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Correlation of serum vitamin A, D, and E with recurrent respiratory infection in children

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Abstract. – OBJECTIVE: To investigate the correlation of serum vitamin A, D, and E levels with a recurrent respiratory infection (RRI) in children.

PATIENTS AND METHODS: The medical records of 422 children with RRI (a study group) in Cangzhou Central Hospital from January 2015 to December 2018 were retrospectively analyzed (the study group was divided into an active group and a stable group). Further 100 healthy children who underwent physical examination at the same time were enrolled as a control group. High-performance liquid chromatography (HPLC) was used to determine vitamin A, D, and E levels, so as to analyze their differences between the groups.

RESULTS: Vitamin A, D, and E in the active and stable groups were significantly lower than those in the control group ($p < 0.001$); in the active group they were significantly lower than those in the stable group ($p < 0.001$). According to partial correlation analysis, in children with active RRI, vitamin A was respectively positively correlated with vitamin D (r=0.945, $p < 0.001$), and vitamin E (r=0.988, $p < 0.001$). Moreover, vitamin E was positively correlated with vitamin D (r=0.959, $p < 0.001$).

CONCLUSIONS: The deficiency of vitamin A, D, and E is positively correlated with the disease activity of children with RRI. Therefore, the supplement of vitamin A, D, and E through dietary adjustment is beneficial to the rehabilitation of the children.

Key Words:
Recurrent respiratory infection, Children, Vitamin A, Vitamin D, Vitamin E.

Introduction

Recurrent respiratory infection (RRI) is the most common pediatric respiratory disease[1,2]. The complex pathogenesis of RRI combined with children's poor resistance to respiratory virus results in the recurrence of the disease after treatment, which seriously affects children's physical and mental health and physical growth[3,4]. According to some reports[5,6], in addition to the infection of pathogenic microorganism, RRI is also closely related to fat-soluble vitamins.

Fat-soluble vitamins are indispensable micronutrients, and different vitamins play different roles in children's growth and development[7,8]. According to some studies[9-11], the decrease in immunity increases the risk of diseases, and the changes of vitamin A, D, and E in fat-soluble vitamins have a great influence on the immunity. The deficiency of vitamin A, D, and E reduces the resistance of the human body, easily leading to RRI. There are currently few such reports, which provide references for the clinical prevention of the disease. Therefore, vitamin A, D, and E levels in children undergoing normal physical examination and children with RRI were detected in this study to explore their correlation with RRI.

Patients and Methods

General Information

The medical records of 422 children with RRI in the department of pediatrics of Cangzhou Central Hospital from January 2015 to December 2018 were retrospectively analyzed. They were enrolled as the study group, and then divided into the active group (n=222) and the stable group (n=200). Further 100 healthy children who underwent physical examination at the same time were enrolled as the control group. Exclusion and inclusion criteria: (1) children clinically diagnosed with RRI were included in the study group[12]; (2) children with cognitive, movement, and language disorders were excluded; children with hepatic, coagulation and renal dysfunction or other infectious diseases were excluded. Children and their families were informed in advance and signed an informed consent form before the study. This study was approved by the Ethics Committee of Cangzhou Central Hospital.

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Experimental Methods

(1) Specimen collection: 2 mL of fasting blood was extracted, and then centrifuged at 3500 rpm/min for 5 min to separate the serum. Then, the separated serum was injected into a centrifuge tube, and stored in a refrigerator at low temperature for determination. (2) The serum vitamin A and E samples were detected quantitatively using high-performance liquid chromatography (HPLC) by Professional examiner [Beijing Hehe Medical Laboratory (Beijing, China)] and the tandem mass spectrometry (TSQ Altis mass spectrometer purchased from Thermo Fisher Scientific, Waltham, USA). Serum 25 (OH) D_2 in the serum was quantitatively detected by Sigma standard (Sigma-Aldrich, Darmstadt, Germany).

Statistical Analysis

The Statistical Product and Service Solution SPSS 19.0 [Bizinsight (Beijing) Information Technology Co., Ltd., Beijing, China] software system was used for statistical analysis. Count data were expressed as [n (%)] and tested by the Chi square (x^2-test). The measurement data were expressed as (x±s), and the One-way ANOVA test was used for comparison between groups. $p < 0.05$ indicates a statistically significant difference.

