leucine balance, an index of the net protein leucine gain, was calculated as NOLD − B.

Statistics

Results are expressed as means ±SEs. Comparisons between groups were performed by using two-tailed, unpaired Student's t tests (11).

RESULTS

Selected relevant clinical variables for the population studied, as well as the babies' nutritional intake on day 4, ie, on the day of the isotopic study, are given in **Table 1**. We detected no significant differences between the groups for birth weight or gestational age.

Both groups were heterogeneous for ventilatory status; they included babies who were breathing spontaneously as well as others who received mechanical ventilation. Because of the small numbers of babies included, no significant difference in ventilatory status was detected between groups. None of the babies, however, received an FiO_2 >36%; the average FiO_2 was 23.7 ± 1.6% in the mixed MCT group compared with 24.7 ± 2.3% in the LCT group (NS). Among the babies who were breathing spontaneously on the day of study (day 4 of life), 2 babies (1 in each group) had received mechanical ventilation before the study; they had, however, been weaned from the ventilator ≥48 h before the isotope infusion. None of the patients was receiving continuous nasal positive airway pressure. All the infants had a blood pH >7.25 and were in a relatively stable condition. None of them had received any dopamine, insulin, theophylline, or sedatives. One patient in the mixed MCT group was receiving caffeine.

Neither $\dot{V}O_2$ (9.1 ± 1.9 compared with 9.0 ± 2.4 $mL \cdot kg^{-1} \cdot min^{-1}$ in the mixed MCT compared with the LCT group; P = 0.85) nor $\dot{V}CO_2$ (8.5 ± 2.0 compared with 8.4 ± 1.8 $mL \cdot kg^{-1} \cdot min^{-1}$; P = 0.92) differed significantly between the groups. Respiratory quotient was not significantly different in mixed MCT compared with LCT group (0.96 ± 0.14 compared with 0.93 ± 0.09; P = 0.64).

Near steady state (as defined by a CV <10% over the sampling period) was achieved in breath $^{13}CO_2$ and plasma [^{13}C]KIC over the last hour of labeled bicarbonate infusion and [^{13}C]leucine infusion (**Figure 1**): the equations for steady state described in the methods section were therefore used to quantitate carbon dioxide recovery and leucine kinetics.

$FRCO_2$, as determined from the excretion of $^{13}CO_2$ at the end of the labeled bicarbonate infusion, was 81.9 ± 14.4% compared with 85.9 ± 24.9% (P = 0.56) in the mixed MCT and LCT groups, respectively. $^{13}CO_2$ recovery did not correlate with gestational age, birth weight, or $\dot{V}CO_2$. When the groups were pooled together, the overall mean $^{13}CO_2$ recovery was 83.9%.

TABLE 2
Estimation of carbon dioxide production by use of [^{13}C]bicarbonate infusion and indirect calorimetry in preterm neonates receiving total parenteral nutrition with medium-chain (MCT) or long-chain (LCT) triacylglycerol emulsions[1]

Study group	Indirect calorimetry	[^{13}C]bicarbonate infusion	Corrected [^{13}C]bicarbonate infusion
		mL · kg^{-1} · min^{-1}	
Mixed MCT	8.5 ± 0.7	10.0 ± 1.2	8.4 ± 1.0
LCT	8.4 ± 0.7	9.9 ± 0.3	7.7 ± 0.4

[1] $\bar{x}$ ± SE; 6 or 7 infants in each group.
[2] Corrected for an assumed recovery of ^{13}C in breath of 83.9%.

The values of R_aCO_2, as determined by using isotope dilution of labeled bicarbonate, and $\dot{V}CO_2$, determined by using indirect calorimetry, are listed in **Table 2**. As expected, because the fractional recovery of ^{13}C in breath is always < 1, R_aCO_2 exceeded $\dot{V}CO_2$. When a mean recovery of 83.9% was used to "correct" the measured R_aCO_2, however, the values obtained were not significantly different from those measured using indirect calorimetry (Table 2).

Leucine appearance rate and leucine release from protein breakdown tended to be slightly, but not significantly, higher in the mixed MCT than in the LCT group (**Table 3**). Leucine oxidation was ≈67% higher in the mixed MCT group than in the LCT group, whereas NOLD, an index of whole-body protein synthesis, was not significantly different between groups. As a consequence, net leucine balance (NOLD − *B*), an index of net protein gain, was negative in 4 of 6 babies receiving mixed MCTs, whereas it was positive in 6 of 7 babies receiving LCTs; overall, NOLD − *B* differed significantly between the groups (Table 3).

