HYPOPHOSPHATEMIA IN CHILDREN WITH INFECTIOUS DISEASES

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ABSTRACT

A case-control study was carried out on 65 infants and children with infectious diseases admitted to pediatric wards of Basrah Maternity and Child Hospital from the 1st of September 2002 till the end of February 2003. Their ages ranged from 1 month-9 years, 37 were males and 28 were females. Seventy-five children (43 males and 32 females) visiting the outpatient department for vaccination or for minor illnesses like common cold were randomly selected as controls. For all children included a complete history and thorough physical examination were done and the following investigations were carried out; hemoglobin level, white blood cell count, serum phosphorus, calcium and albumin. Hypophosphatemia was detected in 20% of patients with infections. The study has revealed that the mean serum phosphorus, calcium, albumin and hemoglobin levels were significantly lower while the mean white blood cell count was significantly higher in patients compared to controls. There was no significant difference in mean serum phosphorus level in relation to age of patients, sex, duration of illness or the type o infection. From this study it is concluded that hypophosphatemia is high among infants and children with infections and further studies are needed to explain the causes of hypophosphatemia and the role of early phosphate therapy in such patients.

INTRODUCTION

Phosphorus is an essential mineral that is required by every cell in the body for normal function.[1] Plasma phosphorus concentration are high during infancy and decline throughout childhood until adult levels are reached. The range of values is 3.8- 6.5 mg/dl in infants and children younger than 3 years of age, declining to 3.7-5.6mg/dl in children 4-11 years of age and 2.5-4.5 mg/dl in adult. [2,3] Moderate hypophosphatemia was defined as serum phosphorus 1.5-3 mg/dl and severe hypophosphatemia when serum phosphorus < 1mg/dl [1,2] Hypophosphatemia may result from many conditions including starvation, protein-calorie malnutrition, malabsorption, respiratory or metabolic alkalosis, and during treatment of ketcacidosis. Hypophosphatemia is also common in patients treated in intensive care unit. [1,2,4] Hypophosphatemia was also reported in patients with legionella pneumophilia pneumonia, toxic shock syndrome secondary to S.aureus infection, gram-negative sepsis and rarely gram-positive sepsis. [5] In addition to that hypophosphatemia is considered to be an early indication of sepsis in critically ill neonates. [5] The effects of hypophosphatemia may include loss of appetite, anemia, muscle weakness, bone pain, rickets, and increased susceptibility to infection. Severe hypophosphotemia may result in death. [1,6] In patients with sepsis, severe hypophosphatemia (S.phosphatc <lmg/dl) may be considered as a superimposed cause of myocardial depression, inadequate peripheral vasodilatation and acidosis. A rapid correction of phosphate may have beneficial effects both on myocardium and vascular system and can reduce mortality. [7,8] Prevention of severe hypophosphatemia should always be the goal. [2] Therefore the frequency of low serum phosphorus in children with different infectious diseases and its relation to other variables that might change during infections like white blood cell count, serum calcium and albumin are important to be investigated.

SUBJECTS AND METHODS

Subjects

This is a case-control study, which was carried out on infants and children with infectious diseases who were admitted to Basrah Maternity and Child Hospital over 6 months (from the 1st September 2002 till the end of February 2003). Sixty-five patients were included (37 males and 28 females), the ages ranged from 1 month - 9 years (mean age 22 ± 22.1 months).

Criteria of inclusion

Infants and children admitted to pediatric wards of Basrh Maternity and Child Hospital for the management of different types of infections like gastroenteritis, bronchopneumonia…etc were included. Patients on medications especially theophyllin, steroids & inhalers or vitamin D

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supplement were excluded, these drugs may affect serum phosphate level. [5]

- ***Control group***

Seventy-five children (43 males and 32 females) visiting the out patient department for vaccination or for minor illnesses like common cold were randomly selected. Their ages ranged from months to 7 years, mean age was 17.8 ± 14 months.

- ***Data collection***

Informations were obtained using a questionnaire form designed for the purpose of the study. For each child included, the following informations were obtained; age, sex, duration of illness, complaints (fever, cough, vomiting, diarrhea... etc). Complete physical examination was done for each child and positive physical signs were recorded including hydration status and anthropometric measurements (wt/ht.) for each child (cases and controls), and the final diagnosis for each patient was recorded. An informed consent was obtained from at least one of the parents before enrolling in the study.

Methods

- One milliliter of blood was taken into EDTA tube for hematological estimation (Hb, WBC; **t**otal and differential).
- Three milliliters of blood were taken and kept in plane tube centrifuged and utilized for the estimation of phosphorus, calcium and albumin. Hemolysed samples were ignored.
- S.phosphorus and calcium were estimated by coloromatric methods, while serum albumin was measured by Bromocres Green using kits from Randox lab. UK. Other investigations were performed according to the patient complaints and provisional diagnosis including chest x-ray, general stool examination, general urine examination, blood, urine or CSF for culture and sensitivity, bone marrow aspiration... etc, as indicated.

Statistical analysis

Data were expressed as mean ± SD. The comparison between groups was performed with one way analysis of variance (ANOVA). Chi-square (X2) test was carried out to determine the relative importance of various variables. P-value of less than 0.05 was considered as statistically significant (S), P-value < 0.01 as highly significant (HS)

RESULTS

A total of 140 infants and children aged 1 month to 9 years were included in the study. The characteristics of the studied children (cases and controls) are illustrated in (Table-1). This table shows that there was no significant statistical difference in the mean age, sex and residence of both groups.

