ORIGINAL ARTICLE

To Identify the Prevalence of Hypophosphatemia in Critically ill Patients

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ABSTRACT

Phosphorus plays an important part in metabolism as a main intracellular anion, enzyme constituent, and component of phosphorylated intermediate compounds, and phosphorus is also a component in cellular membranes, nucleic acids, and nuclear proteins. Hypophosphatemia is the most neglected electrolyte deficiency in our medical practice. A number of clinical conditions and drugs can cause hypophosphatemia. Transient hypophosphatemia seldom causes symptoms but severe hypophosphatemia may contribute to increased morbidity and mortality in seriously ill patients. Fifty critically ill patients were admitted in medical unit and intensive care unit over a period of six months in the study. The mean age was 49.5±17.4. Thirty one (62%) patients were male and 19 (38%) were female. During hospital admission, sixteen (16%) patients had hypophosphatemia (<2.5mg/dl), eighty four (84%) had either normal phosphate levels or hyperphosphatemia. The mean phosphate concentration was 3.27±0.79mg/dl (range 1.8 to 5.1mg/dl). The prevalence of hypophosphatemia was comparable with the international studies. Important clinical diagnosis with hypophosphatemia in our study were diabetic ketoacidosis (16%), respiratory alkelosis (18%), septicemia (32%), chronic obstructive pulmonary disease (32%), respiratory failure (42%), hepatic coma (38%), renal failure (10%). Patients presenting with shortness of breath had higher frequency of hypophosphatemia (p=.047). Patients receiving ß2-agnosists had low serum phosphate levels though it was statistically insignificant while patients with renal failure had higher level of serum phosphate. Prevalence of hypophosphatemia was higher in patients with more than one disease. Mortality among hypophosphatemic patients with septicemia was higher (32%). Ninteen (38%) received mechanical ventilation had hypophosphatemia, hepatic coma and respiratory alkeolosis were present in 60% of patients. Serum calcium and serum albumin levels were low in patients of hypophosphatemia. Severe hypophosphatemia (<1.5mg/dl) was not observed in this study. Haemoglobin levels were not affected significantly below serum phosphate levels. The prevalence of hypophosphatemia was higher in patients admitted with shortness of breath. The hypophosphatemia was 15% in critically ill patients admitted in Medical and ICU Units. Patients with septicemia, respiratory failure and chronic obstructive pulmonary diseases were more prone to develop hypophosphatemia.

Key words: Hypophosphatemia, Phosphorus, Critically ill patients.

INTRODUCTION

Despite the fact that monitoring of sodium, potassium, and calcium ions is part of the routine of intensive care unit services, little attention has been devoted to phosphorus during the follow-up of critically ill patients.[1] Phosphorus plays an important part in metabolism as a main intracellular anion, enzyme constituent, and component of phosphorylated intermediate compounds, and phosphorus is also a component in cellular membranes, nucleic acids, and nuclear proteins[2,3,4].

It is absorbed in greater proportions in the jejunum, mainly by passive transport. Excretion takes place essentially by the kidneys, whereby 80% of the phosphorus is reabsorbed passively within the proximal tubule, linked with sodium, and regulated by hormonal action and food ingestion[2,3,5].

Approximately 1% of the body's total phosphorus reserve is found in the blood and phosphorus is primarily stored within mineralized tissues (bone and teeth). Phosphorus is also present in soft tissues in the form of phospholipids, phosphoglycides, and phosphoproteins[3-7].

Similar to that of calcium, homeostasis of phosphorus also involves direct participation of the intestine, bones, and kidneys, being maintained by the action of Vitamin D (1.25-dihydroxicolecalciferol), parathyroid hormone (PTH), and calcitonin. Vitamin D acts in the intestine, increasing both calcium and phosphorus absorption. Phosphatemia, however, is practically controlled by renal excretion. PTH secretion, stimulated by a decrease in calcium serum levels, acts in renal reabsorption, reducing urinary

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excretion of calcium while simultaneously inhibiting the tubular reabsorption of phosphorus. Conversely, when calcium levels are high, calcitonin is released, acting in reverse fashion, i.e. reducing phosphaturia while increasing calcium excretion[8,9].