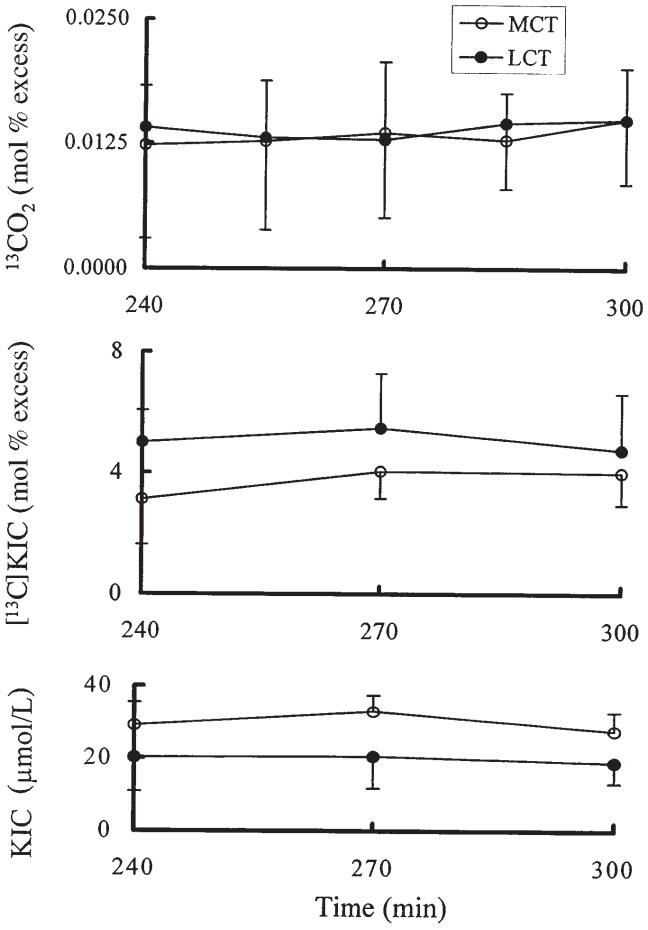

FIGURE 1. Time course of plasma α-ketoisocaproate (KIC) concentration (bottom panel), plasma [^{13}C]KIC enrichment (middle panel), and breath $^{13}CO_2$ enrichment (top panel) over the last 60 min of L-[1-^{13}C]infusion in preterm infants receiving parenteral nutrition with medium-chain (mixed MCT group) or long-chain (LCT group) triacylglycerol emulsions. Each point represents the mean ± SD of measurements performed in 6–7 infants.

DISCUSSION

To our knowledge, the current study is the first to show that in preterm infants receiving TPN on the fourth day of life, whole-body leucine oxidation was higher and net leucine balance lower when parenteral lipid was supplied as a mixture of MCTs and LCTs rather than as pure LCTs. Assessment of leucine oxidation using infusion of [^{13}C]leucine relies on numerous assumptions (12) because it is based on the determination of labeled carbon dioxide excretion in expired air. Because of the differences in ^{13}C abundance in various nutrients, infusion of unlabeled nutrients (eg, dextrose derived from corn starch) affects baseline $^{13}CO_2$ abundance in breath, and it takes ≥4 h for breath ^{13}C to reach steady state after intravenous infusion of natural dextrose is initiated (13). Because tracer infusion was started ≈16 h after the daily change of TPN bags, baseline $^{13}CO_2$ concentrations were, in fact, stable in our patients and did not differ between the groups (data not shown).