Results

General Information

There was no statistically significant difference in the general information between the three groups ($p > 0.05$). The two groups of children were comparable. More details are shown in Table I.

Comparison of Vitamin A, D, and E

Comparison of vitamin A: vitamin A was (0.37±0.09) mg/L in the control group, (0.19±0.05) mg/L in the active group, and (0.28±0.07) mg/L in the stable group. Vitamin A in the active and stable groups was significantly lower than that in the control group ($p < 0.001$), and it was significantly lower in the active group than in the stable group ($p < 0.001$). More details are shown in Figure 1.

Comparison of vitamin D: vitamin D was (66.24±1.76) nmoL/L in the control group, (51.26±1.23) nmoL/L in the active group, and (60.10±1.05) nmol/L in the stable group. Vitamin D in the active and stable groups was significantly lower than that in the control group ($p < 0.001$), and it was significantly lower in the active group than in the stable group ($p < 0.001$). More details are shown in Figure 2.

Comparison of vitamin E: vitamin E was (8.24±2.10) mg/L in the control group, (5.86±1.58)

Table I. General information.

Groups	Study Group		Control group (n=100)	X^2	p
	Active group (n=222)	Stable group (n=200)			
Gender				0.691	0.708
Male	120 (54.05)	106 (53.00)	58 (58.00)		
Female	102 (45.95)	94 (47.00)	42 (42.00)		
Age (years)					
<1	80 (36.04)	64 (32.00)	32 (32.00)	0.930	0.628
≥1 and <3	70 (31.53)	69 (34.50)	34 (34.00)	0.460	0.795
≥3	72 (32.43)	67 (33.50)	34 (34.00)	0.095	0.954
Lack of exercise				1.382	0.501
Yes	130 (58.56)	114 (57.00)	64 (64.00)		
No	92 (41.44)	86 (43.00)	36 (36.00)		
Passive inhalation of smoke				0.930	0.628
Yes	80 (36.04)	64 (32.00)	32 (32.00)		
No	142 (63.96)	136 (68.00)	68 (68.00)		
Particular about food				1.609	0.447
Yes	140 (63.06)	127 (63.50)	70 (70.00)		
No	82 (36.94)	73 (36.50)	30 (30.00)		
Chronic medical history of nasopharynx				1.979	0.372
Yes	110 (49.55)	105 (52.50)	58 (58.00)		
No	112 (50.45)	95 (47.50)	42 (42.00)		

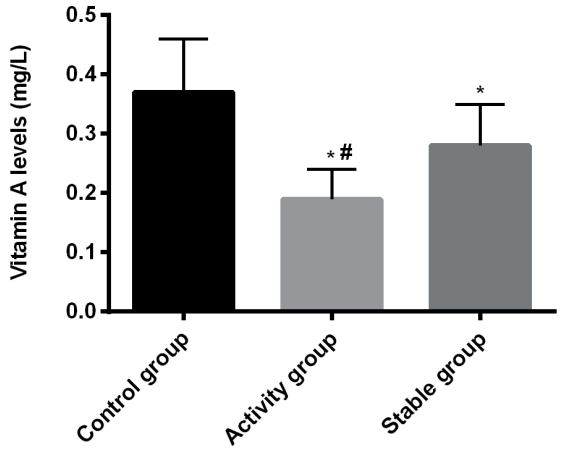

Figure 1. Comparison of vitamin **A,** According to HPLC and tandem mass spectrometry, * indicates that vitamin A in the active and stable groups is significantly lower than that in the control group ($p < 0.001$); # indicates that vitamin A in the active group is significantly lower than that in the stable group ($p < 0.001$).

