Published in final edited form as:

Semin Dial. 2014 ; 27(5): 505. doi:10.1111/sdi.12253.

Letter to the Editor of Seminars in Dialysis

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Dear Dr. Sherman

The recent paper by Chen and Kalantar-Zadeh on serum bicarbonate and the risk of death (1) provides an excellent review and offers new information about a potential role of malnutrition-inflammation. In their critical comment about our 2013 DOPPS publication by Tentori et al. (2), however, the authors dismissed our main finding that higher *dialysate* bicarbonate concentration was associated with mortality, saying, “the presence of significant confounding by indication bias is a more likely explanation. It is likely that high-bicarbonate bath was prescribed to treat more severe metabolic acidosis” (p. 2).

The authors seem to have missed our key analysis, noted in the abstract and page 741, which specifically dealt with confounding by indication by only including dialysis facilities where a single dialysate bicarbonate level was used for virtually all (>90%) patients (confirmed when requiring 100%). In this analysis, there could be no confounding by indication since all patients received the same dialysate bicarbonate and the prescription is not individualized based on specific patient characteristics (e.g., more severe acidosis). The estimated effect of higher dialysate bicarbonate on mortality was nearly identical for patients in non-individualized and individualized facilities. Because of concerns that the dialysate bicarbonate effect may be confounded with other practices that affect mortality, we not only adjusted for case mix and detailed comorbidities, but also for two other dialysis facility practices - the percentage of patients using a catheter and the percentage with Kt/V <1.2.

We also found the inverse association between *serum* bicarbonate and mortality to be the same in facilities where dialysate bicarbonate was uniform as in facilities where it was individualized. That finding is consistent with the inverse association between pre-dialysis serum bicarbonate and mortality, reported by Chen and Kalantar-Zadeh in their fully adjusted model.

In order to advance our understanding of dialysis practices using observational studies, we agree that possible bias due to confounding by indication must be carefully considered in the analysis and in the interpretation of results. Taking advantage of a natural experiment in which patients are “assigned” to facilities that do not individualize a treatment, as all patients at that facility are given a uniform dialysate bicarbonate, eliminates confounding by indication.

Additional studies are needed to address the impact of total base in the dialysate-bicarbonate plus acetate, since neither of these two studies had information about the acetate component in the dialysate. Thus, we recommend randomized clinical trials with different total dialysate base levels.

Sincerely.

References

1. Chen JLT, Kalantar-Zadeh K. Is an Increased Serum Bicarbonate Concentration during Hemodialysis Associated with an Increased Risk of Death? *Semin Dial.* 2014;1–4.
2. Tentori F, Karaboyas A, Robinson B, Morgenstern H, Zhang J, Sen A, Ikizler TA, Rayner H, Fissell R, Vanholder R, Tomo T, Port FK. Association of dialysate bicarbonate concentration with mortality in the Dialysis Outcomes and Practice Patterns Study. *Am J Kidney Dis.* 2013; 62(4):738–746. [PubMed: 23707043]