The Role of the Micronutrients; Vitamin A, Vitamin B12, Iron, Zinc, Copper Levels of Children with Lower Respiratory Tract Infections

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Abstract

Objective: Lower respiratory tract infection is common in children younger than 5 years and is the leading infection cause of childhood mortality and hospitalization. Deficiencies in vitamin A, zinc (ZN), copper (Cu), iron (Fe), and micronutrients, such as vitamin B12, are thought to be causes of respiratory tract infections as a trigger. We aimed to detect levels of the micronutrients vitamin A, Zn, Cu, Fe, and vitamin B12 in children with lower respiratory tract infections.

Material and Methods: A total of 98 patients between 1 month and 5 years of age with a diagnosis of lower respiratory tract infection were enrolled between February 2011-2012 at Ankara Eğitim ve Araştırma Hospital, Clinic of Child Health and Diseases. The control group included 47 healthy children with the same age who did not have any pathologic findings and history of chronic diseases. In these patients, the clinical and radiological findings of acute phase reactants, vitamin A, vitamin B12, Zn, Cu, and Fe levels were studied, and the groups were compared.

Results: Of the patients in the study, 63 (64.3%) were men and 35 (35.7%) were females; mean age was 21.4 (±17.6) (1-60) months. The most common findings on physical examination were tachypnea in 85 (86.7%), cracles 73 (74.5%), and rhonchi 59 (60.2%), respectively. White blood cell (WBC) (p=0.001), sedimentation (Sed) (p<0.001), and CRP (p=0.010) levels were significantly higher in the patient group. Vitamin A levels in all patients (p=0.001) and Fe levels (p=0.001) were found to be significantly lower than the control group. Zn level was lower in the patient group than in the control group but was not statistically significant. C and vitamin B12 levels in terms of the difference between groups was detected.

Conclusion: In patients with lower respiratory tract infection, vitamin A, Zn, and Fe levels were lower. In patients diagnosed with lower respiratory tract infections vitamin A and Zn supplementation is recommended. Fe is recommended to prevent lower respiratory tract infections.

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Introduction

Pneumoniais an inflamotary process that develops inalveoli andinterstitium as a response to infection-causing factors such as bacteria and viruses. Since pneumonia in infancy is difficult to discriminate from acute bronchiolitis, the term acute lower respiratory tract infection (LRTI) inclusive of these both diseases is used (1-5). According to the 2005 report of the World Health Organization, ALTIs account for the 20% of 10 million under 5-year-old pediatric mortality annually (6, 7). Thirty to forty percent of all hospitalizations are due to pneumonia and mortality rate in developing countries is 7-250 times more than in developed countries (6-8).

Vitamin A deficiency pneumounae in children under 5 years old impact 140-250 million children all over the world. The prevalence of vitamin A and zinc deficiency is 20-60% in Africa and Southeast Asia and <5% in the developed countries (9, 10). Vitamin A deficiency increases

the tendency to anemia and infections (6-8). The World Health Organization (WHO) reports that pediatric mortality will decrease 23% when children are supplemented with vitamin A (9, 10).

Zinc and vitamin A are important antioxidants and the zinc and vitamin A taken in by diet are crucially necessary for the body to function healthily (11). In pneumonia, it is commonly known that there is an imbalance between cellular antioxidants and oxidant mechanisms. Similarly, they play a crucial role in the prevention of diarrhea and lower respiratory tract infections.

Zinc deficiency is involved in 1/3 of the world population, most of whom are children and is responsible for 0.8 million childhood mortality (9). A study found that zinc was acytoprotective agent against toxin and inflammatory mediators just like in respiration epithelium (12-14).

It is commonly thought that the lack of micronutrients such as vitamin A, zinc (Zn), copper (Cu), iron (Fe), vitamin B^{12} is a trigger for respiratory tract infections. In this study, we aimed to establish the levels of micronutrients such as vitamin A, zinc (Zn), copper (Cu) , iron (Fe), vitamin B^{12} in respiratory tract infections.

Material and Methods

98 pediatric patients aged between one month and 5 years clinically (according to the criteria set up at the consensus report of Turkish Thoracic Society in 2009) diagnosed with LRTI and hospitalized and monitored in the Pediatric Diseases Clinic of Ankara Training and Research Hospital were included in this study (15). The control group children were selected from a group of 47 same-age children without pathological symptoms in their physical examination and chronic disease.

This study was planned as cross-sectionally and approved by the Local Ethical Committee of our Hospital. Written consent was taken from patients and/or their families. The study was carried out between 2^{nd} of February, 2001 and 2^{nd} February, 2012 for the period of 12 months. Patients with chronic diseases such as congenital heart disease and malnutrition were excluded from the study.