Normal serum phosphate ranges from 2.8-4.5mg/dl (0.4-1.8mmol/L). Serum levels of less than 2.5mg/dl refer to hypophosphatemia. Severe hypophophatemia is a serum level of less than or equal to 1.5mg/dl (0-48mmol^3/L). Most of the phosphorus is absorbed in the duodenum and jejunum. The net amount of phosphate absorbed from gastrointestinal tract is about 600-700mg/day. Almost 80% of filtered load is reabsorbed along the proximal tubule, 10% in distal nephron and rest appears in the urine[10].

Hypophosphatemia results from poor dietary intake, decreased intestinal absorption, increased urinary excretion and shift of phosphate from extracellular fluid into the cell. Severe hypophosphatemia may be found in diabetic ketoacidosis, respiratory alkalosis, hyperalimentation, nutritional recovery syndrome and drugs such as gluco-corticoids, diuretics, intravenous glucose administration in patients of diabetic ketoacidosis and antacids[11,12].

Clinical features of hypophosphatemia include irritability, confusion, convulsions, coma, neuromuscular abnormalities. Rhabdomyolysis, erythrocyte dysfunction and hemolysis, leukocyte and platelet dysfunction, hepatic enzyme alteration and myocardial muscle derangements as well as respiratory muscle weakness and multiple organ failure.[13-15] It is associated with increased morbidity and mortality in hospitalized patients. In our set-up, phosphate abnormalities are also neglected, so a study is designed to see the prevalence of hypophosphatemia in seriously ill patients.

Objective: To identify the prevalence of hypophos-phatemia in critically ill patients and assess the morbidity and mortality associated with hypophosphatemia.

METHODOLOGY

This observational descriptive study was conducted at Nawaz Sharif Social Security Hospital/University College of Medicine, The University of Lahore during the period of six months. In this study fifty patients were included during a period of 6 months w.e.f. 10-02-2010 to 10-08-2010. All patients above 16 years of age presenting to medical out patient department, accident & emergency department and admitted in medical unit. In our study, normal serum phosphate level was 2.5 to 4.5mg/dl. A level below 2.5mg/dl was taken as hypophosphatemia. Severe hypophosphatemia was taken as level of PO4 <1.5mg/dl. Patient's serum phosphate level was checked on 1st, 3rd and 10th day (if applicable) during the hospital stay to identify any decrease in serum phosphate levels. Lowest value of the serum phosphate level was used for analysis. Serum phosphate was measured by using automatic Dade Dimension Chemistry Analyzer. Flex reagent kit was used. Serum calcium was measured on same analyzer. Serum albumin was measured manually on LAB. system.

Statistical analysis: All information collected from the proforma was entered into SPSS version 16 computer software and analyzed through its statistical programme. Descriptive statistics were calculated. The quantitative variables age was presented in the form of mean and standard deviation. The qualitative variables like sex, status of phosphate and hypophosphatemia were presented as frequencies and percentages in tabulated forms.