In addition, the calculation of leucine oxidation assumes that the recovery of labeled carbon dioxide in breath is known. The latter is known to rise in the transition from the fasting to the fed state (14), to correlate with rates of energy expenditure (15), and to depend on the route of tracer delivery (14). Carbon dioxide recovery is unlikely to be consistent from one patient to the next in preterm neonates who experience rapid growth and various degrees of stress. Therefore, in the current study we used an approach initially proposed by Van Goudeover et al (16, 17) to quantitate the recov-

TABLE 3
Leucine kinetics in preterm neonates receiving total parenteral nutrition with medium-chain (MCT) or long-chain (LCT) triacylglycerol emulsions[1]

Study group	PN_{Leu}	R_a	*B*	Ox	NOLD	NOLD − *B*
			μmol · kg^{-1} · h^{-1}			
Mixed MCT	98.5 ± 4.0	408.3 ± 27.7	309.3 ± 30.1	112.8 ± 8.2	295.6 ± 26.7	−13.8 ± 7.7
LCT	95.4 ± 0.7	352.0 ± 46.6	256.6 ± 46.0	67.4 ± 10.2[2]	284.6 ± 48.8	28.0 ± 10.3[3]

[1] $\bar{x}$ ± SE; 6 or 7 infants in each group. PN_{Leu}, leucine in parenteral nutrition; R_a, rate of leucine appearance; *B*, breakdown rate; Ox, oxidation rate; NOLD, nonoxidative leucine disposal.
[2,3] Significantly different from mixed MCT (*t* test): [2] $P = 0.007$, [3] $P = 0.011$.

ery of labeled carbon dioxide in each individual neonate on the same day that [^{13}C]leucine kinetics was determined. We therefore believe that the difference in leucine oxidation between the groups cannot be accounted for by methodologic errors.

In vitro studies consistently show inhibition of branched-chain ketoacid dehydrogenase (3-methyl-2-oxobutanoate dehydrogenase; EC: 1.2.4.4), the key enzyme for leucine oxidation, by palmitate, a long-chain fatty acid. In contrast, octanoate, a medium-chain fatty acid, may activate the decarboxylation of branched-chain keto acids under specific conditions in rat or human muscle (18–20). It is tempting to speculate that the same mechanism may operate in vivo in TPN-fed preterm neonates.

Conflicting data have appeared in the literature with regard to the compared effects of MCTs and LCTs on the preservation of body protein. Nitrogen balance was less negative when critically ill adults admitted to an intensive care unit received for 6 d TPN containing MCTs compared with LCT emulsions (21). Similarly, there was a trend toward an improved nitrogen balance in adult patients undergoing major elective surgery of the gastrointestinal tract (22) who received 10 d of MCT-containing TPN, compared with LCTs. However, no difference was observed in rates of urea production and protein breakdown between MCT- and LCT-based emulsions within 12 h of initiation of TPN in critically ill patients (23). Finally, the lesser anabolic effect of MCT in the current study is consistent with earlier studies carried out in dogs (5) and healthy adult humans (6). Both of these studies, which involved the determination of leucine metabolism by tracer methods, documented a higher rate of leucine oxidation during short-term infusion of MCT compared with LCT emulsions. To our knowledge, the current study is the first to compare the protein anabolic effects of MCTs and LCTs in a population of premature neonates. NOLD $-$ *B*, the difference between leucine released from protein breakdown and leucine utilization for protein synthesis, was positive in the LCT group, whereas it was not in the mixed MCT group. Extrapolation from the current data must, however, be done with caution. Because leucine metabolism was assessed on a single occasion on the fourth day of life, it cannot be ascertained from the data whether differences in leucine kinetics would persist after longer exposure to the same doses or to different doses of MCTs. In summary, the higher rate of leucine oxidation and less positive leucine balance observed with MCTs than with LCTs suggest that intravenous MCTs may not be as effective as LCTs in promoting protein deposition in preterm infants receiving TPN in the first few days of life.

We thank the nursing staff of the Neonatology Unit at Hôpital Mère-Enfant for their superb care of the infants, Odile Desfontaines and Isabelle Grit for their excellent technical assistance, Philippe Mauran for dispensing the fat emulsions, and Alain Mouzard and Michel Krempf for their support and advice in performing these demanding studies.

