The level of zinc, vitamins A and E in the blood of neonates, who need a mechanical ventilation of lungs

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Abstract

The number of infants who need mechanical lung ventilation in the neonatal period increases due to the increasing number of premature births. The prolonged lung ventilation is associated with the development of ventilation-associated complications. It is important to search the means of reducing the duration of traditional invasive ventilation and more common non-invasive methods of ventilation. The aim of this study is to determine the levels of vitamins A, E and zinc in the blood of neonates with respiratory disorders, needing lung ventilation, and evaluate the prognostic value of the above. According to the applied methods of respiratory therapy the infants have been divided into 2 groups: 1st – 17 children, who have had synchronized intermittent ventilation with pressure support (invasive ventilation), 2nd – 11 children with spontaneous breathing along with continuous positive airway pressure via nasal cannulas (non-invasive ventilation). The levels of vitamins A and E in serum have been determined by means of liquid chromatography, the levels of zinc – by means of atomic adsorption spectrophotometry. The results show that the serum level of vitamin A has been by 3.2 times, of vitamin E – by 2.1 times and of zinc – by 2.2 times lower in the neonates of group 1 than in group 2. Low serum levels of vitamins A, E and low zinc blood levels are associated with the necessity of more prolonged ventilation in neonates with respiratory disorders. We have concluded that using zinc, vitamins A and E in the complex treatment of neonates with respiratory disorders being on mechanical ventilation will help to reduce the duration of invasive ventilation and decrease the frequency of its complications.

Key words: zinc, vitamins, neonates, mechanical lung ventilation.

Уровень цинка, витаминов А и Е в крови новорожденных, нуждающихся в искусственной вентиляции легких

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Реферат

Число младенцев, нуждающихся в механической вентиляции легких в неонатальном периоде, увеличивается с ростом числа преждевременных родов. Длительная вентиляция легких связана с риском развития вентиляторно-ассоциированных осложнений. Важно найти средства снижения продолжительности традиционной инвазивной вентиляции, а также более распространенного использования неинвазивных методов. Цель данного исследования – определить уровни витаминов А, Е и цинка в крови новорожденных с дыхательными расстройствами, нуждающихся в вентиляции легких, и оценить их диагностическое и прогностическое значение. В зависимости от применяемой методики респираторной поддержки младенцы разделены на 2 группы: 1 группа – 17 детей, которые были на синхронизированной перемежающейся вентиляции при поддержке давления (инвазивная вентиляция), 2 группа – 11 детей на самостоятельном дыхании с постоянным положительным давлением в дыхательных путях через носовые канюли (неинвазивная вентиляция). Уровни витаминов А и Е в сыворотке определяли с помощью жидкостной хроматографии, уровни цинка – с помощью атомно-адсорбционной спектрофотометрии. Результаты исследования показывают, что сывороточные уровни витамина А в 3,2 раза, витамина Е в 2,1 раза и цинка в 2,2 раза ниже у новорожденных первой группы, чем у новорожденных второй группы. Низкие уровни витаминов А и Е в сыворотке и низкий уровень цинка в крови ассоциируются с необходимостью более длительной вентиляции у новорожденных с респираторными расстройствами. Опираясь на полученные результаты, мы пришли к выводу, что применение препаратов цинка, витаминов А и Е в комплексном лечении новорожденных с дыхательными расстройствами, находящихся на вентиляции легких, даст возможность уменьшить продолжительность инвазивной вентиляции и, следовательно, снизит риск осложнений.

Ключевые слова: цинк, витамины, новорожденные, искусственная вентиляция легких.

Introduction

Traditional mechanical ventilation (MV) is the most common method to treat infants with respiratory failure and one of the cornerstones of intensive care unit treatment [1]. Despite the improved modes of ventilation and surfactant replacement therapy, which reduce the mortality of infants, in some cases the MV leads to serious complications in both term and preterm neonates. The pathogenesis of ventilation-associated complications is not quite clear, but several studies support the role of oxidative stress [2]. The increase of lipid peroxidation activity occurs due to either inadequate concentrations of antioxidants at birth or inability to increase the synthesis of antioxidants in response to oxidative stress [3]. The antioxidant defense system consists of both enzymatic (glutathione peroxidase catalase, superoxide dismutase – Mn- and Cu/Zn-dependent) and non-enzymatic (vitamins A, E and C, ubiquinone, carotenoids, glutathione, urea, uric acid, bilirubin, epinephrine, polyamines, ceruloplasmin, transferrin, ferritin, haptoglobin, melatonin, neuropeptides) components [4-6].

Vitamin A plays an essential role in the functioning of retina (adaptation to dim light), it is also necessary for the growth and differentiation of epithelial tissue, as well as for the growth of bone, reproduction and embryonic development. Along with certain carotenoids vitamin A enhances the immune function, reducing the consequences of some infectious diseases. The antioxidant function of vitamin A is the protection of biological membranes from the damage by reactive oxygen species [7].

