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Original Article

STUDY ON 25 (OH) VITAMIN D STATUS IN HOSPITALIZED CHILDREN WITH ACUTE RESPIRATORY INFECTIONS: PRELIMINARY RESULTS

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Summary

Our study aimed to determine and analyze the serum levels of 25 (OH) vitamin D and parathyroid hormone (PTH) to assess vitamin D deficiency as a risk factor for increased morbidity of acute respiratory infections (ARI) in childhood. The changes in the serum parathormone level were used as a criterion for vitamin D sufficiency since an optimal level of 25 (OH) vitamin D is required for normal PTH values. The study included 87 children divided into four subgroups, respectively – children with acute bronchopneumonia (n=49), children with acute laryngotracheitis (n=11), children with acute bronchiolitis (n=16), and a control group (n=11). Subnormal Vit. D levels were found in the individual groups: in the bronchopneumonia group, 18 children showed evidence of insufficiency; in the group of children with laryngotracheitis, five children showed insufficiency, and one child had Vit.D deficiency; children with acute bronchiolitis showed abnormalities in vit. D levels: seven children with insufficiency and two children - with deficiency. The preliminary results showed that Vit. D status deviations are more common in children with acute respiratory infections than in healthy children.

Keywords: 25-Hydroxyvitamin D3, parathormone, respiratory tract diseases, children

Introduction

Vitamin D deficiency is a global public health problem. Evidence shows an association between vitamin D deficiency and an increased risk of morbidity and mortality from respiratory infections in children [1, 2]. Adequate vitamin D level is essential for maintaining the key immunological defence mechanisms in the developing lungs. In recent years, the study of additional pleiotropic effects of vitamin D has been widely advocated because of the discovery of vitamin D receptors (VDRs) in various peripheral (non-renal) tissues, e.g., lymphoid and myeloid tissue cells, antigen-presenting dendritic cells and macrophages, which upregulate their VDR expression upon infection

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[3, 4]. This stimulates the synthesis of the active form of vitamin D and the formation of the so-called endogenous antibiotics (antimicrobial peptides) – catechilidine and defensin [5].

A study by Loeb suggested that low vitamin D levels are associated with an increased incidence of viral infections during winter [6]. In the past, vitamin D was used as an effective method of treating pulmonary tuberculosis in the form of cod liver oil or by exposure to direct sunlight [7]. There is a high percentage of children with vitamin D deficiency in groups with upper respiratory tract infections [8]. In a randomized clinical trial, the preventive effect of vitamin D administration against influenza A virus in school-age children has been demonstrated [9]. Available data support the importance of vitamin D deficiency in childhood as a risk factor predisposing to the occurrence of diseases such as acute bronchiolitis, recurrent tonsillopharyngitis, acute rhinosinusitis and community-acquired pneumonia [10].

In this sense, maintaining adequate vitamin D-levels is of great importance for children's health, and its monitoring in clinical practice may prove an effective method for preventing ARIs in childhood. Currently, the number of studies in Bulgaria examining vitamin D in the context of childhood respiratory diseases is limited. Thus, researching this matter could be of scientific value for better understanding the role of vitamin D in the development and progression of respiratory diseases and determining the need for adequate prophylaxis among Bulgarian children.

Material and Methods

This prospective study was conducted at the Dr G. Stranski University Hospital – Pleven, Department of Pediatrics. The study included 87 children divided into four subgroups, respectively: children with acute bronchopneumonia (n=49), children with acute laryngotracheitis (n=11), children with acute bronchiolitis (n=16), and a control group of healthy children (n=11).

The inclusion criteria were: age one month to 18 years and acute respiratory infections that required hospitalization; children with acute non-infectious diseases of the respiratory system (aspiration of a foreign body, congenital

anomalies); chronic diseases affecting the respiratory and cardiovascular systems (bronchial asthma, cystic fibrosis, primary ciliary dyskinesia, congenital immunodeficiency states, congenital heart malformations). The Vit D levels were not studied in children with renal and endocrine diseases. The serum levels of 25(OH) Vitamin D3 and parathyroid hormone (PTH) by electrochemiluminescent immunoassay for Roche Cobas e411 immunological analyzer were assayed. The reference range for serum vitamin D levels, according to the criteria of the Bulgarian Society of Endocrinology, was used: vitamin D deficiency: less than 25 nmol/l, vitamin D insufficiency: 25-50 nmol/l, and vitamin D sufficiency: 50-120 nmol/l, respectively. The reference range for serum PTH is 15-65 pg/ml [4, 5]. The ethics commission at the Medical University – Pleven approved the study. Informed consent for the clinical trial was obtained from the parents or guardians of all included patients.

