Feeding behavior in neonates whose diet contained medium-chain triacylglycerols: short-term effects on thermoregulation and sleep

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ABSTRACT
Background: Feeding formulas for premature infants often contain medium-chain triacylglycerols (MCTs). However, previous studies in animals and adults showed that MCTs may decrease food intake. Objectives: The objectives were to determine in hospitalized premature infants whether food intake is modified by dietary MCT supply and to assess the effects on thermoregulation and sleep, which are involved in the regulation of energy metabolism and in the optimal physiologic development of the neonates. Design: Food intake, body mass, and nutritional efficiency during 3 consecutive days were compared in 2 groups of neonates according to the fat composition of their feeding formula [MCT group: 37% MCT, 63% long-chain triacylglycerols (LCTs); LCT group: 100% LCT]. On the third day, sleep and metabolic rate were recorded in the morning during an interval between meals. Results: Regardless of day, energy intake was greater in the MCT group than in the LCT group (Δ difference: 67.3 kJ·kg⁻¹·d⁻¹; \( P = 0.007 \)). Metabolic rate (1.8 mL·min⁻¹·kg⁻¹; \( P < 0.001 \)), cheek skin temperature (0.31°C; \( P = 0.04 \)), and total sleep time (52 min; \( P = 0.01 \)) were also higher in the MCT group. Conclusion: The ratio of MCTs to LCTs in neonates’ feeding formulas can modify physiologic functions involved in energy-balance regulation. Am J Clin Nutr 2002;76:1091–95.

KEY WORDS Feeding behavior, medium-chain triacylglycerols, neonate, thermoregulation, sleep

INTRODUCTION
Milk formulas for premature infants (whose digestive function is immature) often contain medium-chain triacylglycerols (MCTs), ie, those containing saturated fatty acids with carbon chain lengths of 6–10 atoms, which confer nutritional characteristics that differ from those of long-chain triacylglycerols (LCTs) (1). Compared with LCTs, MCTs are more easily hydrolyzed, better absorbed (2), and more rapidly oxidized (3). As a consequence, MCTs are often referred to as a source of readily available energy for premature infants.

However, MCTs could well have adverse effects, especially on feeding behavior. Dietary MCTs decreased short-term food intake in chickens (4), rats (5), and adult humans (6, 7). This effect could be attributed to the fact that MCTs increase the plasma concentrations of cholecystokinin (CCK) (8), a satiety hormone (9). Thus, in neonates, the MCT content of the diet may modify daily energy intake with potential long-term adverse effects on growth. This hypothesis remains the subject of debate.

The type of nutrient could also interfere with thermoregulatory and sleep processes, both of which are implicated in energy-balance regulation. The thermic effect of diet is an important component of body temperature maintenance in premature infants (10, 11). The duration and structure of sleep are also altered by the quality and quantity of food ingested (12–16). Modifications in body temperature and sleep patterns could be of paramount importance in the maturation of neonates’ central nervous system (17).

The present study aimed to determine whether neonates’ food intake is modified by the dietary supply of MCT. Repercussions of the diet on thermic effect and sleep were also assessed.

SUBJECTS AND METHODS
Subjects and feeding
Seventeen healthy premature neonates, nursed in closed incubators in a hospital pediatric department, were enrolled in this study after their parents were informed of the protocol and had given written, informed consent. The protocol was approved by the Regional Ethics Committee of Picardy. Neonates with neurologic or cardiorespiratory problems or infections, or any combination of those conditions, were not included in the experiment.

Neonates were randomly assigned to 1 of 2 groups (Table 1). No significant differences were observed between the 2 groups with regard to general clinical variables. The neonates were fed with 2 commercially available formulas, currently used in the hospital’s pediatric department, spanning the highest and the lowest rates of MCT supply. The 2 formulas were isonitrogenous and isocaloric [293 kJ/100 mL energy content, 57.7% carbohydrate (by wt), 14.6% protein, 24.8% fat, and 2.9% mineral components] and differed only in their relative fat composition, ie, the ratio of MCT to LCT (Table 1). The MCT group was fed with a formula enriched with MCTs, containing 37% MCT and...
Each neonate was studied over 3 consecutive days (day 1–day 3), during which time food intake, body weight, and nutritional efficiency (ie, the ratio of energy supply and body weight gain, calculated over a 24-h period measured from 0800 on day 1 to 0800 on day +1) were recorded. Each neonate was weighed before each experimental session. Feeding nursing care corresponded to the usual procedure and was not modified by the experimental signals. Eye movements were monitored with the use of a mechanogram attached to an eyelid (21). Throughout the experiment, visual observation of the neonate’s behavior was made by the same experimenter.

