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An Alternative Approach to Treatment of Hypophosphatemia in Nonsurgical Critically Ill Patients in Countries With Limited Resources

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Abstract

Background: Hypophosphatemia can complicate and prolong the treatment of critically ill patients, and it is even thought to be related to mortality rate.

Objectives: The aim of this study is to determine whether using extemporary prepared phosphate buffer in pharmacy would help correct serum phosphate in critically ill patients.

Methods: A prospective study was conducted at the medical intensive care unit over a period of 1 year and included 50 patients who were diagnosed with hypophosphatemia. Phosphate buffer was prepared at the pharmacy, and the dose range was recommended by a clinical pharmacist.

Results: Patients were administered phosphate buffer via the nasogastric tube, and the doses chosen by the physicians depended on serum phosphate level and the severity of the patients' clinical status. Serum phosphate levels were successfully corrected in all treated patients. The most frequently used dose was 60 mmoL/d, and in most patients 1-day therapy was sufficient. No adverse effects were observed.

Conclusion: The phosphate buffer is an adequate alternative for the treatment of hypophosphatemia of nonsurgically critically ill patients. One-day therapy with the 60 mmoL phosphate dose divided into 3 single doses resulted in normalization of serum phosphate values in most patients.

Keywords
phosphorus, buffer, intensive care unit, critically ill

Background

Electrolyte imbalance is common in critically ill patients treated in medical intensive care units (MICUs).[1] Hypophosphatemia may develop through 3 mechanisms: reduction of intestinal absorption, increased renal excretion, and redistribution of phosphate in intracellular space.[2] The last mechanism is most commonly observed in critically ill patients.[3] The serum phosphate concentration is inversely proportional to the concentration of inflammatory cytokines, interleukin-6, and tumor necrosis factor α, and it is often seen in septic patients, especially those with infection caused by gram-negative microorganisms[4]; it is in good correlation with the severity of the disease and is considered to be a reliable prognostic factor of survival.[5] The reference range of the serum phosphate value is

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Table 1. Patients' Characteristics and Outcomes.

	All	Severe Hypophosphatemia	Moderate Hypophosphatemia	Mild Hypophosphatemia	Difference
Gender (N)					
Male	22	6	12	10	$P > .05$[a]
Female	28	1	10	11	
Age (years)	59.72 ± 16.41	55.86 ± 23.89	60.91 ± 12.92	59.76 ± 17.52	$P > .05$[b]
Sepsis (N)					
Yes		3 (42.9%)	14 (63.6%)	16 (76.2%)	$P > .05$[a]
No		4 (%)	8 (%)	4 (%)	
Drugs that may induce hypophosphatemia (N)					
None		1 (14.3%)	7 (31.8%)	10 (47.6%)	$P > .05$[a]
1		3 (42.9%)	8 (36.4%)	9 (42.9%)	
2		3 (42.9%)	6 (27.3%)	1 (4.8%)	
3		0	1 (4.5%)	1 (4.8%)	
Phosphate dose (mmoL)	77 ± 53.50	91.43 ± 101.23	80 ± 53.36	69.05 ± 28.27	$P > .05$[b]
Length of MICU hospitalization (days)	11.37 ± 11.27	6.14 ± 0.52	9.95 ± 7.06	14.52 ± 15.05	$P > .05$[b]
Length of treatment (days)					
1	40 (80%)	6 (15%)	18 (45%)	16 (40%)	$P > .05$[a]
2	7 (14%)	0	3 (42.9%)	4 (57.1%)	
4	3 (4.2%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	

[a]χ^2 test.
[b]Mann-Whitney test.

0.8 to 1.45 mmoL/L. Most of the authorities state 3 stages of hypophosphatemia: mild hypophosphatemia (0.6-0.8 mmoL/L), moderate-to-severe hypophosphatemia (0.3-0.6 mmoL/L), and severe hypophosphatemia (<0.3 mmoL/L).[1] The choice of therapy depends on the severity of hypophosphatemia and the presence of disease symptoms. Intravenous phosphate therapy is preferred in severe and sometimes moderately severe hypophosphatemia in critically ill, while other patients are treated via peroral route.[6] In Bosnia and Herzegovina, which is low-income country, there are no supplements of phosphate available, neither for peroral nor intravenous administration. Literature data on treatment of hypophosphatemia in critically ill patients using alternative source of phosphates are scarce. Therefore, we aimed to find appropriate, inexpensive, and safe treatment option.

