L-carnitine serum level in healthy and septic neonates

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Received 26 February 2018
Accepted 4 April 2018

Kasr Al Ainy Medical Journal
2018, 24:26–31

Objective
The aim was to measure plasma l-carnitine concentration in healthy and septic neonates, and the relation between l-carnitine concentration and gestational age, birth weight, and presence of neonatal sepsis.
Background
Neonatal sepsis and endotoxemia result in impaired lipid metabolism and hepatic energy generation from fatty acid oxidation which could put those neonates at risk of l-carnitine deficiency.
Materials and methods
The study was carried out at the Menoufiya University Hospital over 1 year on 40 of healthy and septic neonates. All neonates were subjected to full history taking, clinical examination, and laboratory investigations included measurement of serum l-carnitine level, sepsis workup, and other laboratory investigations.
Results
Our study included 40 neonates, They were divided into four groups. Group 1: 10 healthy preterm neonates with a mean gestational age of between 33.50±1.18 weeks and mean birth weight of between 1.82±0.18 kg. Group 2: 10 healthy full-term neonates with a mean gestational age of between 38.80±1.03 weeks and mean birth weight of 2.98±0.23 kg. Group 3: 13 septic preterm neonates with a mean gestational age of between 33.46±1.13 weeks, and mean birth weight of 1.95±0.31 kg. Group 4: seven septic full-term neonates with a mean gestational age of between 38.57±1.27 weeks and mean birth weight of between 3.00±0.34 kg. Septic neonates groups (groups 3 and 4) have a low level of l-carnitine than healthy neonates groups (groups 1 2) and among septic groups the septic preterm neonates group (group 3) have a high level of l-carnitine than septic full-term neonates group (group 4). Also among healthy groups, the healthy preterm neonates group (group 1) have a high level of l-carnitine than healthy full-term neonates group (group 2). There was no correlation between l-carnitine and maternal age, gestational age, birth weight, and laboratory investigations in all groups.
Conclusion
There is a significant decrease of serum l-carnitine level in septic neonates, so they need assessment and supplementation. There is no correlation between serum level of l-carnitine and both gestational age and birth weight.

Keywords:
l-carnitine, neonatal sepsis, prematurity

Kasr Al Ainy Med J 24:26–31

1687-4625

Introduction

Neonatal sepsis is a systemic infection occurring in infants at less than or equal to 28 days of life and sepsis still contributes significantly to mortality and morbidity among very low birth weight (<1500 g) infants in Neonatal Intensive Care Units (NICUs) [1].

Early-onset neonatal sepsis has been variably defined based on the age at onset, with bacteremia or bacterial meningitis occurring at less than or equal to 72 h in infants hospitalized in the NICU, versus less than 7 days in term infants [2].

In preterm infants, early-onset neonatal sepsis is most consistently defined as occurring in the first 3 days of life and is caused by bacterial pathogens transmitted vertically from mother to infant before or during delivery [3].

Late-onset sepsis is sepsis occurring after 72 h in NICU infants and 7 days of life in term infants, and has been

 DOI: 10.4103/kamj.kamj_9_18

variably defined as occurring up to the age of more than 90 or 120 days [4].

Neonatal sepsis is a significant cause of morbidity and mortality of hospitalized newborns and premature infants. Worldwide, sepsis accounts for 15% of neonatal deaths [5]. Neonatal sepsis is clinically diagnosed by a combination of clinical signs, nonspecific laboratory tests, and microbiologically confirmed by detection of bacteria in blood by culture [6].

The early stage of sepsis development: the main symptoms of it are from a decrease in systemic vascular resistance due to vasodilation.

The late stage of sepsis development is caused from the body being unable to meet the oxygen demands of tissues. Tissue damage and lactic acidosis can occur, and this is now a hypovolemic state [7].

Carnitine is an amino acid derivative which is synthesized endogenously from the essential amino acids lysine and methionine [8].

Carnitine is stored mainly in muscles. Carnitine has an important role in facilitating medium-chain and long-chain fatty acid transport from the cytosol into the mitochondria for β-oxidation and energy generation. In addition, carnitine stimulates pyruvate dehydrogenase complex activity and the Krebs cycle, increasing branched-chain amino acid oxidation in muscles [9].

L-carnitine in infants

Sepsis and endotoxemia result in impaired lipid metabolism and hepatic energy generation from fatty acid oxidation [10], which could put infants at risk of l-carnitine deficiency.