RESULTS

Fifty patients of both sexes were included in this study conducted at Nawaz Sharif Social Security Hospital/ Lahore. The mean age of patients was 49.5±17.4 years and age range was 16-90 years. Sixty two percent were male patients and 38% were female with male to female ratio 1.63:1 (Table 1). The mean serum phosphate concentration was 3.27±0.79mg/dl (range 1.8 to 5.1mg/dl). Out of fifty patients 8 (16%) were having diabetic ketoacidosis, respiratory failure was present in 21 (42%) patients, 16 (32%) had COAD/asthma, 16 (32%) had septicemia, 5 (10%) were with malignancy. Eighteen percent had respiratory alkolosis, hepatic coma was seen in 19 (38%) and renal failure had in 5 (10%) of patients. Among the disease groups 2 (25%) patients of DKA had hypophosphatemia, 1 (11%) with hepatic coma, 4 (25%) patients of septicemia, 1 (11%) patients of respiratory alkalosis, 2 (12%) patients of COAD, 4 (19%) patients of respiratory failure, 1 (20%) patient of renal failure had hypophosphatemia and malignancy also in 20% of patients (Table 2). During the hospital stay 30 (60%) patients received antacid therapy, 20 (40%) were on ß2-agonists (salbutamol/aminophyline), 16 (32%) had total parenteral nutrition, 26 (52%) received glucose infusion. Steroids were given to 14 (28%) and 10 (20%) patients were on diuretics (Table 3).

Table 4 shows 31 (62%) patients were admitted with shortness of breath and 19 (38%) received mechanical ventilation. Gender had no impact on serum phosphate levels. Analysis of serum phosphate levels with serum calcium, albumin and haemoglobin are shown in Table 5. Serum calcium and albumin were low in patients with

hypophosphatemia. But haemoglobin was not affected by low phosphate levels.

Among 17 patients who died in the study, 3 (17.65%) were found to have serum phosphate levels less than 2.5mg/dl. These patients had more than one disease in combination and septicemia was most common ailment and other 14 (82.35%) had died above >2.5 level in combination of different diseases and remaining 3 (17.65%) were <2.5 level (Table 6).

Table 1: Frequency distribution of demographic variables of patients (n=50)

Sex	**Frequency**	**Percentage**
Male	31	62.0
Female	19	38.0
PO4 mg/dl level (age range in years)		
	Age <40 years	Age 40-90 years
PO4 = <2.5	3 (6%)	9 (18%)
PO4 = >2.5	15 (30%)	23 (46%)

Age range 15-90 years Mean±SD 49.5±17.4

Table 2: Frequency of Prevalence of Hyophosphatemia in Different Diseases

Disease Group	**=n**	**Hypophos-phatemia**
DKA	8(16.0%)	2(25.0%)
Hepatic coma	19(38.0%)	1(11.0%)
Septicemia	16(32.0%)	4(25.0%)
Resp. Aklalosis	09(18.0%)	1(11.0%)
COPD	16(32.0%)	2(12.0%)
Resp. failure	21(42.0%)	4(19.0%)
Renal failure	05(10.0%)	1(20.0%)
Malignancy	05(10.0)	1(20.0%)

Table 3: Frequency Status of Phosphate in Different Treatment Modalities

Treatment Categories	**=n**	**Hypophos-phatemia**
Antacids	30(60%)	5(10%)
ß2 Agonist	20(40%)	4(8%)
Ionotrips	16(32%)	3(6%)
Dextrose	26(52%)	4(8%)
Diuretics	10(20%)	1(2%)
Steroids	14(28%)	3(6%)
Total parenteral nutrition	08(16%)	2(4%)

Table 4: Analysis of Shortness of Breath and Mechanical Ventilation of Hypophosphatemia

Patients with Hypophospha temia	**SOB**	**=n**	**%age**	**P value**
31 (62%)	Present Absent	27 4	87.0 13.0	<0.05
Mechanical ventilation 19 (38%)	<2.5 >2.5	3 16	16% 84%	<0.05

Table 5: Analysis of PO4, Hb, Albumin and Calcium Level

	PO4 (mg/dl) Level	**=n**	**Mean**
Hb	<2.5 >2.5	8 42	11.30±2.35 10.81±2.60
Albumin	<2.5 >2.5	8 42	3.51±0.42 3.51±0.58
Calcium	<2.5 >2.5	8 42	7.80±0.59 8.75±0.68

P value: >0.05

Table 6: Frequency of Mortality and PO4 Level

Deaths (total)	**PO4 Level**	**=n.**	**%age**
17 (34%)	< 2.5 > 2.5	3 14	17.65 82.35

DISCUSSION

In a study reported by Geerse the critically ill patients have a high prevalence of hypophosphatemia because of the presence of multiple causal factors. Hypophosphatemia may lead to a multitude of symptoms, but most often remains asymptomatic. Hypophosphatemia, however, is associated with increased mortality in important patient subgroups. It is important to investigate whether hypophos-phatemia causes higher mortality in itself, or rather is associated with a higher severity of illness[16].