Experimental design

Each infant was studied over 3 consecutive days (day 1–day 3), during which time food intake, body weight, and nutritional efficiency (ie, the ratio of energy supply and body weight gain, calculated over a 24-h period measured from 0800 on day 1 to 0800 on day +1) were recorded. Each neonate was weighed before each experimental session. Feeding nursing care corresponded to the usual procedure and was not modified by the experimenter. Each neonate was fed by bottle, with feeding episodes occurring every 3–4 h according to the neonate’s feeding demands, eg, awakening, body activity, and crying. Food was given until the neonate appeared to be satiated, ie, stopped sucking the bottle.

The metabolic rate and body temperatures were measured at 10-s intervals throughout the experiment. Because of a technical problem, the abdominal skin temperature was not recorded for one neonate.

Sleep stages (active sleep, intermediate sleep, and quiet sleep) were scored for each 30-s period (20) on the basis of electrophysiologic recordings: electroencephalograms from the right and the left Rolando-occipital leads, electrocardiogram, and respiratory signals. Eye movements were monitored with the use of a mechanogram attached to an eyelid (21). Throughout the experiment, visual observation of the neonate’s behavior was made by the same experimenter.

Statistics

Two-factor analysis of variance for repeated measures using the T2 correction of Geisser and Greenhouse (22) and t tests were carried out to test the effects of various amounts of MCT on food intake, nutritional efficiency, metabolic rate, body temperatures, and sleep. Values expressed as percentages have undergone arcsine transformation to stabilize the variance (23).
accepted as the level of significance. Indicative results (ie, non-significant, 0.05 < P < 0.10) are sometimes given when relevant.

RESULTS

Food intake and nutritional efficiency

No significant differences in digestive physiologic function (regurgitation, presence of residue in the stomach, diarrhea, or constipation) were observed between the groups. The daily energy intake as a function of the 3 consecutive days is shown in Figure 1. No significant interaction between time and type of feeding was observed. It is striking that, throughout the experiment, food intake was significantly higher in the MCT group than in the LCT group (by 67.3 kJ · kg⁻¹ · d⁻¹; P = 0.007). The interaction between energy intake and the day was not significant.

Feeding episode; the number of feeding episodes each day did not differ significantly (MCT group: 7.1 ± 0.3 episodes; LCT group: 7.4 ± 0.5 episodes).

Over the duration of the experiment, intergroup differences in body mass gain (MCT group: 16 ± 13 g/kg; LCT group: 15 ± 11 g/kg) and nutritional efficiency (MCT group: 0.033 ± 0.026 g/kJ; LCT group: 0.036 ± 0.027 g/kJ) were not significant.

The thermic effect of diet

On the third day of the experiment, oxygen consumption was significantly higher (P < 0.001; Figure 3) in the MCT group (7.0 ± 0.5 mL · min⁻¹ · kg⁻¹) than in the LCT group (5.2 ± 1.1 mL · min⁻¹ · kg⁻¹), whereas the incubator air temperature did not differ significantly between the 2 groups (MCT group: 33.29 ± 0.22°C; LCT group: 33.25 ± 0.58°C) and remained in the thermoneutral range defined by Sauer et al (19). The level of carbon dioxide production (V̇CO₂) was 7.1 ± 0.5 mL · min⁻¹ · kg⁻¹ in the MCT group and 5.4 ± 1.3 mL · min⁻¹ · kg⁻¹ in the LCT group. The respiratory quotient did not differ significantly between the groups (MCT group: 1.02 ± 0.22; LCT group: 1.02 ± 0.12).

Esophageal temperature tended to be higher in the MCT group (37.12 ± 0.26°C) than in the LCT group (37.03 ± 0.24°C), but the difference was not significant. The intergroup difference was indicative for overall mean skin temperature (MCT group: 36.88 ± 0.24°C; LCT group: 36.66 ± 0.25°C; P = 0.08), but this was due only to a significantly higher cheek skin temperature (0.31°C, P = 0.04) in the MCT group.