Statistical analysis with Statgraph and SPSS software was performed. A statistically significant difference was defined as a p-value < 0,05.

Results

We found subnormal vitamin D levels in all separate groups: In the children with bronchopneumonia, 18 (41%) showed evidence of vit. D insufficiency with an average of 40.8 ± 4.8 nmol/L. In the rest of the children in the group, the vitamin D levels remained within the normal range. Five children (33%) were found to have insufficient levels in the group of children with laryngotracheitis, and one child – with deficiency (23 nmol/L). Children with acute bronchiolitis had subnormal vitamin D levels: 7 (44%) with insufficiency and two children (12%) – with deficiency. Children with respiratory infections exhibited significantly lower serum levels of vitamin D compared to the control group (p=0.01, Fig. 1).

The mean values of 25 (OH) vitamin D and PTH in the four studied groups are presented in Table 1 and Table 2. In the comparative analysis of the vitamin D status in the general population of children with ARI compared to the control group, significant differences of 25(OH)D were

found (Table 1).

No deviations in the mean PTH levels in the children we studied were found ($p > 0.05$, Table 2).

Vitamin D insufficiency was found in 43% of the examined patients with ARI compared to 18% in healthy children. Vitamin D deficiency in 5% of children with ARI was established. In the

group of healthy children, vitamin D deficiency was not found (Fig. 2).

Six children had increased levels of vit. D in the absence of clinical symptoms of hypervitaminosis D. One of the children showed a toxic level of 25(OH) D – 250 nmol/l, necessitating additional tests and monitoring the vitamin D status in the first and third months.

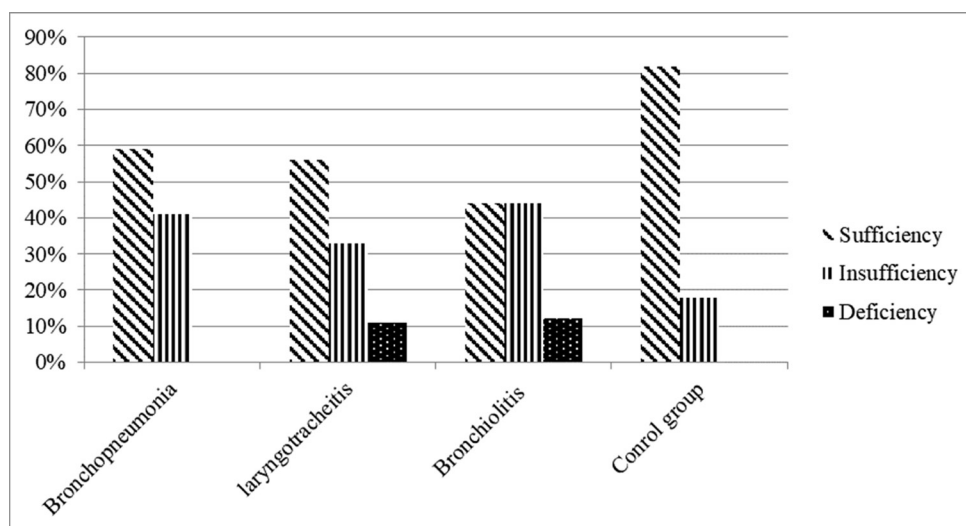


Figure 1. Distribution of the studied groups according to levels of 25 (OH) vitamin D.

Table 1. Mean values of 25(OH) D in the four groups of the studied children

Groups	N	Mean (nmol/L)	SD
Bronchopneumonia	44	56.2*	17.3
Acute laryngotracheitis	9	53.9*	21.9
Acute bronchiolitis	16	54.27*	26.9
Control group	11	73.38	31.1
Total	80	59.41	24.3

* $p = 0.01$ – statistical significance between the ARI groups and the control group.

