

Determinants of pre-dialysis serum sodium trends and variability and their associations with survival in incident hemodialysis patients: Results from the Monitoring Dialysis Outcomes (MONDO) initiative.

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Background

Recent studies in incident hemodialysis patients receiving treatment in Renal Research Institute clinics in the United States showed stable monthly pre-hemodialysis (HD) serum sodium (SNa⁺) to be associated with reduced mortality (Raimann, ASN 2011 and ERA-EDTA 2012). The current analysis aimed to extend this analysis to other countries and continents.

Methods

The global MONDO initiative encompasses patients from 26 countries who started HD between 2000 and 2010 (Usvyat, Blood Purif 2013). Individual pre-HD SNa⁺ average, SNa⁺ trend and variability as slope and standard deviation (SD), respectively, were calculated over the first year. Patients were stratified in 3 strata of average SNa⁺ (<137; 137 to 141; >141 mEq/L) groups and tertiles of SNa⁺ SD (<1.9, 1.9 to 2.9; >2.9 mEq/L), and SNa⁺ slope (<-0.1, -0.1 to 0.1; >0.1 mEq/L/month). Multiple linear regression (MLR) models including pathobiologically plausible parameters were developed to identify predictors of SNa⁺ variability and trends. Time to death in the second year was assessed by two Cox regression models, one each with SNa⁺ slope and SNa⁺ variability, adjusted for SNa⁺, age, gender, diabetes and interdialytic weight gain as % of body weight (IDWG%).

Table 1: Hazard Ratio (HR) for mortality of pre-dialysis serum sodium (SNa⁺) trends and variability at different levels of SNa⁺.

Average SNa ⁺	SNa ⁺ variability (tertiles in ascending order) Hazard Ratio (95% CI)	SNa ⁺ trends (tertiles in ascending order) Hazard Ratio (95% CI)
<137 mEq/L	2.8 (1.7 to 4.7)*	3.9 (2.3 to 6.5)*
	2.7 (1.7 to 4.5)*	3.5 (2.1 to 5.9)*
	3.6 (2.2 to 5.8)*	3 (1.8 to 5.1)*
137 to 141 mEq/L	1.7 (1 to 2.7)*	2.3 (1.3 to 3.8)*
	1.7 (1.1 to 2.8)*	1.8 (1.1 to 3.1)*
	2.3 (1.4 to 3.7)*	2.1 (1.3 to 3.6)*
>141 mEq/L	Reference group	2.2 (1.2 to 4)*
	1.8 (1 to 3.2) [†]	Reference group
	2.3 (1.3 to 4.1)*	2.3 (1.2 to 4.2)*

*P<0.05; [†]P<0.1

Results

We studied 10771 HD patients [60±15 years, 5923 males, 4668 diabetics, IDWG% 3.8±1.4 %]. SNa⁺ variability was positively related to diabetes, IDWG%, serum potassium and dialysate to SNa⁺ gradient, and inversely to albumin, normalized Protein Catabolic Rate (nPCR), SNa⁺ and RRF. SNa⁺ trends were related positively to age and nPCR. Survival analysis identified higher SNa⁺ variability and unstable SNa⁺ trends as significant predictors of death in some strata. Patients with SNa⁺ below 137 mEq/L showed the highest HRs without any discernible effect of SNa⁺ variability and trends (Table 1).

Conclusion

Our analysis in an international cohort of HD patients corroborates previous findings that unstable SNa⁺ are associated with poor survival. HR was, regardless of variability, highest in those with SNa⁺<137, but the risk increase with increased variability was particularly pronounced in patients with an average SNa⁺>141 mEq/L. This suggests that patients with unstable SNa⁺ may require close observation.

