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# Phoxilium vs Hemosol-B0 for continuous renal replacement therapy in acute kidney injury☆

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Acid-base balance;
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**Abstract**

**Purpose:** This study aimed to compare the biochemical effects of Phoxilium (containing phosphate at 1.2 mmol/L; Gambro Lundia AB, Lund, Sweden) and Hemosol-B0 (Gambro Lundia AB) as dialysate and/or replacement fluid during continuous renal replacement therapy (CRRT).

**Methods:** We examined serum biochemistry in critically ill patients for 42 hours of Phoxilium administration for the prevention of hypophosphatemia during CRRT and compared them with corresponding results in random historical controls who received Hemosol-B0.

**Results:** We studied 15 patients in each arm (Phoxilium vs Hemosol-B0). Respective median ages were 57 (49-68) and 64 (57-67) years. Baseline patient illness severity scores, prescribed CRRT effluent rates, and cumulative phosphate intakes were comparable. After 36 to 42 hours of Phoxilium administration, serum phosphate levels increased from 0.95 (0.81-1.13) to 1.44 (1.23-1.78) mmol/L, in contrast to the decline from 1.71 (1.09-2.00) to 0.83 (0.55-1.59) mmol/L with Hemosol-B0 ($P = .0001$). Serum ionized calcium levels decreased from 1.27 (1.22-1.37) to 1.12 (1.06-1.21) mmol/L with Phoxilium, compared with an increase from 1.09 (0.90-1.19) to 1.20 (1.16-1.25) mmol/L with Hemosol-B0 ($P < .0001$). Serum bicarbonate, base excess levels, and effective strong ion difference decreased with Phoxilium and were lower than those with Hemosol-B0 at 36 to 42 hours ($P < .05$).

**Conclusion:** Phoxilium effectively prevented hypophosphatemia during CRRT but was associated with relative metabolic acidosis and hypocalcemia compared with Hemosol-B0 use.



☆ Disclosures/Conflicts of interest: Phoxilium replacement fluid for continuous renal replacement therapy (Gambro Lundia AB, Lund, Sweden) was purchased from Gambro and used (on trial basis) in our hospital under the Therapeutic Goods Administration Australia's Special Access Scheme. The authors have no financial or consultancy agreement with Gambro.

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## 1. Introduction

Continuous renal replacement therapy (CRRT) and hybrid therapies are the preferred treatment modalities for critically ill patients with acute kidney injury (AKI) and hemodynamic instability [1–3]. In the initial stages of AKI, hyperphosphatemia predominates because of reduced renal phosphate excretion. Owing to the continuous nature and prolonged duration of CRRT, systemic phosphate loss will be significant [4–6]. Indeed, up to 65% of patients develop subsequent hypophosphatemia during CRRT [7], which usually manifests itself after 3 to 4 days of therapy [8]. Hypophosphatemia can theoretically deplete intracellular adenosine triphosphate and result in tissue hypoxia [9]. It can precipitate complications such as cardiac arrhythmias, seizures, rhabdomyolysis, and haemolysis [10–12] and is also strongly associated with prolonged respiratory failure and ventilator dependence in critical illness [8,13].

Correction of hypophosphatemia can be achieved via intravenous replacement when levels are low or prophylactically by incorporating phosphate into CRRT fluids, thereby limiting excessive loss. The latter approach is similar to hypokalemia prevention [14] and has been shown to effectively prevent hypophosphatemia during CRRT [15]. However, the addition of phosphate and/or change in fluid composition may alter the systemic calcium and acid-base balance owing to interaction with phosphate or its weakly acidic properties [12,16]. It is also unclear if the addition of physiological phosphate content in CRRT fluids will lead to corresponding optimal serum phosphate levels. Such changes in serum biochemistry may affect clinical assessment of the critically ill. Thus, we aimed to examine these changes in detail. We hypothesized that using a phosphate-containing vs a conventional phosphate-free solution for CRRT would effectively maintain serum phosphate levels but induce relative systemic metabolic acidosis and lower ionized calcium levels.

## 2. Methods

### 2.1. Study design and comparators

This was a retrospective case-control study of the use of Phoxilium vs Hemosol-B0 (both from Gambro Lundia AB, Lund, Sweden) during CRRT, in critically ill patients with AKI admitted to the intensive care unit (ICU). Phoxilium is a new commercially available solution for CRRT, which contains phosphate at 1.2 mmol/L and potassium at 4.0 mmol/L. Phoxilium is used for CRRT when patients' pH and hyperkalemia have normalized and when they need phosphate supplementation for effluent phosphate loss. In comparison, Hemosol-B0 by itself does not contain phosphate or potassium and is subsequently modified by the addition of potassium chloride at 4.0 mmol/L to prevent hypokalemia during therapy. The compositions of both solutions are shown in Table 1. The Human Research Ethics Committee in our institution approved this study.

**Table 1** Composition of study fluids

| Composition (mmol/L) | Phoxilium | Hemosol-B0 (with added 4 mmol/L of KCl) | Accusol |
|---|---|---|---|
| Phosphate | 1.2 | 0 | 0 |
| Bicarbonate | 30 | 32 | 35 |
| Calcium | 1.25 | 1.75 | 1.75 |
| Magnesium | 0.6 | 0.5 | 0.5 |
| Sodium | 140 | 140 | 140 |
| Potassium | 4.0 | 4.0 [a] | 4.0 |
| Chloride | 115.9 | 113.5 [a] | 113.5 |
| Lactate | 0 | 3 | 0 |

KCl indicates potassium chloride.
[a] Estimated composition change after the addition of 4 mmol/L of KCl into the solution.

### 2.2. Phoxilium arm

From January till October 2011, Phoxilium was made available for patient use in our ICU under the Special Access Scheme, which allowed preliminary access to products (on trial basis) yet to be approved by the Therapeutic Goods Administration in Australia. The CRRT mode used during this period was continuous venovenous hemofiltration (CVVH). The blood flow was set at 200 mL/min, and replacement fluid (RF) was adjusted for the desired prescribed effluent rate of 30 mL $kg^{-1}$ $h^{-1}$, with 50% infused prefilter. The default RF used was Accusol (Baxter Healthcare Limited, Norfolk, UK; see Table 1). Clinicians could switch therapy to Phoxilium during CVVH in adults older than 18 years deemed at risk of hypophosphatemia, following informed consent from the patient or proxy in accordance to Special Access Scheme regulations. The patients' phosphate intake, supplement, and serum biochemistry were retrieved and studied for 42 hours after the change of RF to Phoxilium.

Patients with the following biochemical criteria were excluded: (i) serum potassium level higher than 6 mmol/L, which precludes the use of potassium containing RF; (ii) serum ionized calcium level higher than 1.6 mmol/L; (iii) serum phosphate level higher than 2.0 mmol/L; and (iv) current use of citrate-based RF, which is not interchangeable with Phoxilium.

### 2.3. Hemosol-B0 arm

Random controls who received CRRT for more than 48 hours were obtained from the Austin Hospital cohort participating in the Randomized Evaluation of Normal versus Augmented Level (RENAL) Replacement Therapy study, from April 2006 to April 2008 [7]. The CRRT mode used was continuous venovenous hemodiafiltration (CVVHDF). The blood flow was set at 200 mL/min. The prescribed effluent rate was set at 25 or 40 mL $kg^{-1}$ $h^{-1}$ as