Sleep

Total sleep time was significantly (P = 0.01) shorter in the LCT group (−52 min) than in the MCT group (Table 2) as a consequence of an earlier awakening. The time of the sleep onset, wakefulness after sleep onset, and the frequency of sleep stage changes were not modified by the regimen. No significant differences in sleep structure were observed.
tract nucleus in the satiety center within the hypothalamus’s signals from stomach distension, which project via the solitary Another possible explanation relates to the sensory vagal nervous fixation cannot explain the greater energy intake by the MCT group. Namely contains LCT) in mixed flavored drinks (7). Differences between the viscosity of MCT (25–30 cP) and of caloric, or auditory stimulation, which could affect cortical control of the case in the present study. This rules out possible bias due to visual, mechani-
cal, or auditory stimulation, which could affect cortical control of

### DISCUSSION

#### Food intake

In the present study, in contrast with the findings reported for adult humans and animals, MCT increased the daily energy intake in comparison with LCT by increasing the average food intake per feeding episode. Various hypotheses, all relating to signals that alter food intake, such as chemical signals from the intestines, mechanical signals from the stomach, and sensory stimulation, can explain this observation.

MCT ingestion elicits the endogenous secretion of CCK in rats (8). Furuse et al (5) used a CCK-A receptor antagonist to show that the inhibitory effect of MCT on food intake in rat is related in part to the CCK satiety signal. In neonates, CCK is produced in part to the CCK satiety signal. In neonates, CCK is produced in the 2 groups. This was greater in the MCT group. This extra energy expenditure induced an increase in cheek skin temperature, but there was no significant change in esophageal and abdominal skin temperatures. The increase in cheek skin temperature—attributable to increased cutaneous perfusion at the face level—could be interpreted as a thermoregulatory process involving selective brain-cooling activation. This mechanism could be particularly important in neonates, because the head is a major site of heat production (40% of energy metabolism) and of heat transfer to the environment (25% of the total body skin surface area) (35, 36). These observations suggest that the effect of MCT on energy expenditure could be related to the activation of the brain metabolism. This is supported by the fact that ketone bodies, the plasma concentration of which is positively correlated with the MCT supply (37), can be used as a major source of energy for developing the neonatal brain (38–40).

Several explanations can be posited for the high value of the respiratory quotient. First, the error of measurement by indirect calorimetry (1%) is sufficient to obtain a respiratory quotient just > 1. Second, indirect calorimetry does not take into account the biosynthetic process. When the rate of lipogenesis is higher than that of lipid oxidation (as is the case in a growing neonate), the respiratory quotient is often 1.0–1.1.

#### Sleep

The reduction in total sleep time in the LCT group was mainly attributed to earlier awakening, and it could be considered an integral part of the behavioral component of a feeding episode. As suggested by Himms-Hagen (41), in a hypothesis of thermoregulatory feeding in newborns, the interval between meals (ie, the duration of sleep before the next meal) depends in part on the amount of the preceding food intake and therefore on the thermic effect of the food. As a result, the lower food intake in the LCT group could be lead to a shortened intermeal interval, which would reduce sleep time. It would be interesting to test this assumption over a 24-h period to ascertain the consequences of feeding behavior on the sleeping-waking cycle in neonates.

#### Summary

In conclusion, the ratio of MCT to LCT in neonates’ feeding formulas can modify physiologic functions involved in energy-balance
regulation. Food intake, energy expenditure, and sleep time were greater in an MCT-fed group than in an LCT-fed group. It is interesting to point out the physiologic consequences of 2 formulas currently used in neonates, which differ only in the type and characteristics of the lipids they supply. This finding could improve the physician’s criteria for choosing the formula according to the neonate’s requirements. For example, when the physician is confronted with an insatiable neonate, it is better to prescribe the LCT formula. In contrast, the MCT formula is better for premature infants who have difficulty in maintaining their body temperature.

We dedicate this study to Professor Bernard Risbourg, Head of the Department of Pediatrics II of the University Hospital of Amiens, who died recently. We thank Marie-Christine Godefroy, supervisor of the nursing staff of Pediatrics II (CHU Amiens), and wish to acknowledge the work of the nursing staff.

REFERENCES