The correlation between fat-soluble vitamin levels and inflammatory factors in pediatric community-acquired pneumonia: a retrospective study.

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Research Article

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Abstract

Objective: To analyze the correlation between vitamin A, D, E levels and tumor necrosis factor (TNF-a), interleukin-1 (IL-1), interleukin-10 (IL-10), neutrophil, C-reactive protein (CRP) levels in pediatric community-acquired pneumonia (CAP).

Methods: 110 children with CAP and 100 normal children were collected. The concentrations of fat-soluble vitamin A, D, E, the proportion of leukocytes and subtypes, the concentration of CRP, and the concentration of cytokines TNF-a, IL-1, and IL-10 were tested. Differences between vitamin levels and inflammatory factor levels were compared between the two groups. The correlation between vitamin levels and inflammatory factor levels was analyzed in children with CAP.

Results: The hemoglobin, leukocyte concentration, neutrophils, monocytes and CRP concentration in the CAP group showed significant differences (P < 0.05). The levels of vitamin A, D, and E in the CAP group were lower than those in the control group, and the levels of TNF-a and IL-1 were higher than those in the control group, and the difference was statistically significant (P<0.05). IL-10 levels have no significant between 2 groups (P > 0.05). The Pearson analysis showed that the vitamin A, D, and E levels were all correlated with the TNF-a, IL-10, and CRP levels (P < 0.05).

Conclusion: The vitamin A, D, E levels of CAP children were lower than normal children. The content of fat-soluble vitamins are somewhat correlated with the secretion of TNF-a and IL-10.

Background

Community-acquired childhood pneumonia (CAP) is a common respiratory disease that is mostly caused by mixed infections of various pathogens. It remains the primary cause of early childhood death in many areas due to the susceptibility of children to the disease, and low childhood rates of immunization. At present, the diagnosis of CAP mainly depends on the clinical manifestations of patients, chest radiography, and the pathogen detection of respiratory secretions. We hope that there are other aids to diagnose pediatric CAP on the basis of routine diagnosis and treatment. Currently, part of the studies suggest that have shown that the vitamin levels in CAP patients have a certain relationship with the treatment and prevention of the disease. But some scholars believe that vitamin supplementation alone does not reduce the risk of acquired pneumonia. The clinical manifestations of CAP in children is mainly inflammatory effect, and the therapeutic effect of the disease can be evaluated by the inhibition and elimination of inflammation. The mediating factors of inflammation mainly include the cytokines TNF-a, IL-1, IL-10, CRP and others. Since most of the existing literature studies the effect of only one vitamin on pneumonia, this study specifically analyzed the levels of three lipid-soluble vitamins in CAP patients in children aged 4-9 years. In addition, we also studied the relationship between vitamins and inflammatory-mediated factors in pediatric CAP patients.

Data And Methods
1.1 Data

A total of 350 pediatric cough patients who first visited the ED between January 2019 and January 2021 were collected. After excluding other respiratory diseases besides CAP and patients who had been used and were unwilling to participate in this experiment, 110 patients diagnosed with CAP were included in the study. The type of hospital in which patients were recruited was a specialized children's hospital emergency room in the urban area, where children were routinely vaccinated in the area. A total of 100 normal children aged 4-9 years who underwent physical examination in the child health department of our hospital were randomly collected as negative controls. Considering factors such as large individual differences in children, we chose the child's age range between 4 and 9 years, excluding differences in sex, height, weight, etc. The study was reviewed and approved by the ethics committee of our hospital, all methods were performed in accordance with the relevant guidelines and regulations.

1.2 Methods

1.2.1 CAP Diagnostic criteria: Refer to the relevant diagnostic criteria for community acquisition of pneumonia in children, children who meet the following conditions can be diagnosed as CAP: 1. Recent cough, sputum or the original respiratory symptoms of aggravation and purulent sputum. 2. Symptoms of fever occur (Mercury thermometer subaxillary temperature > 37.5°C). 3. Wet rale appears in the lungs. 4. More percentage of leukocytes or neutrophils. 5. Chest radiographs or CT showed large areas of dense or interstitial changes. All patients in this study met more than one of the one to four symptoms of the above diagnostic criteria plus the fifth criteria.

1.2.2 Exclusion criteria: Patients with hospital-acquired pneumonia, pulmonary tuberculosis, lung tumor, pharyngitis, bronchitis and other upper respiratory tract diseases were excluded. Patients with recent supplementation with various forms of vitamin or folic acid were excluded. Lesions in the adjacent organs of the lung, abnormal immune function, and patients with a long history of chronic disease were excluded.

