THE IMPORTANCE OF CARNITINE IN THE PERINATAL PERIOD

Low birth weight infants may be at risk for carnitine deficiency with resulting impairment of lipid and energy utilization.

Key Words: carnitine, total parenteral nutrition, low birth weight infant, fatty acid oxidation

Carnitine plays an important role in the oxidation of fatty acids by facilitating their transport across the mitochondrial membrane via carnitine acyltransferase and translocase systems.[1] In the immediate postnatal period, increased carnitine acyltransferase activity and accumulation of carnitine have been reported in several species including man.[2] This period is characterized by an abrupt transition from reliance upon carbohydrates as energy substrate to a state in which lipids are the major energy source. It is apparent therefore that carnitine availability may be crucial to the neonate in the transition from fetal to extrauterine life.

Although carnitine has been measured in amniotic fluid, maternal and cord blood and in the urine of newborn infants before the onset of feeding,[3,4] it is not understood whether placental transfer or de novo synthesis of carnitine is of greater importance to the fetus. Neonatal adipocytic carnitine accretion coincides with the onset of feeding, suggesting that the oral intake of carnitine is important during this stage of development.[2] Low birth weight infants and newborn infants with medical or surgical conditions that preclude oral feeding may be nourished parenterally on intravenous regimens of fat, glucose and amino acids. Borum and colleagues[5] have measured the carnitine content of selected infant formulas and special diets whose main protein source is soy protein isolate, casein or egg white solid. All such products have been found to contain only 4 nmoles carnitine per milliliter or less, most of them having undetectable amounts of carnitine. In contrast, infant liquid formulas and special diets based on cow's milk or beef contain 50 to 656 nmoles carnitine per milliliter. It is evident that patients receiving certain commercial formulas receive a subnormal carnitine dietary intake.

The development of a modified radiometric method for the measurement of total, acyl- and free carnitine concentrations in very small volumes of plasma[6] has allowed investigators in the rapidly expanding field of research on total parenteral nutrition in infancy and childhood to explore the complexities of fat metabolism with special reference to carnitine. Studies designed to determine the effect of intravenous lipid infusion on plasma triglyceride and free fatty acid concentrations in the newborn have established that both gestational age and weight for gestational age influence the infant's ability to tolerate the lipid infusion.[7,8] Low birth weight infants achieve very high plasma levels of triglycerides and free fatty acids during the infusion which are cleared only slowly. Impaired hydrolysis of triglyceride and deficient uptake and/or utilization at a cellular level may be a reflection of immature enzyme systems but also could be explained by a deficiency in carnitine availability. Abnormalities of lipid tolerance during total parenteral nutrition may have consequences other than those on the provision of energy substrate to various tissues in the body. For example, when the molar ratio of free fatty acids to albumin in plasma is greater than six, bilirubin is displaced from albumin with an increased risk of kernicterus.[9] There have been several cases of liver disease reported following parenteral nutrition using lipid infusions which have lead to the conclusion that lipid toxicity may, in certain cir-

cumstances, be a major metabolic complication of total parenteral nutrition in the newborn.[10]

Two recent studies have attempted to establish whether low birth weight infants receiving total parenteral nutrition are at risk of developing carnitine deficiency.[11,12] In one study, the carnitine blood levels and urinary excretion of 12 premature infants receiving total parenteral nutrition were compared with those of eight infants of similar gestational age and birth weight who received carnitine-containing milk formulas. In the parenterally nourished infants the levels of total and free carnitine in the serum fell after five days and urinary excretion also was reduced significantly. In contrast, the infants fed enterally with formula showed no significant changes in the circulating concentration of carnitine between the first and fifth days of life and a rise subsequently. It is noteworthy that when the parenterally fed infants were subsequently transferred to oral feeding, their plasma carnitine levels were still significantly below those of the control group at 17 days suggesting that they may have had a deficiency of tissue carnitine levels as well as a lower plasma carnitine concentration.

