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Absence of responses in energy metabolism and respiratory quotient to carnitine infusion in premature infants

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Plasma levels of total, free and acylcarnitine, as well as oxygen consumption and respiratory quotient were determined in premature infants maintained at neutral temperature. The effects on these parameters of intravenous infusion of 24 mg/kg/day carnitine were studied. Total, free and acylcarnitine increased and the acyl/free carnitine ratio decreased significantly during the four-hour study period. Resting heat production and respiratory quotient remained practically unchanged throughout the study period, indicating that in the face of carnitine sufficiency exogenous carnitine did not influence whole body heat production and substrate utilization pattern in premature infants. Further examinations in carnitine depleted infants will be required to clarify the regulatory role of carnitine in neonatal fatty acid metabolism and non-shivering thermogenesis.

Interesting findings and observations concerning the effects of carnitine on lipolysis and energy generation in white adipose tissue [6, 7] raised the question as to the possible capacity of exogenous carnitine to influence total body heat production in premature infants with and without carnitine deficiency. The exploration of this aspect may help in understanding the functional role of carnitine in postnatal fat and energy metabolism. This study examines the effect of intravenously infused carnitine on total oxygen consumption and RQ in premature infants exhibiting a satisfactory plasma carnitine level.

Material and Methods

Ten premature infants fed on human milk and without serious postnatal complications were admitted to the study. They were single births with a mean gestational age of 34.4 weeks (range, 33—36 weeks) and mean birthweight of 1961 g (range, 1660—2200 g). The study was performed at 3.8 postnatal days (range, 2—5 day). The caloric and volume intake prior to the study averaged 86 kcal/kg/day and 136 ml/kg/day, respectively.

The design of the study was as follows. Two hours after the last feed carnitine with a quarter physiological NaCl solution was infused at a rate of 24 mg/kg/day during a 4 hour-period. Blood samples were withdrawn before and by the end of the second and fourth hour of carnitine infusion. The samples were placed in heparinized test tubes and after centri-

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fugation stored at −20°C until laboratory analysis. Free and esterified carnitine were measured radiochemically [4] with some modification [14]. Total carnitine refers to the sum of esterified and free carnitine.

Oxygen consumption and CO_2 production were measured using the Kipp diaferometer, which allowed a continuous measurement of respiratory gas exchange and of the respiratory quotient [12]. Readings were made every minute, except when reference was made to room air. The studies were performed within the zone of thermoneutrality. Energy metabolism was expressed as kcal and kJ/kg/day. Each value of heat production and RQ represented the average 30 minute intervals throughout the study period.

Results

Fig. 1 shows the plasma carnitine values prior to and during carnitine infusion. It is seen that the significant increase in total, free and acylcarnitine concentration was associated with a significant fall of the acyl/free carnitine ratio by the end of the four-hour infusion period indicating a much larger increase in the plasma level of free than of esterified carnitine.

In Fig. 2 are seen the average values of resting heat production and respiratory quotient at neutral tem-

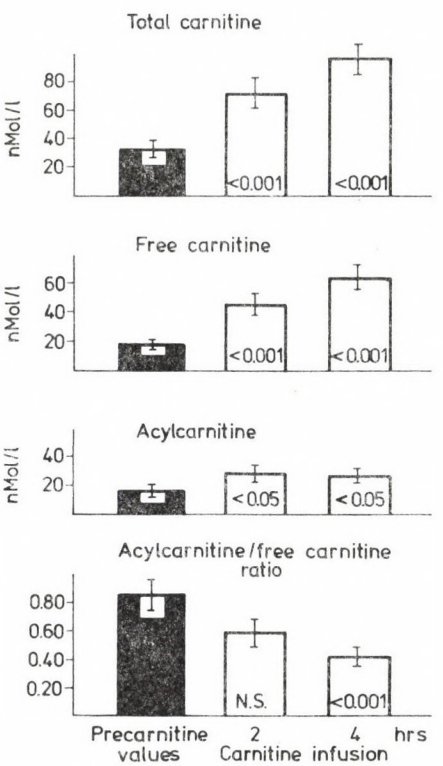

Fig. 1. Mean plasma total free acylcarnitine and acylcarnitine/free carnitine ratio prior to and during carnitine infusion

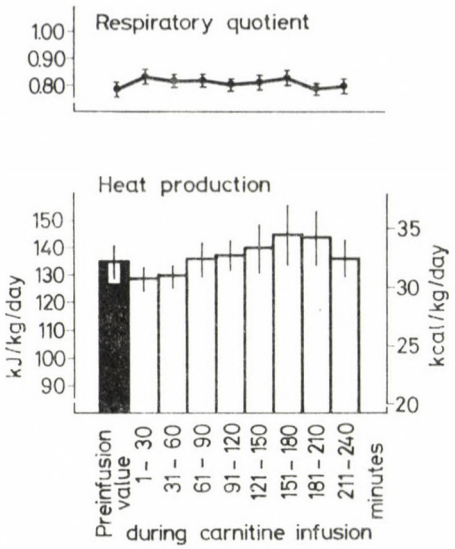

FIG. 2. Mean heat production and respiratory quotient calculated for 30 minute periods before and during carnitine infusion

perature calculated for periods of 30 minutes, and also that no significant changes occurred in these metabolic parameters during carnitine infusion.

DISCUSSION

It is well known that after birth a marked increase in fatty acid oxidation occurs, reflected by a large fall in the respiratory quotient [2, 18]. As a result, the energy metabolism of the unfed newborn is dominated by fat utilization, about 80—85% of energy is produced by this pathway [5]. It is, in fact, this metabolic transition which has brought into focus the functional role of carnitine for optimum oxidation of fatty acids in the neonatal period. So far no examinations aimed at the effect of exogenous carnitine on heat production in the newborn infant have been reported. The findings of an increase in core and skin temperature in response to carnitine administration in newborn rabbits [16] fit in with the in vitro observations, that carnitine stimulated lipolysis and oxygen consumption in the human white adipose tissue [7]. However, a direct proof of the capability of exogenous carnitine to enhance non-shivering thermogenesis as suggested by Hahn and Skala [3] is still lacking. Therefore, further work will be required to clarify the regulatory role of carnitine in neonatal fatty acid metabolism and non-shivering thermogenesis. This has led us to examine heat production and RQ during carnitine infusion in premature infants. The results were negative, no significant change could be observed in oxygen consumption

and respiratory quotient in response to carnitine.

Further understanding of the suggested role of carnitine in a better energy generation by fat metabolism will come from the exploration of its influence on heat production and substrate utilization in carnitine depleted infants maintained at and below the neutral temperature. The relationship between carnitine deficiency and cold induced thermogenesis appears to be of particular interest. Plasma carnitine and substrate measurements in themselves cannot answer some important questions arising from a number of investigations [8, 9, 10, 11, 15, 17]. What does, for example, represent the low serum level of carnitine during intravenous fat alimentation? Does it indicate deficiency and hence an impaired fatty acid oxidation or is it simply due to the increased fatty acid utilization? It is conceivable that in different conditions associated with an increased fat metabolism, a low plasma carnitine level may develop without depletion in tissues (heart, skeletal muscle, brown fat) oxidizing fatty acids as a major source of energy. It would also be necessary to know what degree of deficiency matters in energy generation and does exogenous carnitine exert the same regulatory function in fatty acid oxidation as suggested for the endogenously produced carnitine.

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