1.2.3 Detection of leukocyte classification: 3ml of peripheral blood from CAP patients and control groups, EDTA anticoagulant tube anticoagulation, and percentage of leukocyte classification and other cells using XN-3000 (Sysmex, Germany).

1.2.4 Detection of CRP concentration: 20μl of whole blood samples were injected into the detection tube, and the blood CRP concentration was read out in a specific proteometer BC5390 (Mindray Biomedical Electronics Co., Ltd., Shenzhen, China).

1.2.5 Detection of fat-soluble vitamin levels: Plasma was isolated by high-speed centrifugation, 200μl of serum was absorbed, and the serum concentration of vitamin A, D and E was measured by high-performance liquid chromatography (HPLC) (Agilent, USA).
1.2.6 Detection of related inflammatory cytokines: Detect the concentration of cytokines TNF-a, IL-1 and IL-10 in serum in a microplate reader (Edkang Biotech Co., Ltd. Yantai, China) according to the operating instructions of ELISA kit (Enzyplate Biotechnology Co., Ltd. Jiangsu, China).

1.3 Statistical analysis

Data analysis was performed using SPSS17.0 statistical software (IBM, Armonk, NY, USA), measurement data in mean ± standard deviation, independent sample t-test; count data in rate (%), continuous corrected chi-square test, and P<0.05. difference. The correlation of the two was analyzed by Pearson, whose correlation coefficient is indicated as r, and P<0.05 indicates a correlation between the two.

Results

2.1 Comparison between the two groups of basic cases

No anemia was observed between both groups (RBC>4×1012/L), there were no statistical differences in age, sex ratio, body mass index (BMI), first diagnosis rate, and medication history between the two groups (P>0.05). The hemoglobin (Hb) levels were lower than the control group, and the white blood cell (WBC), neutrophils (NE)%, monocyte (MO)% and CRP levels were higher than the control group, which were statistically significant (P<0.05). (Table 1)

2.2 Comparison of fat-soluble vitamins and inflammatory factors between the two groups

Vitamin A, D and E in CAP group were lower compared with control group, and levels of TNF-a and IL-1 were higher than controls were statistically significant (P<0.05), cytokine IL-10 levels were slightly higher in CAP group than in control group, but not significant (P>0.05). (Table 2)

2.3 Correlation analysis between vitamins and inflammatory factors in pediatric CAP patients

A negative correlation between vitamin A, D, E and TNF-a, CRP in pediatric CAP patients and a positive correlation between IL-10 (P<0.05). (Table 3, Fig. 1.)

2.4 Correlation analysis between the absorption of various lipid-soluble vitamins in children

There was no correlation between the absorption of vitamin A and the absorption of vitamin D and E in children (P>0.05), and there was a significant correlation between the absorption of vitamin D and vitamin E (P<0.05). (Table 4)

Discussion

Infectious diseases in children are a common cause of death in children. According to reports, more than 3 million children dying under the age of 5 worldwide are caused by infections. Community-acquired pneumonia in children is a common infectious disease and whose clinical manifestations are fever,
cough, infection, dyspnea, etc. As the clinical manifestations of childhood CAP are very similar to other respiratory diseases, some children lack typical clinical symptoms, which are easy to cause missed diagnosis or misdiagnosis. There are many causes of CAP in children, and various factors are interrelated. At present, it is believed that viral and Mycoplasma pneumoniae and bacterial infections are the leading causes of CAP in children. In addition, the decreased level of immunity caused by malnutrition is also an important cause of CAP.

The existence of certain vitamin levels in the body is necessary to maintain the body's metabolism, most vitamins can not be synthesized by themselves, it mainly comes from food. Vitamins are divided into two categories: lipid-soluble and water-soluble. Although their content in the body is very small, it is of important significance to maintain the body's immune self-stability, immune surveillance, immune defense and other roles. In recent years, the awareness of purposeful vitamin supplementation in the diet of children has increased. However, due to the greater children's demand for vitamins, the absorption level is smaller than adults, children's self-discipline is not strong, picky eating habits and other reasons, leading to the common phenomenon of low vitamin levels in preschool children. At present, some studies have shown that there may be a certain relationship between the lack of certain vitamins in the body and the occurrence of CAP. The main reasons are: on the one hand, vitamin can promote the expression of inflammatory factors or anti-inflammatory factors, and then enhance the body's immune function. On the other hand, when pathogens invade the respiratory tract, vitamins can promote the differentiation of immune cells, and increase the effect of immune cells phagocytosis bacteria. According to the relevant literature, the standard levels of fat-soluble vitamins in children were VA > 0.30 μg/mL, VD > 20~100 ng/mL, and VE > 7 μg/mL. The fat-soluble vitamin levels of both the CAP and control children met the above criteria. However, the levels of VA, VD, and VE were all lower in the pediatric CAP patients than in the controls, and the difference was statistically significant (P < 0.05). This suggests that vitamin levels are generally lower in CAP patients in this region compared to normal children. In addition, we found a close relationship between vitamin D and E when analyzing the relationship between vitamin A, D, and E absorption in children aged 4-9 years in this region. However, it is interesting that vitamin A absorption is not related with D and E. The result is consistent with the relevant reported results, but the specific reasons are not stated in the report.