Materials and methods

A longitudinal study was carried out at Menoufiya University Hospital and Nursery of Shebin El-Kom Teaching Hospital. Over a period of 1 year from January 2017 to January 2018.

The study protocol was approved by the local ethics committee of the Menoufiya University and written consent was obtained from the parents.

The study done on 40 neonates (20 healthy neonates is divided to 10 preterm and 10 fullterm) and 20 cases of neonatal sepsis is divided to (13 preterm and seven fullterm).

Mothers of the newborns were subjected to the following:

(1) History of any medical diseases such as diabetes mellitus or hypertension before and/or during pregnancy.
(2) History of intake of any medication during pregnancy.
(3) Mode of delivery.
(4) Date of the last menstrual period, and cause of prematurity in case of preterm newborns.

All newborns in this study were subjected to the following:

(1) Attendance of neonatal resuscitation, evaluation, and decisions regarding the resuscitation measures guided by assessment of respiration, heart rate, and color/oxygen saturation.
(2) Apgar score at 1, 5, and 10 min were recorded after birth.
(3) Clinical examination and application of clinical sepsis score.
(4) Laboratory investigations includes the following:
    (a) Complete blood count with differential leukocytic count(application of hematological sepsis score).
    (b) C-reactive protein (CRP).
    (c) Blood culture (for infants with positive hematological sepsis score).
    (d) Other laboratory investigations such as blood glucose level, hemoglobin level, and platelet level.
    (e) Measuring serum l-carnitine using an enzymatic ultraviolet test by peripheral venous samples were collected from healthy groups, also from septic groups (after diagnosis of sepsis clinically and by laboratory investigations).

Exclusion criteria

Neonates with congenital anomalis.

Age above 28 days.

Neonates exposed to asphyxia.

Statistical analysis

Data were collected, coded, revised, and entered into the Statistical Package for the Social Sciences (IBM SPSS) version 20 (IBM Corp. Released 2010, IBM SPSS Statistics for widows,version 20.0, Armonk, NY: IBM Corp). The data were presented as number and percentages for the qualitative data, mean, SD, and ranges for the quantitative data with parametric

Table 1 Comparison between demographic data regarding septic group and healthy group

	Septic group (*N*=20) [*n* (%)]	Healthy group (*N*=20) [*n* (%)]	χ^2/t^*	*P* value
Maternal age (mean±SD) (years)	29.40 (5.08)	29.15 (4.27)	0.168	0.867
Weight (mean±SD) (kg)	2.32 (0.60)	2.40 (0.63)	–0.428	0.671
Sex				
Female	10 (50.0)	11 (55.0)	0.100	0.752
Male	10 (50.0)	9 (45.0)		
MOD				
Cesarean section	13 (65.0)	14 (70.0)	0.114	0.736
Vaginal delivery	7 (35.0)	6 (30.0)		
Gestational age (mean±SD) (weeks)	35.25 (2.75)	36.15 (2.92)	–1.002	0.322
Birth weight for gestational age				
AGA	18 (90.0)	20 (100.0)	2.105	0.147
LGA	2 (10.0)	0 (0.0)		

AGA, appropriate for gestational age; LGA, large for gestational age; MOD, mode of delivery. *Independent *t*-test.

Table 2 Distribution of causes of prematurity

Causes of prematurely	Healthy (preterm) (*N*=10) [*n* (%)]
Idiopathic	
No	6 (60.0)
Yes	4 (40.0)
PROM	
No	9 (90.0)
Yes	1 (10.0)
Antepartum hemorrhage	
No	9 (90.0)
Yes	1 (10.0)
Maternal health disorders	
No	6 (60.0)
Yes	4 (40.0)

Table 3 Distribution of causes of prematurity in septic preterm

Causes of prematurely	Septic (preterm) (*N*=13) [*n* (%)]
Idiopathic	
No	9 (69.2)
Yes	4 (30.8)
PROM	
No	6 (46.2)
Yes	7 (53.8)
Ante partum hemorrhage	
No	12 (92.3)
Yes	1 (7.7)
Maternal health disorders	
No	12 (92.3)
Yes	1 (7.7)

distribution and median with interquartile range for the quantitative data with nonparametric distribution.

χ^2-Test was used in the comparison between two groups with qualitative data and Fisher's exact test was used instead of the χ^2-test when the expected count in any cell was found to be less than 5.