Lower respiratory tract infection diagnosis was made by clinical symptoms and findings and/or presence of infiltration in the chest radiography. Here we aimed clinically to find the presence of acute respiratory symptoms in patients. For pneumonia diagnosis, age-based tachypnea criteria set up by the World Health Organization was used (Table 1) (16). In order to determine the severity of pneumonia, symptoms such as retraction in the chest wall and cyanosis were made use of.

Information regarding admission date, age, gender, pulse rates, chest cell retraction, rale, rhonchus and other examination findings of the children included in the study were recorded down. Blood samples were taken from al the patients for complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), iron, (Fe), zinc (Zn), vitamin B^{12} and vitamin A tests. All the blood samples were analyzed at the laboratory of Ankara Training and Research Hospital.

Table 1. Pulse rates and tachypnea criteria set up by age by the World Health Organization

Age	Normal breathing rate (Breathing rate/ minute)	Tachypnea limit (Breathing rate/ minute)
0-2 months	40-60	60
3-11 months	25-40	50
12-59 months	20-30	40
>5 years	15-25	30

The level of Vitamin A was analyzed by the method of High Performance Liquid Chromatography (HPLC) (Agilent 1100, Germany, kit-chromsystems, Germany); and zinc, iron and copper were analyzed by the immunoturbidimetric method on 570-700 wave length (Olympus AU 2700, Japan, kit-randox, UK). Serum was divided into two parts as normal and low based on the reference values whose vitamin A levels were given. While considering the zinc level, the values between 9.8-18.1 µmol/L were defined as normal for the 0-19 age group.

The data analyses was performed by the "SPSS for Windows 16" package program. If the data was distributed normally in two-group studies, the Student T test was used; for the comparison of Categorical variables, chi-square test was used. Statistical signiŞcance was accepted as $p<0.05$.

Results

Ninety-eight patients diagnosed with LRTI were included in the study. Sixty-three (64.3%) of the patients were male and thirty-five (35.7%) female, and average age of both groups was 21.4 (±17.6) months, (range is 1-60 months). The control group was composed of same age group (1-60 months) with average age of 25.0 (±20.8) months, involving 47 health children of whom 26 (55.3%) were male and 21 (44.7%) female patients. In regard of the demographic features, no difference was found between the patients and control group with regards to age and gender.

The most common findings in physical examination were tachypnea 85 (86.7%), rale 73 (74.5%), rhonchus 59 (60.2%), intercostal retractions 39 (39.8%) and subcostal retractions 21 (21.4%).

Table 2. Comparison of the symptoms of acute phase reactants oh the patients

Blood count	Control (n=47)	Patient (n=98)	P
BK (10^9/L)	8.33±2.42 (3.5-12.1)	11.67±4.66 (3.3-28.5)	0.001*
Neutrophil (%)	32.9±16.4 (11.3-66.0)	46.15±22.01 (3.7-92.0)	0.001*
Lymphocyte (%)	60.8±14.5 (32.0-86.0)	48.5±19.8 (6.4-80.0)	0.001*
Eosinophil (%)	2.1±1.9 (0.0-5.4)	2.15±4.4 (0.0-34.2)	0.106
Hb (gr/dL)	11.7±1.2 (8.9-14.4)	11.2±1.3 (8.5-15.0)	0.285
Plt (10^3/mL)	300.42±1.01 (32.0-397.0)	362.80±1.3 (145.0-1104.0)	0.010*
Sed (mm/saat)	10.4±10.4 (2.0-46.0)	26.4±22.1 (2.0-120.0)	<0.001*
CRP (mg/L)	0.39±0.58 (0.01-1.20)	2.3±4.5 (0.100-10.900)	0.010*
SPO_2	98.5±1.1 (98.0-99.0)	95.7±2.3 (90.0-99.0)	0.378

*p<0.05
BK: leukocyte; Hb: hemoglobin; Plt: thrombocyte; Sed: sedimentation; CRP: c-reactive protein SPO_2: arterial blood oxygen saturation

Table 3. Comparison of micronutrient levels of patient group and control group

	Control	Patient	P
Fe (mg)	44.2±25.3 (7.0-98.0)	28.1±21.4 (4.0-152.0)	0.001*
Zn (mg)	14.3±4.8 (7.6-30.0)	12.7±5.5 (4.0-25.4)	0.412
Cu (mg)	18.9±6.2 (8.5-35.0)	20.2±5.6 (6.3-32.4)	0.068
Vit A (µg)	0.92±0.36 (0.70-1.85)	0.67±0.31 (0.28-2.14)	0.001*
Vit B^{12} (µg)	402.8±197.4 (38.0-743.0)	443.4±24.2 (171.0-4999.0)	0.340
*p<0.05			

When whole patient group was compared with the control group, it was found that white blood cell (WBC), sedimentation (Sed) and CRP levels were significantly higher in the patient group (p=0.010) (Table 2).