Of the 110 patients in this study, 93 patients had inflammatory manifestations, accounting for 84.5% of the population, and all the patients developed a febrile response. Its auxiliary examination mainly showed increased leukocytes, increased percentage of neutrophils, and increased CRP levels. Inflammatory response is the main clinical manifestation of CAP patients, and it is the body's defense response to bacteria, viruses and other foreign invasive substances. The occurrence of inflammation mainly depends on the activation of immune cells and the release of inflammatory factors, mainly including TNF-a, IL-1, IL-6, IL-8, IL-10, etc. Among them, TNF-a and IL-1 belong to the proinflammatory factors, while IL-10 belongs to the inflammatory suppressor. The study showed that the levels of inflammatory mediating factors TNF-a and IL-1 were all higher in pediatric CAP patients than in normal people, with no difference in the levels of IL-10. This is mainly because this population is all first diagnosed patients, and the body is...
in a state of immune activation at the beginning of virus invasion, therefore, the IL-10 level mainly for this immunosuppression is still at a low level. This result suggests that whether the effect of the treatment can be monitored by the detection of inflammatory factors when treating CAP? The pearson analysis showed some correlation between the levels of fat-soluble (VA, VD, VE) in CAP and the levels of cytokine (TNF-α, IL-10) in CAP patients. These results indicate that the levels of vitamin VA, VD, and VE are closely related to the function of immunomodulatory regulation.

There are certain difficulties in the diagnosis and treatment of CAP in children, and inflammation is an important manifestation. At present, the treatment of CAP is mainly oral antibiotics, and the severe patients even need intravenous antibiotics. Aamoxicillin is the first antibiotic in preschool children. Vitamins in the body can promote immune cells to secrete related cytokines, and the level of cytokines has an important relationship with the occurrence and inhibition of inflammation. The intake and supplementation of vitamins are of great significance to the prevention and treatment of CAP in children. Related literature shows that in addition to the use of antibiotics and vaccine vaccination on CAP, patient age, region, nutrition, socioeconomic factors, and immune function also have an important impact on the occurrence of CAP in children.

**Conclusions**

After excluding the influence of the above factors, the results of this study showed that there was a certain correlation between the levels of VA, VD and VE in children with CAP and the cytokines TNF-α and IL-10. The results provide new ideas for the prevention of CAP in children.

**Abbreviations**

VA: vitamin A; VD: vitamin D; VE: vitamin E; CAP: community-acquired pneumonia; TNF-α: tumor necrosis factor-α; IL-1: interleukin-1; interleukin-10: interleukin-10; CRP: C-reactive protein; BMI: body mass index.

**Declarations**

**Acknowledgements**

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**Authors’ contributions**

Qing-tai Wang: Project development, Experimental design, Data Collection; Jian-wei Wei: Data Collection; Hua Jiang: Experimental operation; Gangxin Chen: Data analysis, Manuscript writing, Manuscript editing.

**Funding**
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**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

This study was approved by the ethics committee of Fujian Provincial Maternity and Children Hospital. Informed consent was obtained from all subjects and/or their legal guardian(s).

**Consent for publication**

All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work.

**Competing interests**

The authors declare that they have no competing interests.

**References**


### Table 1

Comparison of the fundamentals between the two groups (n=210)

