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Original Investigation

Dialysate Potassium, Serum Potassium, Mortality, and Arrhythmia Events in Hemodialysis: Results From the Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Background: Sudden death is a leading cause of death in patients on maintenance hemodialysis therapy. During hemodialysis sessions, the gradient between serum and dialysate levels results in rapid electrolyte shifts, which may contribute to arrhythmias and sudden death. Controversies exist about the optimal electrolyte concentration in the dialysate; specifically, it is unclear whether patient outcomes differ among those treated with a dialysate potassium concentration of 3 mEq/L compared to 2 mEq/L.

Study Design: Prospective cohort study.

Setting & Participants: 55,183 patients from 20 countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS) phases 1 to 5 (1996-2015).

Predictor: Dialysate potassium concentration at study entry.

Outcomes: Cox regression was used to estimate the association between dialysate potassium concentration and both all-cause mortality and an arrhythmia composite outcome (arrhythmia-related hospitalization or sudden death), adjusting for potential confounders.

Results: During a median follow-up of 16.5 months, 24% of patients died and 7% had an arrhythmia composite outcome. No meaningful difference in clinical outcomes was observed for patients treated with a dialysate potassium concentration of 3 versus 2 mEq/L (adjusted HRs were 0.96 [95% CI, 0.91-1.01] for mortality and 0.98 [95% CI, 0.88-1.08] for arrhythmia composite). Results were similar across predialysis serum potassium levels. As in prior studies, higher serum potassium level was associated with adverse outcomes. However, dialysate potassium concentration had only minimal impact on serum potassium level measured predialysis (+0.09 [95% CI, 0.05-0.14] mEq/L serum potassium per 1 mEq/L greater dialysate potassium concentration).

Limitations: Data were not available for delivered (vs prescribed) dialysate potassium concentration and postdialysis serum potassium level; possible unmeasured confounding.

Conclusions: In combination, these results suggest that approaches other than altering dialysate potassium concentration (eg, education on dietary potassium sources and prescription of potassium-binding medications) may merit further attention to reduce risks associated with high serum potassium levels.

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INDEX WORDS: Dialysate potassium; hemodialysis; hyperkalemia; potassium gradient; mortality; serum potassium; hemodialysis; arrhythmia; sudden death; cardiac instability; electrolyte shift; end-stage renal disease (ESRD); Dialysis Outcomes and Practice Patterns Study (DOPPS).

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Sudden death is a leading cause of death in patients requiring hemodialysis (HD), with 27% of all deaths attributable to arrhythmic mechanisms.[1] In thrice-weekly maintenance HD, these events tend to cluster in the period just prior to the first dialysis session of the week, when fluid overload and levels of various uremic toxins are highest, and in the period during and immediately following HD sessions.[2-4] Although a multiplicity of factors contribute to sudden death, it is speculated that the increased risk during and immediately following the HD session is associated with large fluid and electrolyte shifts that occur during this time.[3]

Hyperkalemia is common in patients with kidney failure due to diminished renal potassium excretion causing disturbances in heart rhythm and cardiac arrest in extreme cases.[5,6] High predialysis serum potassium level is recognized as a risk factor for sudden death and all-cause mortality in HD patients.[7,8] Potassium has the potential to move freely across the dialyzer membrane during the HD session, typically being transferred from a patient's blood into the dialysate.[9] Dialysate potassium concentration is a modifiable factor that can alter serum potassium concentrations throughout the HD session and thus potentially affects the risk for arrhythmias and cardiac arrest.[10] Results of studies examining dialysate potassium effects on sudden death and all-cause mortality have been mixed. Kovesdy et al[7] advised that hyperkalemic patients with a lower dialysate potassium concentration bath may have better survival, whereas 2 large case-control studies investigated sudden death events occurring during dialysis and concluded that there was an increased risk for sudden death for patients dialyzing with dialysate potassium concentrations of 1 mEq/L or even 0 mEq/L.[11,12] Although no recommendation for dialysate potassium concentrations has been provided in the NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative) cardiovascular disease guideline,[13] several recent reviews are in agreement that dialysate potassium concentration < 2 mEq/L should be avoided, particularly in patients with high predialysis potassium levels, to avoid a rapid decrease in plasma potassium levels.[6,14-18] Accordingly, anecdotal reports indicate that the use of dialysate potassium concentrations < 2 mEq/L has become increasingly rare. This prompted us to investigate whether a dialysate potassium concentration of 2 mEq/L was still too low, in comparison to a higher dialysate potassium concentration of 3 mEq/L.

In the absence of conclusive results, many clinicians' dialysate potassium prescriptions often aim to keep serum potassium levels within an "acceptable" range. Some nephrologists make decisions qualitatively based on clinical judgment and experience, others anecdotally use the "rule of 7" and prescribe dialysate potassium concentrations to make the sum of dialysate potassium and predialysis serum potassium level approximately 7,[19] whereas some facilities' medical staff elect to provide a uniform dialysate potassium concentration to all patients. However, optimal prescription practices are unknown: treating with lower dialysate potassium concentrations promotes greater intradialytic potassium flux and increases the likelihood of hypokalemia; conversely, treating with higher dialysate potassium concentrations may predispose patients to hyperkalemia. The former may be worsened among patients with already low predialysis serum potassium levels, and the latter, among patients with high predialysis serum potassium levels. Furthermore, treating patients with a high predialysis serum potassium level with a low dialysate potassium concentration may cause a rapid intradialytic shift in potassium during the first hour of dialysis. Thus, there is reason to speculate that the effect of dialysate potassium concentration may be modified based on patients' predialysis serum potassium levels.

A previous Dialysis Outcomes and Practice Patterns Study (DOPPS) analysis[20] observed associations between sudden death and various modifiable practices: low treatment time, low Kt/V, high ultrafiltration volume, and low dialysate potassium concentration. Given more recent trends toward higher dialysate potassium concentrations and the lack of clear evidence across studies comparing the 2 most commonly used dialysate potassium prescriptions (2 vs 3 mEq/L), we revisited the issue of dialysate potassium concentration and clinical outcomes using a larger and more contemporary cohort of patients. In this study, we leveraged data from the international cohort of in-center HD patients in the DOPPS to assess the risks of different dialysate potassium prescriptions overall and among patients with different serum potassium levels. We also examined associations between predialysis serum potassium levels and outcomes, as well as association between dialysate potassium concentrations and serum potassium levels.

METHODS

Data Source

The DOPPS (www.dopps.org) is an international prospective cohort study of patients 18 years or older treated with in-center HD. The study is designed to observe patients over time and correlate practices and outcomes in different medical settings around the world to help researchers and clinicians identify best practices and other modifiable characteristics that improve dialysis patients' lives. Patients were randomly selected from national samples of dialysis facilities within each country.[21,22] In this analysis, data from participants in DOPPS phase 1 (1996-2001), phase 2 (2002-2004), phase 3 (2005-2008), phase 4 (2009-2011), and phase 5