Methods

This prospective study was conducted at the MICU in the period from February 2017 to April 2018. The study included 50 adult patients (aged 18 years and older) who were mechanically ventilated with mean SAPS II score (SAPS II—simplified acute physiology score) of 61.31 and diagnosed with hypophosphatemia (concentration of inorganic phosphate in serum <0.81 mmoL/L). Phosphate buffer solution that contains 30.4 mg of elemental phosphorus approximately 1 mmoL phosphate per 1 mL of solution (6,762 g $Na_2HPO_4 \cdot 2H_2O$ plus 5,88 g of H_3PO_4, 85% and aqua redestilata in amount that is necessary to have 100 mg of solution) was prepared at the pharmacy as a possible source of phosphate for peroral use in the treatment of patients in the MICU. After diagnosis of hypophosphatemia, clinical pharmacist advised on administration of phosphate buffer in dose 30 to 150 mmoL phosphate daily, divided into 2 to 3 single doses. Phosphate dose for each individual patient was chosen by a physician according to phosphate levels and clinical status of the patient. Phosphates were administered in the form of phosphate buffer solution via nasogastric tube since all patients in the study were on mechanical ventilation and the peroral administration was disabled. The serum phosphate levels were measured 24 hours after administering phosphate buffer to evaluate the efficacy of the administered dose and modify it, if necessary. Further monitoring was carried out as needed and physician decided on additional doses.

For statistical analysis, SPSS 20 was used and this study was approved by the Ethical Board of the hospital.

Results

During the period from February 2017 to April 2018, 50 patients with hypophosphatemia were identified in the MICU. There was no statistically significant difference in the dose of phosphate or length of treatment between patients with different degrees of hypophosphatemia. For most studied patients (80%), 1 day of phosphorus supplementation was enough to normalize serum phosphate levels (Table 1).

The most commonly administered dose was 60 mmoL of phosphate per day divided into 3 single doses for 66% of patients, as shown in Figure 1.

There was no significant difference in the number of drugs that could cause or contribute to hypophosphatemia among patients with severe, moderate-to-severe, or mild hypophosphatemia, as shown in Table 1.

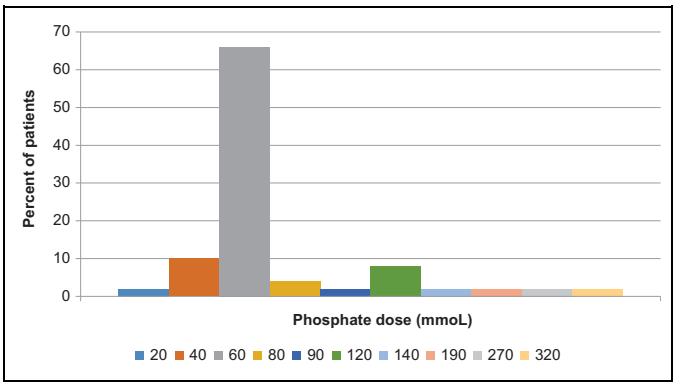

Figure 1. Phosphate dose.

Discussion

Administration of phosphate buffer solution via nasogastric tube proved to be effective alternative source of phosphates for treatment of hypophosphatemia in critically ill medical patients in low-income countries. Some authors advise that severe and moderate hypophosphatemia in mechanically ventilated critically ill patient should be treated using intravenously (IV) administered phosphate, while in patients with mild-to-moderate hypophosphatemia who are not on mechanical ventilation phosphate can be administered perorally.[4] Phosphate for IV administration is not available on the market of Bosnia and Herzegovina, and for the treatment of hypophosphatemia in critically ill patients, we have not had a therapeutic solution so far. In addition, according to the literature, parenteral administration of phosphate carries the risk of significant undesirable effects during administration such as renal insufficiency, hypocalcemic tetany, hypotension, hyperphosphatemia, and heart electrical activity disorders.[7,8]

There are currently no widely recognized guidelines for the treatment of hypophosphatemia in critical illness. Different literature sources recommend 1 mmoL/kg phosphate for the treatment of severe hypophosphatemia, 0.64 and 0.32 mmoL/kg for the treatment of moderate and mild hypophosphatemia,[9] or 0.08 to 0.16 mmoL/kg IV for severe and moderate hypophosphatemia in mechanically ventilated patients and 1000 mg orally for the treatment of moderate and mild hypophosphatemia.[4]

The most patients in our study received daily dose of 60 mmoL phosphate divided into 3 single doses and 1 day of therapy was sufficient for serum phosphate-level normalization in most patients. For 7 patients, therapy was administered for 2 days, and for 3 patients phosphates were given for 4 days. Since all patients were intubated and on mechanical ventilation, the phosphate solution was administered using a nasogastric tube. For all 50 patients included in the study, serum phosphate stayed in reference range during MICU stay, with no patients experiencing gastrointestinal adverse effects (vomiting, diarrhea, mucus bleeding), which often accompany peroral/enteric administration of phosphate.[10]

Most patients in our study who had 1 or 2 drugs in concomitant therapy that may cause or aggravate hypophosphatemia were diagnosed with mild hypophosphatemia, and the difference in the number of drugs between patients with 3 different stages of hypophosphatemia was not statistically significant.

Based on the results of our study, we can conclude that 60 mmoL phosphate per day (divided into 3 single doses) and administered in the form of a phosphate buffer solution via a nasogastric tube is sufficient to correct serum phosphate values in most nonsurgical critically ill patients, regardless of the degree of hypophosphatemia and without the risk of adverse effects.

Authors' Note

This work was performed at the Medical Intensive Care Unit, University Clinical Centre of the Republic of Srpska.

Declaration of Conflicting Interests

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