REFERENCES

1. Micheli JL, Schutz Y, Jéquier E. Protein metabolism of the newborn. In: Plin RA, Fow WW, eds. Fetal and neonatal physiology. Philadelphia: WB Saunders, 1992:462–76.
2. Jeejeebhoy KN, Anderson GH, Nakooda AF, Greenberg GR, Sanderson I, Marliss EB. Metabolic studies in total parenteral nutrition with lipid in man. J Clin Invest 1976;57:125–36.
3. Klein S, Miles JM. Metabolic effects of long-chain and medium-chain triglyceride emulsions in humans. JPEN J Parenter Enteral Nutr 1994;18:396–7.
4. Miles JM. Intravenous fat emulsion in nutrition support. Curr Opin Gastroenterol 1991;7:306–11.
5. Rodriguez N, Schwenk WF, Beaufrère B, Miles JM, Haymond MW. Trioctanoin infusion increases in vivo leucine oxidation: a lesson in isotope modelling. Am J Physiol 1986;251:E343–8.
6. Beaufrère B, Chassard D, Broussole C, Riou JP, Beylot M. Effects of D-β-hydroxybutyrate and long- and medium-chain triglycerides on leucine metabolism in humans. Am J Physiol 1992;262:E268–74.
7. Rozé JC, Chambille B, Dehan M, Gaultier C. Measurement of oxygen uptake in newborn infants during assisted and spontaneous ventilation. Respir Physiol 1994;98:227–33.
8. Rozé JC, Chambille B, Fleury MA, Debillon T, Gaultier C. Oxygen cost of breathing in newborn infants with long term ventilatory support. J Pediatr 1995;127:984–7.
9. Darmaun D, Roig JV, Auestad N, Sager BK, Neu J. Glutamine metabolism in very low birthweight infants. Pediatr Res 1997;41:391–6.
10. Spear ML, Darmaun D, Sager BK, Parsons WR, Haymond MW. Use of [^{13}C]bicarbonate infusion for measurement of CO_2 production. Am J Physiol 1995;268:E1123–7.
11. Zar JH. Biostatistical analysis. 2nd ed. Englewood Cliffs, NJ: Prentice-Hall, 1984.
12. Abumrad NN, Darmaun D, Cynober LA. Approaches to studying amino acid metabolism: from quantitative assays to flux assessment using stable isotopes. In: Cynober LA, ed. Amino acid metabolism and therapy in health and nutritional disease. Boca Raton, FL: CRC Press, 1995:15–30.
13. Robert JJ, Koziet J, Chauvet D, Darmaun D, Desjeux JF, Young VR. Use of ^{13}C-labeled glucose for estimating glucose oxidation: some design considerations. J Appl Physiol 1987;63:1725–32.
14. Hoerr RA, Yu Y, Wagner DA, Burke JF, Young VR. Recovery of ^{13}C in breath from $NaH^{13}CO_3$ infused by gut and vein: effect of feeding. Am J Physiol 1989;257:E426–38.
15. Van Aerde JEE, Sauer PJJ, Pencharz PB, et al. The effect of energy intake and expenditure on the recovery of $^{13}CO_2$ in the parenterally fed neonate during a 4-hour primed constant infusion of $NaH^{13}CO_3$. Pediatr Res 1985;19:806–910.
16. Van Goudoever JB, Sulkers EJ, Chapman TE, et al. Glucose kinetics and glucoregulatory hormone levels in ventilated, preterm infants on the first day of life. Pediatr Res 1993;33:583–9.
17. Van Goudoever JB, Wattimena JDL, Carnielli VP, Sulkers EJ, Degenhart HJ, Sauer PJJ. Effect of dexamethasone on protein metabolism in infants with bronchopulmonary dysplasia. J Pediatr 1994;124:112–8.
18. Wagenmakers AJ, Veerkamp JH. Degradation of branched-chain amino acids and their derived 2-oxo acids and fatty acids in human and rat heart and skeletal muscle. Biochem Med 1984;28:16–31.
19. Buxton DB, Olson MS, Taylor MK, Barron LL. Regulatory effects of fatty acids on decarboxylation of leucine and 4-methyl-2-oxopentanoate in the perfused rat heart. Biochem J 1984;221:593–9.
20. Wagenmakers AJM, Veerkamp JH. Interaction of octanoate with branched chain 2-oxoacid oxidation in rat and human muscle in vitro. Int J Biochem 1984;16:977–84.
21. Ball MJ. Parenteral nutrition in the critically ill: use of a medium chain triglyceride emulsion. Intensive Care Med 1993;19:89–95.
22. Jiang Z, Zhang S, Wang X, Yang N, Zhu Y, Wilmore D. A comparison of medium-chain and long-chain triglycerides in surgical patients. Ann Surg 1993;217:175–84.
23. Muller TF, Muller A, Bachem MG, Lange H. Immediate metabolic effects of different nutritional regimens in critically ill medical patients. Intensive Care Med 1995;21:561–6.