Vitamin E contributes to the normal maintenance of biomembranes by reacting with the hydroxyl radical, absorption of singlet oxygen, inactivation of superoxide radicals and inhibition of lipid radicals. Besides, it provides an antioxidant protection for vitamin A. The activity of vitamin E increases with gestational age [7]. The World Health Organization recommends the supplementation of vitamin A when its level falls below 0.6 mkmol/L. A severe deficiency is indicated at the level less than 0.3 mkmol/L. In turn, the supplementation of vitamin E is recommended when its level is less than 4.6 mkmol/l [7, 8].

Zinc is a part of more than 300 enzymes, including antioxidant zinc-copper superoxide dismutase. It is an essential microelement and, probably, most intensively studied by newborn nutrition specialists, also because it is important for the growth, neuro-psychological development and for the normal function of immune system. Zinc deficiency is diagnosed when its level is less than 15 mkmol/l [9, 10].

The number of infants, who need mechanical lung ventilation in the neonatal period increases due to the increasing number of premature births. The prolonged lung ventilation is associated with the development of ventilation-associated complications. So, it is important to search the means of reducing the duration of traditional invasive ventilation and non-invasive modes of more common use.

The purpose of this study is to determine the levels of zinc, vitamins A and E in the blood of neonates being on mechanical lung ventilation, evaluate their diagnostic and prognostic value.

Material and methods

Blood levels of zinc and serum levels of vitamins A and E have been determined in 28 newborns treated in the neonatal intensive care unit of Lviv City Children's Hospital. All the infants had the symptoms of respiratory distress that appeared on the first day after birth due to the hyaline membrane disease, congenital pneumonia, birth asphyxia and transient tachypnea. The clinical diagnosis has been made on the base of the evaluation of data history and the results of objective, instrumental (chest X-ray, neurosonography, electro- and echocardiography) and laboratory (general blood and urine tests, biochemical parameters of blood serum, standard bacteriological tests) investigations. All the children received respiratory therapy (mechanical ventilation by nCPAP), standard infusion therapy, antibiotics, etc. According to the applied methods of respiratory therapy the infants were divided into 2 groups: 1st – 17 children, who were on synchronized intermittent ventilation with pressure support (SIMV/PS), 2nd – 11 children on spontaneous breathing with continuous positive airway pressure via nasal cannula (by nCPAP). The average gestational age of the children in the first group was 36.4 ± 3.78 weeks, the mean birth weight was 2805.9 ± 1165.58 g. For the newborns of the second group the average gestational age was 36.1 ± 3.57 weeks and the mean birth weight – 2856.4 ± 1007.1 g respectively. Boys predominated in the both groups (82.4 % – 1st group, 63.6% – 2nd group).

The patients received respiratory support with the help of the following medical devices: VIP "BIRD", VIP "Newport", VIP "Inspiration" and nCPAP – Infant Flow system. The respiratory therapy started on the 1st day of life in the both groups. In the first group the mechanical ventilation was launched during the first 6 hours of life in 8 newborns (47.1%), in 1 infant – from 7 to 12 hours of life and in 8 infants (47.1%) – from 13 to 24 hours. In the 2nd group nCPAP was launched during the first 6 hours of life in 2 children (18.2%), in 3 children (27.3%) – from 7 to 12 hours and in 6 children (54.6%) – from13 to 24 hours. The average duration of ventilation in infants of the first group was 5.0 ± 2.6 days, in neonates from the second group – 3.7 ± 1.56 days.

Considering the heterogeneity of lung diseases in the both groups of newborns, the index of the pulmonary injury severity (IPIS) has been determined by the method of M. Palta et al. [11]. According to the received scores 6 infants on mechanical ventilation mode SIMV/PS had the heaviest pulmonary injury (IPIS > 50 scores), 5 – heavy (IPIS > 20 scores), 1 – light pulmonary injury (IPIS < 20 scores). Of the newborns kept on nCPAP one had a moderate lung injury (IPIS = 20 scores) and 9 newborns – a heavy lung injury.

The levels of vitamins A and E in the serum were determined on the 2-3rd day of ventilation by liquid chromatography apparatus "Milihrom-4".

Zinc was determined in blood on 3-4th day of respiratory therapy by means of atomic adsorption spectrophotometry.

The analysis of the data has been made according to the requirements for medical and biological research.

The statistical analysis of the data has been performed by the program STATISTICA 10 (Statsoft, USA). The values are presented as an arithmetic mean (M), standard deviation (SD) of the mean, n-sample size. The differences between the groups have been established by Mann-Whitney test (U-test). The differences in nominal values have been evaluated using χ^2 criteria or Fisher's exact test. All the results have been considered reliable at $p < 0.05$. In order to determine the relationship between the studied parameters we have defined Spearman's correlation coefficient.