<table>
<thead>
<tr>
<th></th>
<th>CAP group n=110</th>
<th>Control group n=100</th>
<th>t / X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>5.78±1.23</td>
<td>5.70±1.18</td>
<td>0.48</td>
<td>0.62</td>
</tr>
<tr>
<td>BMI</td>
<td>14.47±3.07</td>
<td>14.46±2.78</td>
<td>0.01</td>
<td>0.98</td>
</tr>
<tr>
<td>Sex ratio (%)</td>
<td>59.10 65/45</td>
<td>53.00 53/47</td>
<td>0.79</td>
<td>0.37</td>
</tr>
<tr>
<td>First diagnosis rate (%)</td>
<td>95.50 105/5</td>
<td>98.00 98/2</td>
<td>-1.05</td>
<td>0.30</td>
</tr>
<tr>
<td>RBC(10¹²/L)</td>
<td>4.98±0.28</td>
<td>5.01±0.35</td>
<td>-0.56</td>
<td>0.48</td>
</tr>
<tr>
<td>Hb(g/L)</td>
<td>135.21±10.81</td>
<td>156.54±13.68</td>
<td>-4.56</td>
<td>0.00</td>
</tr>
<tr>
<td>WBC(10⁹/L)</td>
<td>11.52±3.35</td>
<td>7.26±2.16</td>
<td>31.25</td>
<td>0.00</td>
</tr>
<tr>
<td>NE(%)</td>
<td>70.35±10.54</td>
<td>51.21±11.16</td>
<td>43.56</td>
<td>0.00</td>
</tr>
<tr>
<td>LY(%)</td>
<td>20.35±8.65</td>
<td>20.89±10.35</td>
<td>0.45</td>
<td>0.71</td>
</tr>
<tr>
<td>MO(%)</td>
<td>9.05±1.65</td>
<td>6.04±0.35</td>
<td>17.88</td>
<td>0.00</td>
</tr>
<tr>
<td>BA(%)</td>
<td>1.03±0.35</td>
<td>1.39±0.48</td>
<td>0.75</td>
<td>0.39</td>
</tr>
<tr>
<td>CRP(μg/ml)</td>
<td>14.71±10.43</td>
<td>0.39±0.22</td>
<td>55.28</td>
<td>0.00</td>
</tr>
</tbody>
</table>

BMI, body mass index; RBC, red blood cells; Hb, hemoglobin; WBC, white blood cell; NE, neutrophils; LY, lymphocytes; MO, monocyte; BA, basophils; CRP, C-reactive protein.

### Table 2

Comparison between fat-soluble vitamins and inflammatory factors in the two groups (n=210)

<table>
<thead>
<tr>
<th></th>
<th>CAP group n=110</th>
<th>Control group n=100</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA(μg /ml )</td>
<td>0.41±0.19</td>
<td>0.48±0.18</td>
<td>-10.13</td>
<td>0.00</td>
</tr>
<tr>
<td>VD (ng /ml )</td>
<td>87.55±8.71</td>
<td>89.89±11.38</td>
<td>-6.49</td>
<td>0.00</td>
</tr>
<tr>
<td>VE(μg /ml )</td>
<td>17.92±7.79</td>
<td>20.68±10.02</td>
<td>-8.63</td>
<td>0.00</td>
</tr>
<tr>
<td>TNF-a(pg/ml)</td>
<td>46.38±9.73</td>
<td>30.06±6.13</td>
<td>56.84</td>
<td>0.00</td>
</tr>
<tr>
<td>IL-1(pg/ml)</td>
<td>8.86±2.53</td>
<td>6.03±1.48</td>
<td>38.71</td>
<td>0.00</td>
</tr>
<tr>
<td>IL-10(pg/ml)</td>
<td>34.27±7.60</td>
<td>33.87±7.21</td>
<td>1.51</td>
<td>0.13</td>
</tr>
</tbody>
</table>

VA, Vitamin A; VD, Vitamin D; VE, Vitamin E; IL-1, interleukin-1; IL-10, interleukin-10; TNF-a, tumor necrosis factor-a;
Table 3

Analysis of the correlation between vitamins and inflammatory factors in pediatric CAP patients (n=210)

<table>
<thead>
<tr>
<th></th>
<th>TNF-a(pg/ml)</th>
<th>IL-1(pg/ml)</th>
<th>IL-10(pg/ml)</th>
<th>CRP (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA (μg/ml)</td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>-0.378</td>
<td>0.000</td>
<td>-0.024</td>
<td>0.167</td>
<td>0.183</td>
</tr>
<tr>
<td>VD (ng/ml)</td>
<td>-0.151</td>
<td>0.000</td>
<td>-0.027</td>
<td>0.134</td>
</tr>
<tr>
<td>VE (μg/ml)</td>
<td>-0.175</td>
<td>0.001</td>
<td>-0.022</td>
<td>0.225</td>
</tr>
</tbody>
</table>

Table 4

Analysis of the correlation between vitamins (n=210)

<table>
<thead>
<tr>
<th></th>
<th>VA (μg/ml)</th>
<th>VD (ng/ml)</th>
<th>VE (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA (μg/ml)</td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>1.000</td>
<td>-</td>
<td>0.041</td>
<td>0.107</td>
</tr>
<tr>
<td>VD (ng/ml)</td>
<td>0.041</td>
<td>0.107</td>
<td>1.000</td>
</tr>
<tr>
<td>VE (μg/ml)</td>
<td>0.037</td>
<td>0.144</td>
<td>0.958</td>
</tr>
</tbody>
</table>

Figures
Figure 1

The correlation between Fat-vitamins and inflammatory factors in pediatric CAP patients