Table 1. ***Characteristics of the studied groups***

Parameter	Patients (No.65)	Controls (No. 75)	P-value
*age (mean ± SD)	22 ± 22.1	17.8 ± 14	NS
★Sex *Male* *Female*	 37(56.9%) 28(43.1%)	 43(57.4%) 32(42.6%)	NS
★Residence *Urban* *Rural*	 37(56.9%) 28(43.1%)	 52(69.4%) 23(30.6%)	NS

*ANOVA was utilized, ★ X^2 test was utilized

The results of hematological and biochemical investigations of the 140 infants and children included in the study are presented (Table-2). The mean hemoglobin level, serum phosphorus, calcium and albumin were significantly lower in patients with infection compared to the control group. However, the mean white blood cell count was significantly higher in patients compared with controls.

Table 2. ***Heamatological and biochemical parameters of patients and controls.***

Parameters	Patients (No. 65)	Controls (No. 75)	P-value★
*Hb %	9.61 ± 2.1	11.48±2.61	<0.001
*WBC	7.04 ± 3.6	5.21 ± 2.41	<0.001
*S.phosphorus	4.71±1.22	5.77 ± 1.22	<0.001
*S.calcium	8.88±0.77	10.19 ± 1.2	<0.001
*S. albumin	4.12±0.83	5.23 ± 1.34	<0.001

*Values were expressed as mean ±SD

★ANOVA test was utilized

The mean serum phosphorus level was statistically not different among patients of different age groups, of both sexes and it was not related to the duration of illness, (Table-3).

Table 3. ***Mean serum phosphorus among patients in relation to selected variables.***

Variable	Mean S.ph.±SD	P-value
-**age (years)**		
<1(No.27)	4.86±1.11	
1-3(No.28)	5.57±1.31	NS
>3(No. 10)	4.25±1.16	
-**Sex**		
Males (No.37)	5.53±1.21	NS
Female (No. 28)	4.88±1 .26	
-**Duration of illness**		
<1 wk. (No.28)	4.74±1.19	
1-2 wk. (No. 27)	4.66±1.23	NS
> 2 wk. (No. 10)	4.92±1.56	

Twenty-six patients (40%) had bronchopneumonia, 15(23.1%) with kala-azar, 14(21.5%) with gastroenteritis and 10(15.4%) with other infections including urinary tract infection 3(4.6%), meningitis 3(4.6%) enteric fever 2(3.1%) and viral hepatitis 2(3.1%). Although patients with gastroenteritis had lower mean serum phosphorus 1evel However, statistically there was no significant difference in the mean serum phosphorus level among patients in relation to the type infection, (Table-4).

Table 4. ***Mean serum phosphorus level among patients in relation to the type of infection.***

Infection	*Mean S.ph±SD
Bronchopneumonia (No. 26)	4.77±1.25
Kala-azar (No. 15)	4.66±1.55
Gastroenteritis (No. 14)	4.45±0.88
Others (No. 10)	4.97±1.06

* P-value NS, ANNOVA test was utilized.

DISCUSSION

Hypophosphatemia is a common finding in acutely ill patients and possibly may occur in the acute phase response syndrome secondary to hyperglycemia and shifts of the extra cellular phosphorus into cells.[9] In this case-control study, the mean serum phosphorus level was significantly lower in patients with infectious diseases compared to controls. Hypophosphatemia was detected in all 13(20%) of patients with infectious diseases. Hypophosphatemia was mild to moderate in cases (no case of severe hypophosphatemia was reported in this study). In comparison with other studies, Ashkenazi et al, have reported hypophosphatemia in 16% of children with diarrhea, be highest in children with shigellosis (39%), followed by salmonella (6%) and rotavirus (3%). [10] In this study 2 (14.3%) children out of 14 patients with diarrhea have hypophosphatemia. Haglin et al, have also reported hypophosphatemia in 16% of patients (children and adults) admitted with infectious diseases. [11] Lower mean serum phosphate was reported in females. However, the difference was statistically not significant, this is in agreement with the results reported by Haglin et al, in Sweden.[11] The mean hemoglobin, serum albumin and calcium levels were significantly lower in patients with infections compared to control while mean white blood cell was significantly higher in patients compared to controls. This is in agreement with the findings report by Haglin et al, (except for hemoglobin level which was not significantly different between patients and controls).[11] Low serum albumin was frequently documented in patients with infectious diseases and has been shown to be of importance for the long term prognosis of patients with pneumonia.[12] Sankaran et al, have found that patients with pneumonia have lower levels calcium, phosphorus and albumin and they demonstrated longer hospital stay, so they concluded that hypophosphatemia, hypocalcemia and hypoalbuminemia may be predictors of the severity of illness in patients admitted to hospital with bacterial pneumonia.[13] In this study 9 patients (13.8%) were malnourished while all children in the control group were well nourished. This finding is similar to that reported by Haglin et al[11] who demonstrated high prevalence hypopho-sphatemia and malnutrition in patients with infections. The exact mechanism behind hypophosphatemia in infectious diseases is not clear but there are many explanations. An acute decrease in serum phosphorus may be the result

of increased excretion of phosphate into the urine and a shift from extra cellular to intracellular compartment. [14] In addition, infection might also cause hormonal and metabolic changes similar to trauma Hypophosphatemia also may be the result of hypermetabolism. Carbohydrates, given enterally or parenterally, probably accentuate the phosphate losses via the urine. [16] Also it would be of interest to know whether the high prevalence of hypophosphatemia seen together with infectious diseases was precipitated by the infection was the result of malnutrition prior to the infection. This study has revealed high percentage of hypophosphatemia among children with infections. Further studies are needed to look the possible causes of this hypophosphatemia like increased urine excretion of phosphate during infection, and also to study the role of early phosphate therapy in such patients.

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