Carnitine Levels in Neonatal Hypoxia

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Summary

Background: The aim of this study is to determine carnitine levels in hypoxic–ischemiac neonates.
Methods: Total and free carnitine levels were measured in 20 normal term neonates and 20 term neonates who were diagnosed as hypoxia–ischemia.
Results: Both total carnitine levels (43.7 ± 10.0 µg/dl vice 27.8 ± 11.8 µg/dl, $p < 0.0001$) and free carnitine levels (28.0 ± 8.8 vice 13.2 ± 6.8 µg/dl, $p < 0.0001$) were lower in the hypoxic–ischemic group). Additionally acyl/total carnitine ratio was higher in the asphyxic group (0.33 ± 0.20 vice 0.56 ± 0.24, $p < 0.0001$).
Conclusions: The findings of this study show that neonates with hypoxia–ischemia suffer carnitine deficiency.

Introduction

Perinatal hypoxia–ischemia is one of the most important factor affecting the neonatal mortality and morbidity.[1–5] Fatty acids are the most important essential metabolic fuel under situations of prolonged fasting or stress especially in neonates. Therefore, the defective or insufficient oxidation of fatty acids may produce pathological situations such as perinatal hypoxia–ischemia. Hypoxia–ischemia in the newborn disturb mitochondrial energy metabolism.[6] Supplements such as carnitine and coenzyme Q can correct the mitochondrial energy metabolism. Carnitine has two major functions; transportation of the fatty acids across the inner mitochondrial membrane and neutralization of toxic intracellular acyl-CoA moieties. The purpose of the present study is to determine whether intrapartum hypoxia plays a role in the development of carnitine deficiency or insufficiency during the early neonatal period.

Subjects and Methods

Forty term asphxiac and normal appropriate for gestational age newborn infants were included in the study. The subjects were subdivided into two groups, homogeneous for gestational age, birth weight and hours of life.

Group I consisted of 20 neonates (11 boys/9 girls) with intrapartum asphyxia, had a mean gestational age of 39.1 ± 1.1 weeks (mean ± SEM), birth weight of 3140 ± 314 g (mean ± SEM). Infants were selected according to the fallowing parameters: Apgar score at 5 min of < 5, umbilical artery pH of < 7.20, lactate in umbilical artery of > 1.8 mmol/l and PaO_2 in umbilical artery of < 30 mmHg.[7,8]

Group II comprised 20 healthy term newborn infants (12 boys/8 girls). They had a mean gestational age of 39.3 ± 1.03 weeks, birth weight of 3268 ± 564 g.

Blood samples for total, free and acyl carnitine were obtained by venipuncture from each infant in the first 24–48 h of life. Total and free carnitine in serum were determined by the method described by Cejka and Kithier, and values were recorded in µmol/dl.[9] Plasma free carnitine concentrations under 20 µmol/dl are considered as a marker of carnitine deficiency.

For statistical calculations in both groups, the Student's *t* test was used for comparison of the mean parametric values.

Results

Table 1 gives the mean values of the plasma concentrations of free, acyl and total carnitine and acyl/total carnitine ratio. The plasma levels of free and total carnitine were significantly lower in asphyxiac babies than those of the control group ($p < 0.0001$). Acyl/total carnitine ratio was higher in the asphyxic group ($p < 0.0001$).

Discussion

The main finding of the present study is the presence of low free carnitine levels and high acyl carnitine

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TABLE 1
Comparison of plasma concentrations of free, acyl and total carnitines, in both normal and asphyxiac babies

	Normal babies ($n=20$)	Asphyxic babies ($n=20$)
Total carnitine (μg/dl)	43.7 ± 10.0* (27.5–61.2)	27.8 ± 11.8* (14.4–60.0)
Free carnitine (μg/dl)	28.0 ± 8.8* (15.8–37.9)	13.2 ± 6.8* (6.7–25.2)
Acyl carnitine (μg/dl)	15.7 ± 11.7 (0.8–38.2)	16.6 ± 12.0 (2.0–44.5)
Acyl/total carnitine ratio	0.33 ± 0.20*	0.56 ± 0.24*

Data are mean ± SD. *$P < 0.0001$, ranges in parenthesis.

(AC) to total carnitine (TC) ratio in neonates with hypoxia–ischemia. Bayes *et al*. also showed that AC/TC ratio was higher in the hypoxic neonates than in the control group.[10]

It is highly probable that ischemic or hypoxic insults inhibit the metabolism of acyl-CoA and related acyl-CoA metabolites accumulate in mitochondria. These toxic acyl-CoA metabolites also inhibit the other vital enzymatic processes.[11,12] Accumulation of these toxic acyl-CoA metabolites leads to elevation of serum carnitine esters and therby reduction of free carnitine levels.[13]

In many animal model studies, it has been shown that myocardial hypoxia–ischemia causes accumulation of long-chain acylcarnitines in myocytes and leads to cardiac dysfunction.[14–20] Studies performed in the light of these results showed that carnitine administration to hypoxic rats corrected the cardiac functions and antihypoxic action of carnitine chloride.[21,22]

Recent data suggested that pletelt-activiting factor (PAF) could play a pathophysiologically important role in progression of hypoxic–ischemic brain injury. Akisu *et al*. indicated that suppressor effect of L-carnitine on PAF production may give new insight into the treatment of hypoxic–ischemic brain injury in rat model.[23] Additionally Rauchova *et al*. showed that the protective effect of carnitine and phosphocreatine administrations were due to their regulation of metabolic reactions during hypobaric hypoxia rather than to their activity in hypoxic rat brain.[24]

In addition to all these studies Wainwright *et al*. recently showed that L-carnitine treatment reduced brain injury after hypoxia–ischemia in newborn rats.[25]

In conclusion the findings of this study show that neonates with hypoxia–ischemia suffer carnitine deficiency. Whether these infants may benefit from carnitine supplements remains to be proven in clinical trials.

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