

The Vitamin D Deficiency as a Marker of Risk of Pneumonia among Children Under 3 Years

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Abstract

The analysis of the maintenance of a metabolite of vitamin D (25-dihydroxyvitamin D) and vitamin D-binding protein in the blood serum of children under 3 years, patients with pneumonia. Found that a child with pneumonia is characterized by a significant decrease in blood serum concentrations of 25-dihydroxyvitamin D and vitamin D-binding protein. Additional risk factors for pneumonia in young children are adverse for the 2nd half of the pregnancy, the risk of miscarriage, the acute respiratory infections during pregnancy, a small body weight at birth; asphyxia at birth, a prematurity, the artificial ventilation in the neonatal period, artificial nutrition in the first year of life, the disease rickets, anemia, delayed motor development.

Keywords: vitamin D, vitamin D-binding protein, pneumonia, risk factors, children

Introduction

The community-acquired pneumonia is a major cause of infant death, according to the world health organization, representing 20% of all deaths among children under the age of 5 years [2]. The risk of developing pneumonia increases

significantly if the child lack of vitamins, such as vitamin D [16]. In the work of H. H. F. Remmelts et al. (2012) showed that vitamin D deficiency is associated with poor outcome in community-acquired pneumonia. Vitamin D is an independent predictor of 30-day mortality rate and along with other biomarkers has prognostic value in assessing the severity of pneumonia [15].

The hypovitaminosis D is recognized as a pandemic with many health effects today [3, 6]. The vitamin D has immunomodulatory properties, in addition to its classic functions in maintaining calcium - phosphate homeostasis. In connection with this recently there has been great interest in the role of vitamin D in protecting the body [1]. Correlation of vitamin D deficiency with a long course of many diseases [6, 18]. Vitamin D is involved in maintaining an adequate level of innate immunity, in particular, by increasing production of antimicrobial peptides (β -defensin, cathelicidin), acting on lymphocytes, neutrophils, macrophages and epithelial cells of the respiratory tract [4]. In addition, vitamin D has a profound impact on the activity of the adaptive immune system through its interaction with vitamin D receptors, which are found in many organs and tissues not related to calcium metabolism, in particular, dendritic cells, monocytes, T -, B- lymphocytes [1]. So vitamin D deficiency in infants is accompanied by the development of secondary immune deficiency (decreased phagocytosis and production of inteferon, retard the synthesis of interleukins) [18]. It is believed that the endogenous vitamin D modulates the normal development of the fetal lung, while intrauterine violation of the synthesis of vitamin D may contribute to impaired lung growth and function in the postnatal period [9, 11].

Despite numerous studies investigating the role of vitamin D in the occurrence of respiratory diseases, at the present stage there is conflicting evidence about the impact of antenatal factors, prenatal, postnatal periods on the availability of vitamin D and its correlation with the risk of pneumonia in children [4, 5, 12]. In addition, identification of risk factors for pneumonia in young children will contribute to the organization of preventive measures of the disease [17].

Objective: to study the characteristics of the supply vitamin D of children with pneumonia and its prognostic value in the occurrence of pneumonia at children of early age.

Methods

The conducted a comprehensive examination of 32 children with community-acquired pneumonia in children aged 2 months to 3 years (the average age of the patients was $1,6 \pm 0,3$ years). Mandatory complex examination included x-rays of the chest, the study of General blood analysis, General urine analysis. The control group consisted of 30 healthy children, representative by age and gender.

Statistical Analyses

The research of a 25-dihydroxyvitamin D, vitamin-D-bindungsprotein was carried out by the method of an enzyme immunoassay with the use of the commercial sets of dough IDS OSTEIA 25-Hydroxy Vitamin D, Vitamin-D-Bindungsprotein (ELISA Kit) respectively.

The received results are processed by the method of variation statistics with the use of a package of the analysis of the Statistic for WINDOWS 6.0 program with the function of calculation of an arithmetic average (M), an average quadratic deviation (σ) and average mistakes (m). For an assessment of distinctions of indexes in the compared groups the student's criterion was used. The distinctions considered reliable at $p < 0,05$.

To assess the risk of developing pneumonia in children of early age this produced a calculation of the odds ratio (OR) in 2x2 contingency tables, with determination of 95% confidence intervals (CI 95%). Among the most significant factors were classified as informative characteristics with the value of the odds ratio more than 1.0. Risk ratio (RR-related risk) calculated as the ratio of risk of an event (pneumonia) in people who have a risk factor, relative to the control group.

