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RESEARCH ARTICLE

THE USE OF L-CARNITINE IN PREMATURE NEWBORNS WITH «VENTILATOR-ASSOCIATED» PNEUMONIA

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ABSTRACT

The rationale for the use of the drug L-carnitine (Levocarnitine) in the complex treatment of neonatal pneumonia was metabolic disorders and carnitine deficiency in premature infants with perinatal pathology. The aim of the study was to increase the effectiveness of treatment of premature newborn infants with respiratory distress syndrome complicated by "ventilator-associated" pneumonia on the basis of correction of carnitine deficiency. We examined 80 premature infants with this pathology. All infants received basic therapy (antibiotics, intravenous immunoglobulin, oxygen therapy, infusion therapy, parenteral and enteral nutrition, oxygen therapy, treatment of anemia). 40 infants received an additional drug L-carnitine at a dose of 100 mg/kg per day enteral for 25 days. The daily dose was divided into two administrations. 40 infants did not receive L-carnitine and were on basic therapy.
The use of L-carnitine in the complex treatment of RDS complicated by VAP had a positive therapeutic effect. We noted an increase in the rate of baby body weight, a reduction in the time of relief of clinical symptoms of the disease, the duration of oxygen therapy, antibiotic therapy, hospital stay in comparison with infants who did not receive this drug.

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INTRODUCTION

Ventilator-associated pneumonia (VAP) in preterm infants remains a serious pediatric problem. This disease is one of the main causes of death in the post-neonatal period and often leads to the formation of chronic lung pathology. The issue of increasing the effectiveness of drug treatment of this disease remains relevant (Cairns *et al.,* 2000). It is known that with severe respiratory failure, the energy costs of the body increase, especially against the background of a bacterial infection (Garmaeva *et al.,* 2007; Garmaeva *et al.,* 2008; Neudakhin *et al.,* 2015; Guseva *et al.,* 2014; Donnell *et al.,* 2002). Noteworthy is the question of a deficiency of carnitine involved in the metabolism of fats - energy sources (Clark *et al.,* 2017; Garmaeva *et al.,* 2008; Ledyaev *et al.,* 2017). In premature infants, the situation is complicated by the immaturity of carnitine synthesis enzymes, reduced its reabsorption in the kidneys, insufficient transplacental transmission of carnitine, which is carried out mainly in the 3rd trimester of pregnancy (Garmaeva *et al.,* 2007; Garmaeva *et al.,* 2008; Ledyaev *et al.,* 2017; Longo *et al.,* 2006; Nasirova *et al.,* 2018; Neudakhin, 2015; Guseva *et al.,* 2014). It is known that respiratory failure, including respiratory distress syndrome (RDS) in premature infants, is accompanied by a deficiency of carnitine in the blood (Garmaeva *et al.,* 2007; Garmaeva *et al.,* 2008; Donnell *et al.,* 2010). RDS is often complicated by the development of VAP, which can contribute to the formation of secondary carnitine metabolism deficiency against bacterial inflammation (Clark *et al.,* 2017; Garmaeva *et al.,* 2017). Carnitine deficiency in premature infants with perinatal pathology can develop due to disorders of the central nervous system (CNS) (Neudakhin, 2015; Guseva *et al.,* 2014) and the cardiovascular system (CVS) (Piksajkina *et al.,* 2012), as well as prolonged parenteral nutrition (Cairns *et al.,* 2000; Neudakhin *et al.,* 2015). Given the possible deficiency of carnitine in premature infants with RDS and VAP, we included a drug based on L-carnitine (Elkar, Levocarnitine) in the complex treatment.

Aim

Improving the effectiveness of treatment of premature infants with respiratory distress syndrome, complicated by "ventilator-associated" pneumonia, based on the correction of carnitine deficiency.