It was found that vitamin A level and iron (Fe) level in the patient group were significantly lower compared to control group (p=0.001); no significant difference was found in zinc (Zn) level between two groups despite it was lower in the patient level (Table 3).

Discussion

The fact that lower respiratory tract infections are still at the top list of pediatric mortality in developing countries and Turkey can be explicated by such reasons as low socio-economic level, low per capita income, high carbohydrate low protein diet, crowded and insufficient family planning.

Zinc and vitamin A taken in through diet is an important antioxidant and are significantly crucial for the healthy functioning of the body (11). It is known that in pneumonia, an imbalance occurs between cellular antioxidants and oxidant mechanisms. Similarly, they play crucial roles in protection from diarrhea and lower respiratory tract infections. The studies revealed that zinc was a cytoprotective agent against toxin and inflammatory mediators just like in respiration epithelium (12-14).

In a study done by Al-Sonboli et al. (17), they found that patients with lower respiratory tract infection disease caused byrespiratory syncytial virus (RSV) and human meta pneumovirus (HMPV) were analyzed for vitamin A and other micronutrient levels together and they were significantly low.

In double-blind placebo controlled study done by Fawzi et al., (18) in Tanzania, half of the patients diagnosed with pneumonia were given vitamin A supplements, the other half of the patients were given placebo. Although the mortality rate in the group given vitamin A was distinctly low, no significant difference was found regarding hospital-stay duration and when compared with group who were given placebo in the clinic.

In a randomized-controlled study done by Imdad et al. (18) in Pakistan, it was found that children aged between 6 months and 5 years diagnosed with lower respiratory tract infections were followed up for the effects of supplementary vitamin A on mortality and morbidity, there was a clear decrease in comparison to the control group.

In a study done by Cameron et al. (20) in Canada, they investigated the relationship between acute otitis media, acute lower respiratory tract infections and incidence of lower respiratory-tract infections-related hospitalization in pre-school children in whose cord blood, vitamin A level was examined. The cord blood vitamin A levelin patients hospitalized for acute otitis media and lower respiratory tract infections was significantly low; but, the cord blood vitamin A level in patients hospitalized for LRTI was in the normal range.

In a study done by Büyükgebiz et al. (21) in Ankara, the vitamin A level in pre-school children with acute

respiratory tract infection and recurrent diarrhea was significantly lower than the control group.

In a study done by Haidar et al. (22) in Ethiopia., children aged between 6 months and 6 years given vitamin A supplement were followed up for morbidity incidence, and it was found that it significantly reduced the development of many infectious diseases such as inflammatory diseases, diarrheaand measles.

A significant decrease of vitamin A levels was found in our cases, a result which is in line with the relevant literature and statistically significant difference was found when compared with the control group (p=0.001).

In a study done by M. Dardenne et al. (23), they explicated the role of zinc in the organization of enzymes, thymic peptides, cytokines, lymphoid cell activities and its significance in key operations such as proliferation andapoptosis.

In a study done by Singh et al. (24), it was found that zinc supplementation in patients who had cold reduced the duration of cold and the severity of the symptoms.

In the study done by Lassi et al. (25), some of the children aged between 2 and 5 years old were given zinc and some other placebo, and it was concluded that there was significant decrease in the pneumonia incidence and prevalence in the group who were given zinc.

In a study done by Arıca et al. (26) in Istanbul, zinc (Zn) and iron (Fe) levels of 25 children aged 0-2 with pneumonia were compared with those of 10 healthy children, and they found that zinc (Zn) and iron (Fe) levels in the patient group was significantly low.

In our study, while iron (Fe) level in the whole patient group was significantly lower than the control group, zinc (Zn) level was low in comparison to the control group even though low level of zinc was not statistically significant.

Conclusion

In conclusion, in our study in which epidemiologic, clinic, radiologic features and micronutrient levels of children aged between 1 month and 5 years diagnosed with lower respiratory tract infection, it was found that the vitamin A, zinc and iron levels of the patients were low. Despite the abundance of studies where it was revealed that the patients diagnosed with “ALTI” had lower levels of morbidity and mortality after vitamin A and zinc supplements, the existing does not support the routine use of this practice in every patient. In order to be able to introduce the data regarding the prevention and treatment of ALTIs and the use of vitamins and trace elements as support treatment, it is vitally important that multicentered studies involving sufficient number of patients be carried out.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Research and Training Hospital/ 26.10.2011/438.

Informed Consent: Informed consent was obtained from patients and their parents who participated in this study.

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