In another study reported by Betro and Pain[17] the prevalence of hypophosphatemia of 2 to 5% in hospitalized patients which increased to 20 to 40% if predisposing conditions such as alcoholism, diabetic ketoacidosis, recovery from burns or sepsis were present. In our study the prevalence of hypophosphatemia was 10% with predisposing conditions. No history of alcoholism was found in our patients.

Fischer[18] et al described low phosphate levels (<2.5mg/dl) in 25% of patients in respiratory illness with a 5% prevalence of severely reduced serum levels (<1.0mg/dl). In our study severe (<1.5mg/dl) hypophosphatemia was not found. Another study carried out by Fiaccardori et al[19] 22 patients with chronic obstructive pulmonary disease. Phosphorus content was measured by spectrophotometric methods on muscle fragments of both peripheral and respiratory muscles. Thirty age and sex matched subjects were used as controls. Muscle phosphorus depletion was present in about 50% of patients with COPD. Mean age was 63±6 years with 19 men, 3 women. In our study 16 (32%) patients had chronic obstructive pulmonary disease. Muscle phosphorus was not measured. Hypophosphatemia was present in 2(12%) patients of COAD. Mean age was 49.5±17.4. There were 31 male and 19 patients were female in our study. There was no control used.

In Fiaccardori's[19] study COPD was primary diagnosis and study was done in pulmonary medicine ward. Serum creatinine level ranged from 0.7 to

1.2mg/dl in contrast to our study. Six of 22 patients with COPD had phosphorus values less than 2.5mg/dl while in our study (16.7%) of patients with COPD had low phosphate values (<2.5mg/dl). But in our study the patients with different combinations of diagnosis were included in the study, and study was done in ward and ICU patients. None of the patients was unconscious or impaired consciousness in contrast. No patient had sepsis or was receiving antacids or parenteral nutrition but in our study 30 (60%) patients received antacids, 20(40%) were on ß2-agonist. Eight (16%) patients were on total parenteral nutrition.

Paleologos[20] in a study reported significant lowering of serum phosphate levels after hyperventilation and dextrose infusion (p<0.0003). In our study respiratory alkalosis and dextrose infusion did not affect the serum phosphate levels significantly (p >0.05). Serum phosphate levels however, were not measured after dextrose loading in our study.

Severe hypophosphatemia may cause acute respiratory failure, myocardial depression or seizures as described by Miller[2] in emergency department with alcoholic patients. In our study one patient with serum phosphate levels of 1.8mg/dl had seizures but it was not possible to correlate this symptom with phosphate levels.

In a retrospective analysis by Ornstein[21] to determine the incidence of hypophosphatemia in adolescents with anorexia nervosa, sixty nine patients (66 females, 3 male) with anorexia nervosa were included. Mean age was 15.5±2.5. Four (5.8%) developed moderate hypophosphatemia (<2.5mg/dl >1.0mg/dl), fifteen (21.7%) had mild hypophsphatemia (<3.0mg/dl & >2.5mg/dl). Phosphorus nadirs were directly proportional to ideal body weight (p 0.01). In our study 8(16%) patients developed moderate hypophosphatemia.

A study carried out by Bollaert[22] study done to see the haemodynamic and metabolic effects of rapid correction of hypophosphatemia in patients with septic shock, phosphorus administration was followed by a 22% increase in left ventricular stoke work index (p <0.01) and a 12% increase in systolic arterial pressure, while in our study no effects on haemodynamics were studied. In our study 3 patietns who died had having hypophosphatemia along with other diseases.

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