Independent *t*-test was used in the comparison between the two groups with quantitative data and parametric distribution and Mann–Whitney test was used in the comparison between two groups with quantitative data and nonparametric distribution

Spearman's correlation coefficients were used to assess the significant relation between two quantitative parameters in the same group.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *P* value was considered significant as the following:

(1) *P* value greater than 0.05: nonsignificant.

(2) *P* value less than 0.05: significant.

(3) *P* value less than 0.01: highly significant.

Results

Our study included 40 neonates and they were divided into four groups. Group 1: 10 healthy preterm neonates with a mean gestational age of between 33.50±1.18 weeks and mean birth weight of between 1.82±0.18 kg. Group 2: 10 healthy full-term neonates with a mean gestational age of between (38.80±1.03 weeks) and mean birth weight of 2.98±0.23 kg. Group 3: 13 septic preterm neonates with a mean gestational age of between 33.46±1.13 weeks and a mean birth weight of 1.95±0.31 kg. Group 4: seven septic full-term neonates with a mean gestational age of between 38.57±1.27 weeks) and a mean birth weight of between 3.00±0.34 kg. Septic neonate groups (groups 3 and 4) have a low level of l-carnitine than healthy neonate groups (groups 1 and 2) and among septic groups the septic preterm neonate groups (group 3) have a high level of l-carnitine than the septic full-term neonate groups (group 4). Also among healthy groups, the healthy preterm neonates group (group 1) has a high level of l-carnitine than healthy full-term neonate

groups (group 2). There was no correlation between l-carnitine and maternal age, gestational age, birth weight, and laboratory investigations in all groups.

Discussion

Our study included 40 neonates. Table 1 shows that there was significant decrease in weight and gestational age in the septic group in comparison to the healthy group, which comes in accordance with Gardner *et al.* [7] who found that the incidence of neonatal infection is higher for infants with lower gestational age, with premature infants having a three to five times greater risk of developing sepsis.

Among group 1, the incidence of causes of prematurity (Table 2) was idiopathic preterm labor in 40%, premature rupture of membrane in 10%, antepartum hemorrhage in 10%, and maternal disorders represent 40%. The high percentage of maternal disorders is in agreement with the study done by Hammond *et al.* [11], which detect changes in risk factors for preterm birth in Western Australia in the period 1984–2006. Over the 23 years of study, there was a fourfold increase in the rates of preexisting medical maternal complications over time, and the estimates for premature rupture of membrane (PROM) were between 10 and 20% [11].

Among group 3, the incidence of causes of prematurity (Table 3) were: idiopathic cause in 30.8%, PROM in 53.8%, antepartum hemorrhage in 7.7%, and maternal disorders in 7.7%; the high percentage of PROM comes in accordance with the study done by Yang *et al.* [12] on 73 patients. In 33 (45.2%) patients, amniotic membranes ruptured before 23 weeks of gestation.

All healthy groups show negative CRP; however, all septic groups show positive CRP (Table 4), which agree with the study of Omran *et al.* [13] on 70 neonates, 35 with sepsis and 35 healthy controls. All the septic cases were positive CRP and was stated that, to date, CRP is the most extensively studied acute-phase reactant, despite the detection of new markers of infection, with wide-ranging sensitivities and specificities (74–98% and 71–94%, respectively).

The l-carnitine level in septic preterm neonates was more than septic full-term neonates (Table 4), which agree with the study of Chace *et al.* [14] which report that no meaningful correlation was found between total carnitine and gestational age or birth weight in any group.

All septic cases of our study were of positive blood culture and regarding the type of blood culture. Table 5 shows that the percentage of Gram-negative organisms in blood culture is 71.4% in septic full-term and 69.2% in septic preterm; however, Gram-positive organisms represent 28.6% in septic full-term and 23.1% in septic preterm and fungal organisms represent only 7.7% in septic preterm which agree with the studies done by

Table 4 Comparison between serum l-carnitine, C-reactive protein regarding septic (fullterm and preterm)

	Septic (fullterm) (*N*=7)		Septic (preterm) (*N*=13)		Independent *t*-test	*P* value
	Mean	SD	Mean	SD		
CRP (mg/l)	86.43	61.61	83.85	40.27	0.114	0.911
Serum l-carnitine (mg/l)	2.30	0.08	2.81	0.29	–4.496	0.000

CRP, C-reactive protein.