In another study, serum carnitine levels were monitored in 33 infants during intravenous feeding and during periods when the infant was fed with expressed breast milk or proprietary formulas. On parenteral feeding, the blood carnitine levels remained relatively constant, but in some cases extremely low; and on transfer to oral alimentation, striking rises in carnitine levels were observed. These findings suggest that there may be an endogenous supply of carnitine present in the preterm infant, but that the blood level is maintained at the expense of tissue stores. Both studies indicate that the preterm infant may not be able to synthesize sufficient carnitine to maintain blood levels in spite of an adequate supply of the necessary amino acids, lysine and methionine. It is clear that carnitine deficiency can occur during or following total parenteral nutrition. The clinical consequences for the infant merit further investigation, particularly in relation to the possibility that the lower acylcarnitine levels observed may contribute to the impairment of fatty acid oxidation which in turn renders the infant incapable of using fat efficiently as an energy substrate.

A positive correlation has been shown to exist between serum β-hydroxybutyrate and acylcarnitine levels.[13] An absence of dietary carnitine therefore leads to a decrease in ketone body production. In this context, it is interesting that the acylcarnitine levels found in the parenterally nourished infants following seven days of oral feeding were lower than those of the control group, but that the free carnitine levels in the two groups were similar.[11] This points to a mechanism by which carnitine deficiency may influence ketone body and fatty acid metabolism in infancy. For example, human infants fed exclusively on carnitine-free, soy bean-base formulas have lower blood levels of carnitine and ketone bodies than babies fed carnitine-containing cow's milk.[4] Warshaw and Curry[14] have shown that higher serum carnitine levels and a higher rate of ketogenesis are observed in breast fed infants than in formula-fed infants. They suggest that the carnitine in breast milk may be better absorbed than that in the commercial formula.

A fuller understanding of human carnitine metabolism, especially in the perinatal period, will help to resolve some of the problems at present encountered in the nutritional management of low birth weight infants. □

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NUTRITIONAL COMPOSITION OF BREAST MILK PRODUCED BY MOTHERS OF PRETERM INFANTS

Milk obtained from mothers delivering preterm infants contains significantly higher amounts of non-protein nitrogen. This and other less consistent differences between milk produced by mothers of preterm and term infants may be related to the nutritional needs of the two groups of neonates.

Key Words: breast milk, premature infants, protein

The development of intensive care neonatal units has resulted in the survival of an increasingly larger proportion of low birth weight infants. Many questions regarding the optimal method of feeding this group of babies remain unanswered. It has been suggested that human milk may offer some protection against infection and necrotizing enterocolitis. One possibility is that the unique nutritional needs of the preterm infant are matched by the composition of breast milk produced by mothers delivering prematurely. On the other hand, it has been observed that rapidly growing low birth weight infants fed human milk in usual amounts may fail to put on weight and height at the rates achieved by formula-fed infants and are at risk of developing deficiencies of certain specific nutrients. These data have led to studies designed to evaluate the nutritional composition and adequacy of breast milk produced by mothers delivering before 37 weeks of gestation.

Gross and coworkers[1] determined the concentrations of protein, minerals and electrolytes in milk obtained from 33 mothers giving birth between 28 and 36 weeks of pregnancy (preterm) and from 18 mothers delivering between 38 and 42 weeks of gestation (term). Morning milk samples were collected by manual or mechanical emptying of both breasts. Protein concentrations estimated by the Kjeldahl method were significantly higher in preterm milk compared to term milk throughout the three- to 28-day period postpartum. The highest levels were observed on the third day after birth. Nonprotein nitrogen (NPN) calculated as the difference between total nitrogen and nitrogen precipitated by 10 percent trichloroacetic acid remain fairly constant at 15 to 19 percent in both groups of mothers. Fat concentrations determined by the mixed ethers extraction method were similar in preterm and term milk samples. Lactose was estimated by an automated colorimetric assay and its levels were lower in milk from mothers delivering preterm than in term milk. In both groups, the lactose concentration