Results and discussion

The analysis of the content of metabolites of vitamin D in the blood serum, found that 27 (84,4 %) of children with community-acquired pneumonia concentration of 25-hydroxyvitamin D was lower compared with healthy children and on average amounted to $69,8 \pm 6,8$ nmol/ml vs. to $104,8 \pm 6,7$ nmol/ml, respectively ($p < 0,05$).

It is believed that 25-hydroxycholecalciferol is the most accurate indicator of vitamin D levels in the body and reflects the rate of accumulation of both endogenous and exogenous vitamin D. Approximately 90-95% 25(OH)D associated with a specific α -globulin vitamin D-binding protein (VDBP), the level of which in blood serum may be a marker of physiological and pathological changes in the body [10], and insufficient amount of it may be the cause of endogenous vitamin D deficiency even when sufficient exogenous intake [7, 8, 10].

In this regard, we studied the content in the blood serum of children of group monitoring the vitamin D-binding protein. The results of the study found a significant decrease in the vitamin D-binding protein most children with pneumonia (30 patients – 93,7 %), the level of which in blood serum averaged $59,90 \pm 3,41$ ng/ml vs. $68,33 \pm 4,02$ ng/ml in children of the control group ($p < 0,05$).

The course of diseases of respiratory system in infants due to, first of all, the peculiarities of the functioning of the immune system. As we know, perinatal pathology may contribute to changes in the immune status of the fetus and child. Currently especially stresses the value transferred during pregnancy, acute respiratory viral infections, and urogenital pathology of the mother that may lead

to the development of immunological failure of fetus and newborn [14]. We studied the obstetric and perinatal histories of patients under the supervision of, and evaluated clinical and laboratory parameters, given the link between intrauterine status of the fetus, the availability of vitamin D and susceptibility to disease in children after birth [6].

The analysis of anamnesis data, clinical and laboratory parameters showed that the development of pneumonia observed in our children was associated with risk factors. Such as unfavorable course of pregnancy in mothers (56,2 %) presented the following disorders: preeclampsia first (5 persons – 15,6 %) or second (8 persons - 25,0%) half of pregnancy, risk of miscarriage (10 persons – 31,2%), acute respiratory infections during pregnancy – (13 persons - 40,6%); complication intrapartum period (acute fetal hypoxia, asphyxia) - 8 children (25,0%), a prematurity – 3 children (9,3%), a small body weight at birth – 7 children (21,9 %).

One third of children with pneumonia were registered with different syndromes of consequences of perinatal lesions of the nervous system in the form of delay motor development (10 children – 31,2%), seizures (3 children – 9,3%), hypertension-hydrocephalic (3 children – 9,3%), and asthenic-neurotic syndrome (2 children – 6,2%). At the time of admission to inpatient treatment 15 (46,9%) with acute pneumonia had signs of rickets. Symptoms of anemia are mild in 7 (21,9%) patients.

We analyzed the nutrition of sick children, in connection with the importance of nutritional factors in the development of hypovitaminosis D. Some children are in the first year of life for artificial nutrition it was 68,7% (22 children) against 21,9 % (7 children) and 9,3% (3 children) breastfeeding and mixed nutrition, respectively ($p < 0.05$).

The next stage of our work was to determine the degree of influence of identified risk factors on the development of pneumonia in children of early age. During the mathematical-statistical processing of data were the statistically significant modifiable factors (clinical and laboratory indicators, historical data) and non-modifiable factors (sex, child age) that determine the risk of pneumonia in children of early age (table 1).

The main risk factors of developing pneumonia with respiratory diseases in children of early age were made by hypovitaminosis D (OR = 6,2, 95% CI = 1,7-21,8, $p < 0,05$; RR = 1,8, 95% CI = 1,3-2,4, $p < 0,05$), the content of vitamin-D-binding protein in blood serum below 56,9 ng/ml (OR = 28,8, 95% CI = 5,7-145,6, $p < 0,05$; RR = 3,1, 95% CI = 1,6-5,1, $p < 0,05$), the pathology of the second half of pregnancy (OR = 4,8, 95% CI = 0,9-26,1, $p < 0,05$; RR = 3,9, 95% CI = 1,7-6,8, $p < 0,05$), the risk of miscarriage (OR = 3,3, 95% CI = 0,5-22,0, $p < 0,05$; RR = 2,6, 95% CI = 1,5-4,0, $p < 0,05$), artificial nutrition (OR = 5,4, 95% CI = 1,1-26,0, $p < 0,05$; RR = 2,4, 95% CII = 1,5-3,5, $p < 0,05$), anemia in children (OR = 4,8, 95% CI = 0,9-26,1, $p < 0,05$; RR = 3,9, 95% CI = 1,7-6,8, $p < 0,05$).