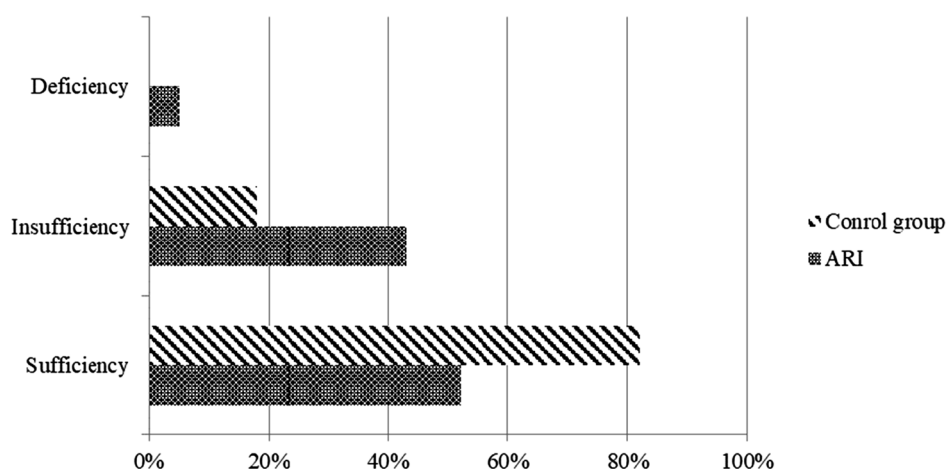


Figure 2. Vitamin D status in the general population of children with ARI compared to the control group.

Table 2. Mean values of PTH in children with ARI and control group

Groups	N	Mean (nmol/L)	SD
Bronchopneumonia	44	22.3	13.9
Acute laryngotracheitis	9	18.47	7.52
Acute bronchiolitis	16	23.77	14.01
Control group	11	19.27	11.35
Total	80	20.9	11.69

Discussion

Vitamin D continues to be a subject of worldwide research with the primary goal of studying its importance in immunity, particularly acute respiratory infections. The number of studies in Bulgaria examining the relationship between vitamin D levels and acute respiratory infections is presently scarce. Our research aimed to elucidate this relationship in the Bulgarian population and thus contribute to improving vit. D prophylaxis in childhood.

Our preliminary results showed that children with ARI more often have abnormalities in the vitamin D status compared to the control group. The lack of deviations in the level of PTH was probably due to the short exposure to various factors in the course of acute respiratory infections leading to vitamin D deficiency and the introduced vit D prophylaxis in infancy and early childhood.

These data coincide with the results reported by many studies – a high frequency of hypovitaminosis D in acute respiratory infections.

Similar findings were presented in a study published in 2015, which investigated the role of vitamin D in the course of acute lower respiratory tract infections in 347 hospitalized children, 38.6% of which were found to be insufficient for vitamin D and 18.7% were deficient. The results showed that 25(OH) D levels were significantly reduced and correlated with disease severity regarding oxygen requirements, clinical scales (Wood-Downes and GENVIP) and respiratory distress [11]. The same conclusion was made in the Vitamin D book by Harvard Medical School. It is stated that acute respiratory diseases, which cause most episodes of childhood broncho-obstructions, are most likely to occur in children with Vitamin D deficiency [12]. A 2015 New Zealand case-control study, which included 469

children aged <2 years and hospitalized for ARI, revealed 29% vit D insufficiency (in both case and control groups) and 26% vit D deficiency. It is concluded that vitamin D deficiency was more common in children hospitalized for acute respiratory infections than those treated in a community setting [13]. A hospital-based study of 25(OH) D levels in Mumbai, India, which included 108 children with recurrent respiratory diseases, reported significant relation between vitamin D deficiency and the incidence of acute respiratory infections. This research reported 75% vitamin D deficiency and 25% vitamin D insufficiency in the case group. [14] A 2021 prospective cohort study in Indonesia involving 422 pregnant women and tracking the vitamin D status of their children from birth to 12 months of age published results showing that vitamin D status at birth or at six months of age was not associated with an increased incidence of pneumonia, and longer maternal sun exposure during pregnancy was associated with a trend toward less frequent acute respiratory illness and pneumonia in infants [15].

Our preliminary results are consistent with the data from the studies mentioned above. Nevertheless, it is necessary to examine the topic on a larger scale to draw correct conclusions for the benefit of prophylaxis.

Conclusions

Our preliminary results prove the importance of vitamin D deficiency as a significant pathogenetic factor in the occurrence of acute respiratory infections. Monitoring the vitamin D status in children with ARI and establishing its deviations provides an opportunity to build a new therapeutic strategy. Maintaining an adequate vitamin D status is essential for children's health, and vitamin D replacement should be carried out in the event of insufficiency or deficiency.

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