MATERIALS AND METHODS

We conducted clinical observation, examination and treatment of 80 preterm infants with RDS complicated by VAP in most of them (72 infants). Infants were divided into two groups. Newborns in the 1st group (n = 40) received L-carnitine (Elkar) at a dose of 100 mg / kg per day by enteral course of 25 days in a complex treatment. The daily dose was divided into

two administrations. L-carnitine was prescribed to infants from 4-9 days of life after removal from the mechanical ventilation apparatus. Infants of the 2nd group (n = 40) did not receive this drug and were on basic therapy. At the age of 4-6 days of life, 37 infants of group 1 (93%) and 35 infants of group 2 (88%) were diagnosed with focal pneumonia, it was confirmed by x-ray studies. Newborns of both groups came under our supervision to the Department for premature infants from the intensive care unit after the termination of mechanical ventilation on the 4-10yh days of life. They were on the same basic treatment for the disease: oxygen therapy (oxygen tent - 60% O2, mask), broad-spectrum antibiotics, intravenous immunoglobulin, infusion therapy to correct homeostasis disorders, and treatment of anemia. All infants received combined parenteral and enteral nutrition. They were in couves (incubators) with temperature and humidity control.

RESULTS

All infants were born in women with a burdened' somatic and obstetric - gynecological history. According to the degree of somatic history in mothers, the course of their pregnancy and childbirth, there were no significant differences between the groups. So, chronic somatic diseases were noted in 24 women in group 1: and in 22 - in group 2 (p> 0.05).Reproductive organ diseases in group 1 were observed in 16 women, and in group 2 in 11 (p>0.05). The pathological course of pregnancy (toxicosis in the 1st and 2nd half of pregnancy, anemia, the threat of abortion) was observed in all women, and the frequency of occurrence of these factors in the selected groups did not significantly differ (p> 0.05). The condition of all newborns at birth was severe. All children from 1 day of life were on mechanical ventilation for RDS. The Apgar score at birth at both the 1st and 5th minute did not significantly differ in the two groups (p <0.05). Indicators of physical development, severity of the condition at birth, the presence of clinical syndromes in the examined infants are presented in Table 1. As can be seen from table 1, groups of newborns were representative in terms of physical development and gestational age. There were no differences between the groups according to the clinical condition at birth and the main clinical diagnosis. Most infants with RDS at birth needed urgent resuscitation and were admitted to the intensive care unit at the age of 8 minutes to 1 day of life. All infants were sucked from the upper respiratory tract. Apparatus ventilation was performed in 16 (40%) infants and 15 (37.5%) infants from birth, 24 (60 %) and 25 (62.5%) infants from 1 day of life in the 1st and 2nd groups, respectively. Of the concomitant pathologies, CNS lesions in the form of cerebral ischemia of the 1st and 2nd degree (in 24 and 23 infants in the 1st and 2nd groups, respectively), conjugation jaundice (in 16 and 17 infants, respectively) were most often encountered, intrauterine malnutrition and intrauterine growth retardation (in 9 infants in each group). By concomitant pathology, there were no differences in children in the groups (p> 0.05). The clinical criteria for the effectiveness of carnitine were the dynamics of respiratory disorders, dependence on oxygen therapy, the timing of the elimination of the symptoms of pneumonia, the dynamics of body weight, the improvement in changes in motor activity, muscle tone, and physiological reflexes. In addition, the duration of antibiotic therapy, infusion therapy, parenteral nutrition, and the length of stay in the clinic were analyzed as a whole. A significant difference was established between the two compared groups in such indicators as: normalization of the gas composition of the blood and the

Table 1. Indicators of physical development, gestational age (M ± m) and condition in premature newborns at birth in the compared groups

Indicators	Group 1 (n=40)	Group2 (n=40)
Body weight (grams)	2026.77±81.98	2125.1±97.62
Body length (cm)	43.74±0.54	44.5±0.49
Gestational age (weeks)	33.32±0.43	34.07±0.37
Extremely serious condition	8	8
Grave condition	29	28
Moderate condition	3*	4*
Clinical Syndromes at Birth:	40	40
Respiratory distress syndrome	40	40
Neurological syndrome	15	14
Oppression Syndrome	5	4
Arousal syndrome	2	1
Inhibition with excitement	2	1
Neonatal cramps	12	11
General edema syndrome	2	2
Ypovolemic syndrome	1	0
Hemorrhagic syndrome	1	0

Note. * - Deterioration on the 4th-6th day of life from moderate to severe condition.