Table 1
Analysis for risk factors associated with pneumonia in children of early age

Risk factors	Odds ratio (OR)	95 % confidence interval (CI)	Relative risk (RR)	95 % confidence interval (CI)
1	2	3	4	5
The child's age :				
2 - 6 mon.	0,5	0,11-0,27	0,65	0,5-0,8
6 mon-1 year	0,85	0,12-6,0	0,87	0,8-0,9
over 1 year	2,1	0,8-6,1	1,53	1,2-1,9
The pathology of pregnancy :				
of the first half of pregnancy	0,85	0,12-6,0	0,87	0,8-0,9
of the second half of pregnancy	4,8	0,9-26,1	3,92	1,7-6,8
The risk of miscarriage	3,33	0,5-22,0	2,62	1,5-4,0
The acute respiratory infections during pregnancy	2,9	0,6-15,5	2,2	1,4-3,1
Cesarean section	0,92	0,28-3,03	0,94	0,9-1,3
Asphyxia at birth	2,2	0,4-18,9	2,0	1,4-2,7
A small body weight at birth	2,1	0,4-11,5	1,7	1,3-2,4
A prematurity	1,45	0,2-9,3	1,4	1,2-1,6
An artificial ventilation in neonatal period	1,45	0,2-9,3	1,4	1,2-1,6
The rickets	2,1	0,7-6,0	1,6	1,3-2,0
The anemia	4,8	0,9-26,1	3,9	1,7-6,8
The delayed motor development	2,1	0,4-11,5	1,7	1,3-2,4

Table 1 (Continued):
Analysis for risk factors associated with pneumonia in children of early age

1	2	3	4	5
The level of 25(OH)D				
< 98,0 nmol/ml	6,2	1,7-21,8	1,8	1,3-2,4
≥ 98,0 nmol/ml	0,85	0,12-6,0	0,87	0,8-0,9
The level of VDBP				
< 57,0 ng/ml	28,8	5,7-145,6	3,1	1,6-5,1
≥ 57,0 ng/ml	0,27	0,03-2,78	0,33	0,2-0,75
Gender (male)	1,04	0,99-1,01	1,02	1,01-1,03
The nutrition:				
a breastfeeding	0,19	0,04-0,89	0,44	0,3-0,6
a mixed nutrition	0,15	0,3-1,5	0,2	0,1-0,3
a artificial nutrition	5,4	1,1-26,0	2,35	1,5-3,5

The risk of pneumonia development in early childhood is much less influenced by the age of the child older than one year (OR = 2,1, 95% CI = 0,8-6,1, p<0,05; RR = 1,5, 95% CI = 1,2-1,9, p<0,05), the acute respiratory infections during pregnancy (OR = 2,9, 95% CI = 0,6-15,5, p<0,05; RR = 2,2, 95% CI = 1,4-3,1, p<0,05), the asphyxia at birth (OR = 2,2, 95% CI = 0,4-18,9, p<0,05; RR = 2,0, 95% CI = 1,4-2,7, p<0,05), the artificial ventilation in the neonatal period (OR = 1,45, 95% CI = 0,2-9,3, p<0,05; RR = 1,4, 95% CI = 1,2-1,6, p<0,05), a small body weight at birth (OR = 2,9, 95% CI = 0,5-17,3, p<0,05; RR = 26, 95% CI = 1,5-4,0, p<0,05), the prematurity (OR = 1,45, 95% CI = 0,2-9,3, p<0,05; RR = 1,4, 95% CI = 1,2-1,6, p<0,05), delay motor development (OR = 2,1, 95% CI = 0,4-11,5, p<0,05; RR = 1,7, 95% CI = 1,3-2,4, p<0,05) and clinical signs of rickets (OR = 2,1, 95% CI = 0,7-6,0, p<0,05; RR = 1,6, 95% CI = 1,3-2,0, p<0,05).

Conclusions

1. The results show that children early age with low levels of vitamin D and vitamin D-binding protein are at risk for the development of pneumonia.
2. The analysis of anamnesis data, clinical and laboratory parameters in children of early age showed that for predicting risk of pneumonia, you must consider several important factors:
 - in the antenatal period: pathology 2nd half of pregnancy, the risk of miscarriage, acute respiratory infectious disease during pregnancy, small body weight at birth;
 - in the neonatal period: asphyxia, prematurity, artificial ventilation;

– in the first year of life: artificial nutrition, the disease of rickets, anemia, delayed motor development.

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