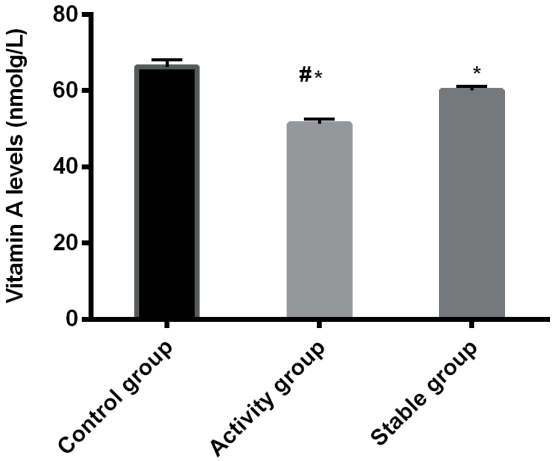

Figure 2. Comparison of vitamin D. According to HPLC and tandem mass spectrometry, * indicates that vitamin D in the active and stable groups is significantly lower than that in the control group ($p < 0.001$); # indicates that vitamin D in the active group is significantly lower than that in the stable group ($p < 0.001$).

mg/L in the active group, and (6.47±1.98) mg/L in the stable group. Vitamin E in the active and stable groups was significantly lower than that in the control group ($p < 0.001$), and it was significantly lower in the active group than in the stable group ($p < 0.001$). More details are shown in Figure 3.

Correlation of Vitamin A, D, and E in Children with Active RRI

Correlation of vitamin A with vitamin D and E: according to partial correlation analysis, in children with active RRI, vitamin A was positively correlated with vitamin D (r=0.945, $p < 0.001$), and vitamin E (r=0.988, $p < 0.001$). More details are shown in Figure 4 A-B.

Correlation of vitamin E with vitamin D: according to partial correlation analysis, in children with active RRI, vitamin E was positively correlated with vitamin D (r=0.959, $p < 0.001$). More details are shown in Figure 5.

Discussion

Vitamin A, D, and E levels in children undergoing normal physical examination and children with RRI were detected in this study to explore their correlations with RRI. Vitamin A, D, and E in the active and stable groups were significantly lower than those in the control group, and they were significantly lower in the active group than in the stable group. Vitamin A, an essential fat-soluble vitamin for human body, has a great influence on maintaining the immune function of the body[13]. The deficiency of vitamin A causes severe infectious diseases, and the long-term deficiency directly increases the mortality rate of the children[14]. Vitamin D regulates the hematopoietic system, inhibits tumor cell growth, and regulates endocrine[15-17]. The supplement of

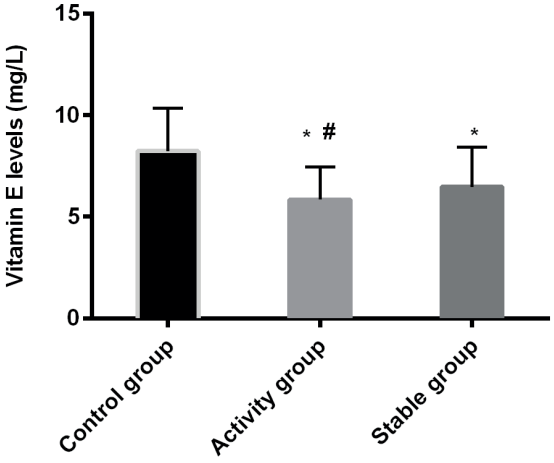

Figure 3. Comparison of vitamin E. According to HPLC and tandem mass spectrometry, * indicates that vitamin E in the active and stable groups is significantly lower than that in the control group ($p < 0.001$); # indicates that vitamin E in the active group is significantly lower than that in the stable group ($p < 0.001$).