Table 2. Comparative characteristics of the clinical effectiveness of treatment in two elected groups

Indicators	Group 1 (n=40)	Group2 (n=40)
The duration of physical changes in the lungs, days (M±m) *	13.72±.,22	17.11±1.02
Inflammatory changes in peripheral blood on the 14th day of observation (% of infants in the group) *	19±2.21	33±3.02
Positive dynamics of body weight (from which day of life) (M±m) *	2.96±0.41	6.26±0.56
Improvement of motor activity, muscle tone, physiological reflexes (observation day) (M±m) **	14.29±1.1	16.89±1.05
Duration of oxygen therapy, (oxygen tent),days (M±m) *	10.6±1.02	13.92±1.1
Duration of infusion therapy, days (M±m) *	13.12±0.52	14.2±0.69'
Duration of parenteral nutrition, days (M±m) *	9.11±0.21	11.34±0.68
Duration of antibiotic therapy, days (M±m) *	15.61±0.98	18.61±0.38
Length of hospital stay, bed-day (M±m) *	28.34±1.26	32.66±1.22

Notes. 1. * - significance of differences between groups, p<0.05.
2. ** - the tendency to decrease the index in group 1 compared to the second.

associated duration of oxygen therapy, the duration of the determination of wet and crepitious wheezing in the lungs, inflammatory changes in the blood. This determined significantly shorter duration of antibacterial and infusion therapy, as well as hospital stay. A tendency to earlier periods of improvement in motor activity, muscle tone, physiological reflexes, and positive dynamics of body weight in the 1st group compared with the 2nd was noted. Our studies showed that complex therapy with the inclusion of L-carnitine was clinically more effective compared to the basic therapy (table 2). This is confirmed by a more rapid elimination of symptoms of respiratory failure and inflammatory changes in the lungs in infants of the 1st group. The daily increase in body weight in the 1st group was significantly greater than in the 2nd. The duration of parenteral nutrition in the 1st group was 2 days shorter than in the 2nd group. The duration of antibiotic therapy was in group 1 on average 3 days less than in group 2.The length of hospital stay was 4 days shorter in children of the first group, compared with the second group (p = 0.01).

DISCUSSION

The use of L-carnitine in premature infants with VAP had a positive clinical result. This is due to the compensatory effect of exogenous carnitine in the composition of the drug, which made up for the deficiency of endogenous carnitine and restored its impaired metabolism (Garmaeva *et al.,* 2007; Garmaeva *et al.,* 2008; Neudakhin *et al.,* 2015). Carnitine deficiency in such infants was associated both with the development of the infectious process and with long parenteral nutrition, the presence of non-infectious perinatal and postnatal

pathology (respiratory failure, persistent apnea, hypoxia, intrauterine growth retardation, hypoxic-ischemic damage to the central nervous system, cardiomyopathy, hypotrophy).In these situations, the importance of lipids as energy sources increases, in the biosynthesis of which carnitine takes a large part (Clark *et al.,* 2017; Garmaeva *et al.,* 2007; Nasirova *et al.,* 2018; Neudakhin *et al.,* 2015). In clinical practice, the use of L-carnitine increased the effectiveness of treatment of postnatal hypotrophy (Ledyaev *et al.,* 2017) and hypoxic-ischemic damage to the central nervous system in premature infants (Neudakhin *et al.,* 2015). L-carnitine has been successfully used to correct maladaptation of the cardiovascular system in premature infants with very low body weight (Piksajkina *et al.,* 2012). The positive effect of L-carnitine in the complex treatment of infants with VAP in our study, apparently, indicates an adequate provision of energy needs for this severe pathology, which involves not only the respiratory tract, but also other organs and systems.

Conclusion

The use of the drug L-carnitine in the complex treatment of premature infants with respiratory distress syndrome, complicated by pneumonia, has a positive therapeutic effect in the form of reducing the duration of relief of clinical symptoms of the disease, the duration of oxygen therapy, antibiotic therapy, hospital stay, increasing the rate of body weight compared to infants who did not receive this drug.

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