Reviewer's report

Title: Dysnatremia, its correction, and mortality in patients undergoing continuous renal replacement therapy: a prospective observational study

Version: 1 Date: 4 September 2015

Reviewer: Arthur Greenberg

Reviewer's report:

The authors attempted to assess the influence of hyponatremia and hypernatremia on 30 day mortality of patients with AKI who required continuous renal replacement therapy. In addition, they examined the effect of correction of dysnatremia on mortality in this same population.

The adverse effect of dysnatremia on mortality is well documented in numerous situations. This manuscript adds another population. Data on effect of correction of dysnatremias in large populations are scarce. The data provided by the authors in this population are an important addition to the literature.

Major Compulsory /Revisions:

1. How the population enrolled was acquired in incompletely specified. Were the cases consecutively ascertained? What percentage of patients approached declined enrollment. The authors should provide a CONSORT diagram detailing patient flow as a supplemental figure.

2. The authors mention correction for comorbidities, but provide details only on the modification to APACHE scores. If they performed a multivariate correction (table 2), they need to provide details on their model.

3. The authors repeatedly state that the available prior studies do not show a survival benefit for correction of hyponatremia. No study performed to date was designed or powered to show a mortality effect. The studies have all used sodium concentration correction as the metric for benefit. The comments on the EVEREST trial in the discussion need either to be deleted or reworked. The objective of this trial had nothing to do with dysnatremia. It was designed only to assess the effect of treatment with a vasopressin receptor antagonist on outcome of acute decompensated CHF. Only 7% of patients were dysnatremic. A secondary analysis of the hyponatremic patients suggests benefit of improved hyponatremia, (Hauptman PJ. J Card Fail 2013;19:390), but this study is merely hypothesis generating.

4. Patients with AKI receiving CRRT are very sick. Numerous trials in patients with AKI, ESRD, sepsis in the ICU, and other highly complex illness have failed to show a mortality benefit of a single simple maneuver, e.g., increased dialysis dose, goal-directed fluid management, glucocorticoids, anti-thrombin 3. The authors should emphasize in the discussion the difficulty of showing
improvement of therapeutic maneuvers in patients with multi-system illness. This is particularly important in this purely observational study.

Minor Essential Revisions:

5. Are figures 4E and 4F correctly labeled? They appear to show higher mortality in patients with hypernatremia at baseline whose sodium fell, i.e., corrected, at 24 or 72 hours. The text describes improved mortality with correction in this group.

6. Suggested language changes:
p4, line 6. substitute "adverse" for "worse"
p. 4, line 23 change to "how sodium levels predict mortality". "Predictability" is not a suitable term here.
p. 12, line 12. meaning of "issues are waived" is unclear. Rewrite.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Within the last 5 years, I have received consulting fees, research support, travel support, and served on a Speaker Bureau for Otsuka, the manufacturer of tolvaptan.