Efficacy and Safety of Phosphate Enema as a therapeutic agent in Hypophosphatemia in Critically Ill Children

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ABSTRACT

The aim of the study was to evaluate the safety and efficacy of oral administration of phosphorous enema in hypophosphatemia (HP) in critically ill children admitted in the pediatric intensive care unit (PICU) of The Indus Hospital, Karachi, from September 2018 to August 2019. This was a retrospective review of 31 critically ill children with hypophosphatemia who received 1 ml/kg/day of phosphate enema through nasogastric tube or orally for phosphate replacement, with serial phosphorus level monitoring along with observation for its side effects. The results showed that the rise of serum phosphorus level was observed in all cases and 64.5% of cases achieved target phosphorus level with no adverse reactions observed. Sample size although limited, it is safe to state that oral phosphate enema is safe and effective for correction of hypophosphatemia in critically ill children.

Key Words: *Hypophosphatemia, Enema, Pediatric intensive care unit.*

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Hypophosphatemia (HP) is a commonly recognised electrolyte abnormalities in acute critically children with frequency of around 40-70% in the recent literature.[1] Phosphorus is a vital electrolyte for physiological homeostasis being the source of body currency (ATP) and many important chemical reactions. Serum phosphorus depletion is not only associated with serious effects on respiratory, cardiac, neurology, hematology, and immune systems; but is associated with increased morbidity and mortality rates in critically ill patients.[1,2]

There are significant dietary sources to replace phosphorus; however, sick patients mostly require replacement either as intravenous preparation or as an oral solution, which are not only expensive but are not easily available.[3] Apart from these few available preparations, there is inadequate knowledge regarding alternative source of phosphorus for the treatment of hypophosphatemia in critically ill patients.[4,5]

Phosphate enema is commonly used as a laxative for constipation and as for bowel preparation before lower gastrointestinal endoscopy. It contains monobasic sodium phosphate (USP) 19.2 grams /120 ml and dibasic sodium phosphate (USP) 7.2 grams/120 ml.[5]

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Not only is it widely available, it is a comparatively cheap alternate source of phosphorous; and can be used orally or via nasogastric tube for phosphorus replacement in hypophosphatemia, if there is no contraindication. This study was conducted to evaluate safety and efficacy of phosphate enema orally or *via* nasogastric tube in critically ill children with hypophosphatemia in pediatric intensive care unit (PICU).

This study was conducted in children admitted in PICU of The Indus Hospital, Karachi from September 2018 to August 2019 after approval of Institutional Ethical Review Committee. Medical records were reviewed for all critically ill children, who had hypophosphatemia and received phosphate enema orally or through nasogastric tube. Patients receiving any other form of phosphorus for hypophosphatemia were excluded from the study.

After diagnosis of hypophosphatemia, clinical pharmacist advised administration of phosphate as a phosphate enema in dose 40mg/Kg/day in four divided doses. This enema has 43 mg of elemental phosphorus per ml. Hence, the replacement dose is 1ml/kg/day *via* nasogastric tube or orally in four divided doses given for three to five days till normalisation of serum phosphorous levels.

Hypophosphatemia was defined as serum phosphorus level less than 3.5mg/dl and return of normal serum level of phosphorus (>3.5mg/dl) was required.[1] Clinical complications of phosphorous replacement like diarrhea, vomiting, arrhythmias, seizures oliguria along with radiological complications like intestinal perforation were observed.

All data were collected on structured data collection sheets.

Demographic data (age, gender) clinical variables (admitting diagnosis, use of mechanical ventilation and vasopressors, medications causing low serum phosphorus like diuretics, steroids along with duration and number of doses of enema received) along with outcome variables (normalisation of phosphorus level and complications) were recorded. Statistical analyses were performed on SPSS version 22. Data were presented as mean ± SD or as frequency with percentages. The serum phosphorus at baseline and day 4 were compared by using paired t-test, p-value ≤0.05 was taken as statistically significant.

The data of 31 patients were evaluated. The mean age was 6.0 ± 4.4 year and 51.6% (n=16) were males. The most common admitting diagnoses were shock and respiratory failure. The mean serum phosphorus level before intervention was 1.56 ± 0.67 mg/dl. The average numbers of doses received were 11.4 ± 6.04. There was a rise in the serum level of phosphorus noted in all cases after 24-48 hours of administration; however, target level was observed in 64.5% cases (Table I).

Table I: Characteristics of children with hypophosphatemia admitted in pediatric intensive care unit (N = 31).

	Mean ± S.D n (%)
Age (years)	6.0 ± 4.4
Gender: Male Female	 16 (51.6) 15 (48.4)
Mechanical ventilation: Yes No	 12 (38.7) 19 (61.3)
Corticosteroid use: Yes No	 13 (41.9) 18 (58.1)
Insulin use: Yes No	 7 (22.6) 24 (77.4)
Diuretic use: Yes No	 20 (64.5) 11 (35.5)
Inotropic support given: Yes No	 13 (41.9) 18 (58.1)
Baseline (D0) phosphate levels (mg/dl)	1.56 ± 0.67
Number of dose received	11.4 ± 6.04
Days of therapy	2.87 ± 1.5
Target phosphate levels achieved: Yes No	 20 (64.5) 11 (35.5)

Statistically significant difference was observed in phosphorous level over time *i.e.* from D0 1.3 ± 0.5 mg/dl to D4 (3.8 ± 1.4 mg/dl) (p = 0.001).

Currently, there are no evidence-based guidelines for the treatment of hypophosphatemia in critically ill patients. Traditionally, intravenous phosphorus is the standard of care for replenishment of phosphorus in most of intensive care units; however, intravenous phosphorus is not easily available, and parenteral administration of phosphorus carries high risk of tetany, hypotension and cardiac arrhythmias. Recently, Kovacevic *et. al*. described an alternative for the treatment of hypophosphatemia in critically ill patients, suggesting that phosphorus buffer solution *via* nasogastric tube 60mmol/day in three divided doses was sufficient for normalisation of serum phosphorus in most of the patients.[4] Similarly, Kimmerly *et. al.* used phosphate enema for treatment of hypophosphatemia in an elderly patient without any adverse effect.[5] We have similar results from phosphate enema solution (1ml/kg/day in 4 divided doses) administration *via* nasogastric tube without any adverse effect. This phosphate enema is easily available, less expensive, easy to administer, and also associated with fewer side effects.

There were several limitations with this study including small sample size, retrospective and being a single centre study. Therefore, large prospective randomised critical trials are needed to prove the safety and efficacy of phosphate enema for treatment of hypophosphatemia in critically ill children. However, this is the first study in children from lower middle income countries like ours that not only explores alternative agents for phosphorous replacement, but also hints at the drug being safe and efficacious.

ETHICAL APPROVAL:

This study was conducted after obtaining approval from the Institutional Ethical Review Committee of The Indus Hospital, Karachi (IRD-IRB-2019 09 009).

PATIENTS' CONSENT:

It was waived because of retrospective data.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

RU: Conception of idea, data collection.
AH: Conception of idea, initial draft.
SM, FR, HJ: Needful correction and advice.
ARA: Manuscript writing, data collection, statistics finalisation, and corresponding author.

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