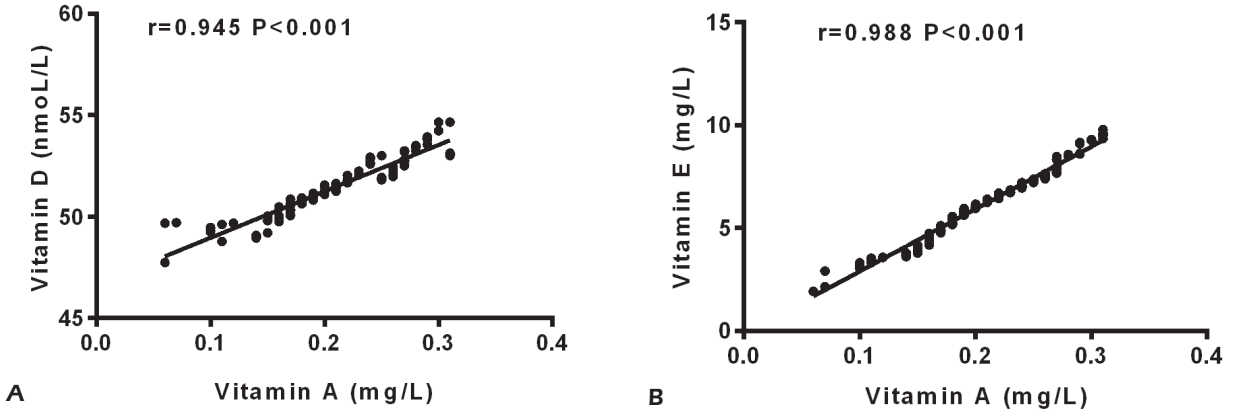

Figure 4. A-B, Correlation of vitamin A with vitamin D and E. According to partial correlation analysis, in children with active RRI, vitamin A was positively correlated vitamin D (r=0.945, $p < 0.001$), and vitamin E (r=0.988, $p < 0.001$).

vitamin D greatly influences the clinical effect on patients with respiratory infection. Martineau et al[18], detected that vitamin E, a good antioxidant equally important to the physiological function of the body, stabilizes the structure of cell membrane and resists lipid peroxidation, and its supplement promotes cellular immunity[19-21]. Patients with respiratory infection have low vitamin A, D, and E levels, proving the results of this paper[22,23]. It is believed that vitamin A, D, and E levels in children with RRI are lower than those in healthy children, and they are significantly lower in children with active RRI than in children with stable RRI. Therefore, the supplement of vitamins should be distinguished in children with RRI of different disease status. Moreover, in children with active RRI, vitamin A was positively correlated with vitamin D and E, and vitamin E was positively correlated with vitamin D. Bergman et al[24] showed that the deficiency of vitamin D was positively correlated with the severity of respiratory infection in children. Beale observed that[25], the serum calcium level affects the cell membrane permeability of capillaries, and the disease in it causes respiratory infection. Serum calcium level is positively correlated with vitamin D level[26], so maintaining the normal level of vitamin D can effectively reduce respiratory infection. Hejazi et al[27] studied the correlation of vitamin levels with respiratory infection. The proper increase of vitamin levels effectively reduces the damage of lipid peroxide to the body, enhances the immunity, and greatly reduces the incidence rate of the related respiratory diseases.

There are deficiencies in this study. For example, the regional limitations of subjects included and the failure to analyze the correlation of vitamin levels in stable RRI have affected the statistics. Therefore, to improve this work, in later investigations, children in different regions will be added, and the latest research will be referred to add corresponding research programs.

Conclusions

The deficiency of vitamin A, D, and E is positively correlated with the disease activity of children with RRI. The number of respiratory infections is significantly reduced, so it is believed that the supplement of vitamin A, D, and E through dietary adjustment is beneficial to the rehabilitation of the children.

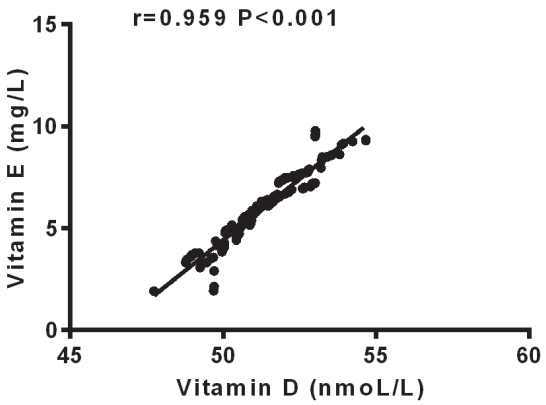

Figure 5. Correlation of vitamin E with vitamin D. According to partial correlation analysis, in children with active RRI, vitamin E was positively correlated with vitamin D (r=0.959, $p < 0.001$).

Conflict of Interests

The Authors declare that they have no conflict of interests.

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