Results and discussion

The analysis of data history has revealed that 12 neonates (70.6%) of the first group were born as a result of pregnancies with complicated course (threatened miscarriage, hypamnion, preeclampsia, gestosis of the second half of pregnancy). In 9 cases (52.9%) the labour was with complications (premature discharge of amniotic fluid, fetal distress, weakness of labour, tight loop of cord around the neck, placental presentation). In addition, in 10 cases (58.8%) the delivery was realized by Cesarean section, 6 of them – repeatedly. Five babies (29.4%) were born with Apgar score at the 1st minute less than 4 points, 5 infants (29.4%) – with Apgar scores from 4 to 6 points. Ten newborns (58.8%) needed the resuscitation procedures in the delivery room.

In the 2-nd group 2 children (18.2%) were born from the pregnancies with complicated course (threatened miscarriage, hydramnion). In 2 cases (18.2%) the labour was with complications (bleeding due to the placental presentation, tight loop of cord around the neck). In 4 cases (36.4%) Cesarean section was performed, in 1 of them – repeatedly. One child was born with Apgar score at the 1st minute less than 4 points and 1 infant – 4-6 points. Two infants (18.2%) needed the resuscitation in the delivery room.

There have not been significant differences found between these groups in terms of maternal infectious morbidity.

Among the primary diseases, which have been presented with respiratory distress in infants, the hyaline membrane disease (HMD) has made up 458%, congenital pneumonia – 28.6%, birth asphyxia – 25%, transient tachypnea – 3.6%. No significant difference has been found between the groups concerning the frequency of HMD ($\chi^2 = 0.35$, $p = 0.56$), congenital pneumonia ($\chi^2 = 0.26$, $p = 0.61$), asphyxia ($\chi^2 = 0.81$, $p = 0.37$). We have not revealed significant differences between the groups regarding the age of neonates at the beginning of respiratory support either – in 9 neonates (52.9%) from the 1st group and 5 ones (45.5%) from the 2nd the ventilation was started during the first 12 hours of life ($\chi^2 = 0.15$, $p = 0.70$).

The resulting data of the conducted experiment are presented in table 1.

The level of zinc is by 2.2 times, of vitamin A – by 3.2 times, of vitamin E – by 2.1 times lower in newborns on synchronized intermittent ventilation with pressure support compared to the neonates on spontaneous breathing with continuous positive airway pressure via nasal cannula.

Table 1

Zinc, vitamins A and E levels in the blood of neonates being on synchronized intermittent ventilation with pressure support and on spontaneous breathing with continuous positive airway pressure via nasal cannula

Data	Group 1 n = 17	Group 2 n = 11	p 1-2
Vitamin A, mkmol/l	0.7 ± 0.45	2.2 ± 0.39	< 0.01
Vitamin E, mkmol/l	7.6 ± 3.15	16.1 ± 2.58	< 0.01
Zinc, mkmol/l	10.5 ± 3.74	22.8 ± 6.16	< 0.01

The vitamins deficiency may be associated with neonatal hypoxia (due to the respiratory failure), which disrupts the synthesis of coenzyme forms of vitamins. Besides the persistent inflammation in the airways with increased activity of lipid peroxidation, the catabolism of vitamins dramatically increases. The reliable inverse correlation has been found between the duration of ventilation and levels of vitamins A and E ($r = -0.37$, $p < 0.05$; $r = -0.38$, $p < 0.05$ respectively).

The literary data show that zinc deficiency in fetuses causes the development of congenital lesions, low birth weight, low Apgar scores and a severe respiratory distress [10]. We have also revealed some significant direct correlations between Apgar scores at the 1st and 5th minutes and zinc levels in the blood of neonates ($r = 0.71$, $p < 0.001$; $r = 0.69$, $p < 0.001$ respectively). The reliable inverse correlation has been found between the IPIS, duration of ventilation and zinc blood level ($r = -0.54$, $p < 0.01 r = -0.44$, $p < 0.01$ respectively). Furthermore, the significant direct correlation has been found between the vitamins A and E levels and zinc level ($r = 0.62$, $p = 0.0005$; $r = 0.67$, $p = 0.00008$ respectively).

Our previous study proved that the prolonged ventilation leads to the development of serious complications in neonates [12]. So, zinc, vitamins A and E supplementation in the treatment of the neonates with established deficiency of these elements can, evidently, reduce the duration of ventilation and the risk of the development of ventilation-associated complications.

The received results show, that further studies are necessary to determine the maternal blood levels of zinc, vitamins A and E and compare them with cord blood levels and serum levels in newborns. We suppose that initial deficiency of these compounds in mothers leads to pregnancy and labour complications, which, in turn, lead to the births of neonates with severe respiratory distress when the invasive mechanical ventilation is necessary.

Conclusions

In infants on mechanical ventilation mode SIMV/PS a decrease of antioxidant vitamins A, E and zinc is observed.

Low serum levels of vitamins A, E and low blood levels of zinc are associated with the necessity of more prolonged mechanical ventilation in the neonates with respiratory disorders.

Zinc, vitamins A and E supplementation in the complex

treatment of neonates with respiratory disorders being on ventilation will, obviously, help to reduce the duration of invasive ventilation and decrease the frequency of its complications.

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