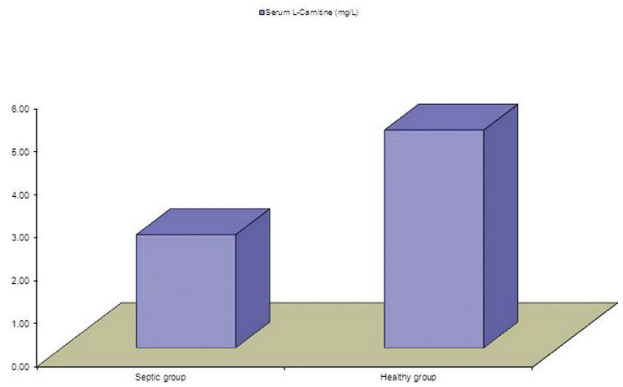
Table 5 Comparison between type of blood culture regarding septic group (preterm and fullterm)

	Septic (fullterm) (*N*=7) [*n* (%)]	Septic (preterm) (*N*=13) [*n* (%)]	χ^2	*P* value
Blood culture				
Fungal	0 (0.0)	1 (7.7)	0.597	0.742
Gram negative	5 (71.4)	9 (69.2)		
Gram positive	2 (28.6)	3 (23.1)		

Table 6 Comparison between serum l-carnitine regarding healthy (preterm and fullterm)

	Mean	SD	Mean	SD	Independent *t*-test	*P* value
	Healthy (preterm) (*N*=10)		Healthy (fullterm) (*N*=10)			
Serum l-carnitine (mg/l)	5.94	0.60	4.18	0.38	7.872	<0.001
	Septic (preterm) (*N*=13)		Septic (fullterm) (*N*=7)			
Serum l-carnitine (mg/l)	2.81	0.29	2.30	0.08	4.496	0.000

Figure 1



Serum l-carnitine regarding septic group and healthy group.

Table 7 Correlation between Serum l-carnitine (mg/l) as regards the studied parameters in healthy group (preterm and fullterm) and septic group (preterm and fullterm)

	Serum l-carnitine(mg/l)	
Healthy group (preterm)	*r*	*P*
Gestational age (weeks)	0.394	0.260
Weight (kg)	0.222	0.538
Healthy group (fullterm)		
Gestational age (weeks)	0.019	0.959
Weight (kg)	0.018	0.960
Septic group (preterm)		
Gestational age (weeks)	0.210	0.492
Weight (kg)	0.457	0.116
Septic group (fullterm)		
Gestational age (weeks)	0.092	0.845
Weight (kg)	0.393	0.383

Ozkan [15] and Lim [16] which reported that Gram-negative organisms as the most frequent microorganism.

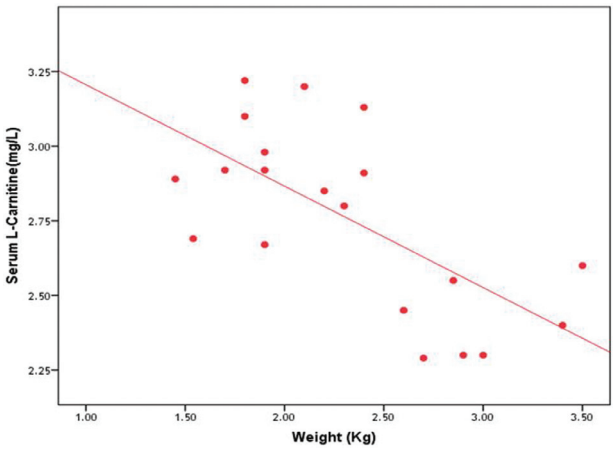
Table 6 and Fig. 1 report that there was significant increase in serum l-carnitine (mg/l) in the healthy group in comparison to the septic group.

The serum l-carnitine (mg/l) in the healthy group was 5.06±1.03 mg/l and serum l-carnitine (mg/l) in the septic group was 2.63±0.35 mg/l.

Hatamkhani *et al.* [17] report that it seems reasonable not to consider carnitine as a mandatory and beneficial supplement under septic conditions.

There is no correlation between l-carnitine level and birth weight and gestational age among all studied groups which is opposite to the study done by Sánchez-Pintos *et al.* [18], which report that l-carnitine deficiency was demonstrated in all very low birth weight babies. However, birth weight restriction has been suggested as a risk factor for impaired carnitine status (Table 7 and Fig. 2).

Figure 2



Weight regarding serum l-carnitine.

Conclusion

There is a significant decrease of serum l-carnitine level in septic neonates, so they need assessment and supplementation. There is no correlation between serum level of l-carnitine and both gestational age and birth weight.

Financial support and sponsorship

Nil.

Conflicts of interest

There are conflicts of interest.

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