MEASUREMENT OF CARNITINE IN PRETERM NEONATES SUFFERING RESPIRATORY DISTRESS SYNDROME AND THE EFFECT OF ITS SUPPLEMENTATION

Thesis

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List of Abbreviations

Abbr.	Full-term
AAP	: American Academy of Pediatrics
AT	: Antitrypsin
CLD	: Chronic lung disease
COXIs	: Cyclooxygenase inhibitors
CP	: Cerebral palsy
CPAP	: Continuous positive airway pressure
DPPC	: Dipalmitoyl phosphatidylcholine
ELBW	: Extremely low birth weight
FiO2	: Fractional inspired oxygen
EPT	: Extremely preterm
FRC	: Functional residual capacity
HF	: High-flow nasal cannulae
HFOV	: High-frequency oscillatory ventilation
HMD	: Hyaline membrane disease
LBW	: Low birth weight
LCAD	: Long-chain acyl-CoA dehydrogenase
MCAD	: Medium-chain acyl-CoA dehydrogenase
MV	: Mechanical ventilation
NDI	: Neurodevelopment impairment
NEC	: Necrotizing enterocolitis
NICHD	: National Institute of Child Health and Human Development

NIPPV : Nasal intermittent positive pressure ventilation

NRN : Neonatal Research Network

PCVC : Peripherally inserted central venous catheter

PDA : Patent ductus arteriosus

PEEP : Positive end expiratory pressure

PIP : Peak inspiratory pressure

PPHN : Persistent Pulmonary hypertension

PPV : Positive-pressure ventilation

PVR : Pulmonary vascular resistance

RDS : Respiratory distress syndrome

ROP : Retinopathy of prematurity

SCAD : Short-chain acyl-CoA dehydrogenase

SCHAD : Short-chain 3-hydroxyacyl-CoA dehydrogenase

SM- score : Silverman score

SP-D : Surfactant protein–D

SPSS : Statistical package for the social science

TPN : Total parenteral nutrition

V/Q : Ventilation-perfusion

VLBW : Very low birth weight

VLCAD : Very long-chain acyl-CoA dehydrogenase

VPT : Very preterm

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Abstract

Respiratory distress syndrome (RDS) is among the *most* common diseases of preterm infants. RDS is caused by a decreased production or secretion of pulmonary surfactant. Numerous causes of RDS have been identified, and the factors suspected to be involved in the pathogenesis of RDS are numerous. Carnitine is essential for the fetus and is provided via placental transport. As the gestational age increases, fetal tissues store increasing amounts of carnitine, therefore, preterm infants require exogenous carnitine supplementation for carnitine homeostasis. Treatment with carnitine has shown benefit in the respiratory status of ventilator-dependent adults, as well as stabilization of respiratory parameters and increased physical performance in adult patients with chronic respiratory insufficiency.

Aim of the work: The present study was designed to measure the level of free carnitine in preterm neonates with RDS and to evaluate the efficacy of L~ camitine therapy on those neonates.

Methodology; Forty preterm infants, including 14 females and 26 males. Study group were divided in to 2 groups, group A: received L-camitin in a dose of 30 mg/kg/day for 7 days and group B: did not receive supplementation.

Results:
Our results show non statistically significant difference between group A (with Carnitine supplementation) and group B (no supplementation) at day 1. There was statistically significant higher serum carnitine level in group A compared to group B at day 7 (after supplementation). Seven neonates (35%) in group A, and 13(65%) in group B, needed surfactant administration and MV after 24 hs from admission and this difference was statistically significant. Dose of surfactant was statistically significant lower in group A compared to group B (P=0.001) and duration of mechanical ventilation was statistically significant lower in group A compared to group B (p=0.03).

Key words: RDS, Carnitine supplementation, Surfactant, MV

Respiratory distress syndrome (RDS) is the most common threatening respiratory disorder of newborns and it is the most common cause of respiratory failure in the first days after birth. It occurs mainly in preterm neonates ***(Jackson et al., 1994).***

RDS occurs as a result of deficiency or absence of surfactant which is very important for lung maturity as it decreases the surface tension of alveoli and keeps the stability of the alveoli, so its absence leads to atelectasis and respiratory distress syndrome ***(Moya et al., 1994).***

The incidence and severity of respiratory distress syndrome (RDS), also known as hyaline membrane disease (HMD), are related inversely to the gestational age of the infant. The classic clinical presentation of RDS includes grunting respiration, retractions, nasal flaring, cyanosis, and increased oxygen requirement together with diagnostic radiographic findings and the onset of symptoms shortly after birth ***(Rodriguez et al., 2006).***

Fanaroff et al. (2007) reported results of the National Institute of Child Health and Human Development (NICHD), neonatal research network study, which showed that rates of RDS were 42%, 71%, 54%, 36%, and 22% in infants weighing 501-1500 g, 501-750 g, 751- 1000g, 1001-1250 g, and 1251-1500 g, respectively.

Surfactant is synthesized and secreted by type II epithelial cells in the alveolus. It is composed primarily of phospholipids; Phosphatidylcholine and phosphatidylglycerol ***(Whitsett et al., 2005).***

Carnitine is a small amino acid derivative, plays a major role in fatty acid oxidation as well as in other central metabolic pathways. Fatty acid oxidation is an important energy-providing pathway in early postnatal period. Carnitine has a role not only in energy production, but also as a secondary antioxidant, favoring fatty acid replacement within previously oxidatively damaged membrane phospholipids ***(Arenas et al., 1998)***.

Carnitine is a naturally occurring hydrophilic amino acid produced endogenously in the kidneys and liver and derived from meat and dairy products in the diet. It plays an essential role in the transfer of long-chain fatty acids into the mitochondria for beta oxidation ***(Scaglia, 2006).***

The low levels of L-carnitine present in plasma during pregnancy and the immaturity of liver L-carnitine biosynthetic pathway in preterm neonates may be important determinants in the pathogenesis of respiratory distress syndrome (RDS) ***(Arduini et al., 2001).***

Antepartum administration of L-carnitine has been shown to enhance the dipalmitoyl phosphatidylcholine (DPPC) content of fetal rat lung. DPPC is the most important constitute, functionally and quantitatively, of the surfactant complex ***(Lohninger et al., 1996).***

Decreased neonatal serum carnitine levels in preterm infants with RDS during the first week of life might be caused by increasing consumption of carnitine in lung tissue for surfactant synthesis ***(Ozturk et al., 2006).***

The aim of the present study was to measure the level of free carnitine in preterm neonates with respiratory distress syndrome (RDS) and to evaluate the effect of its supplementation on them regarding, the respiratory distress course, the duration of mechanical ventilation and the RDS outcome.