



Opinion

Choice of the Optimal Dialysate Sodium Concentration

Christopher W. McIntyre^{1,2}

¹ HemoLab and the Lilibeth Caberto Kidney Clinical Research Unit, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON N6A5W9, Canada; cmcint48@uwo.ca

² Kidney Clinical Research Unit Room ELL-101, London Health Sciences Centre, Victoria Hospital, London, ON N6A5W9, Canada

Abstract: The choice of dialysate sodium concentration remains amongst the most crucial and difficult to address challenges, in the care of hemodialysis (HD) patients. Our understanding of the determinants of sodium transport, as well as the consequences of getting the decisions wrong, remains both imperfect and evolving. This question has been subject to far less study than it deserves. In this short piece we consider what we are trying to achieve with dialysate sodium choices and how best to individualize those choices to address the symptomatic and survival-based needs of our patients.

Keywords: sodium; hemodialysis; hemodialysate



Citation: McIntyre, C.W. Choice of the Optimal Dialysate Sodium Concentration. *Kidney Dial.* **2022**, *2*, 534–536. <https://doi.org/10.3390/kidneydial2040047>

Academic Editors: Manfred Hecking, Peter Kotanko and Jochen G. Raimann

Received: 11 January 2022

Accepted: 30 May 2022

Published: 13 October 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Although this seems a relatively simple and straight forward question, it is mired in the complexities surrounding the movement of sodium during hemodialysis (HD), limitations in our knowledge relating to these processes and the dearth of high quality empirical clinical study. The challenge needs to be carefully thought through, with clear enunciation of what the purpose of HD is (with respect to sodium homeostasis), our evolving understanding of the pathophysiological consequences of failure and the constraints relating to this decision-making process.

What is the principle therapeutic aim? HD aims to remove the entire interdialytic sodium load that was ingested between sessions, that was not eliminated through residual renal function and gastrointestinal losses (both modest in this scenario). Failure to do so results in aggravation of interdialytic fluid gains, congestion, aberrant cardiac remodeling, hypertension [1] and exacerbation of multi-organ ischemic injury as a consequence of inappropriately high ultrafiltration requirements and associated circulatory stress [2–4]. Failure of clearance leads to tissue deposition of sodium in skin, muscle [5] and directly into cardiac tissue, further driving mortality. Exposure to inappropriate intradialytic circulating serum sodium concentrations also directly results in injury to the vascular epithelial glycocalyx [6,7]; exacerbating the ischemic vulnerability of tissue by inducing additional intradialytic endothelial dysfunction. Excessive sodium depuration results in failure to maintain plasma tonicity and plasma refill—resulting in hypotension and circulatory collapse (also leading to worsening HD-associated cardiovascular injury to heart, brain, gut and kidneys) [4,8–10].

Manipulation of dialysate sodium concentration is the principal instrument to manage sodium homeostasis in HD patients: Sodium ingestion (in patients without other osmotic drives for thirst such as hyperglycemia) is the major determinant of interdialytic weight gain (IDWG). Lower dialysate sodium concentrations lead to more modest IDWG and reduced tissue deposition of sodium; as directly measured using sodium MRI [11]. Ultrafiltrate is characteristically hypotonic—with respect to plasma—therefore, this requires some additional diffusive element in addition to convection to clear the interdialytic ingested sodium load. Higher ultrafiltration volumes result in additional decoupling of sodium mass transfer from assumptions based on diffusion gradient. The terms 'high'

and 'low' can be somewhat meaningless in the way they are often applied to the study of dialysate sodium concentrations. Sodium ions in plasma interact with a variety of other dissolved materials (proteins, bicarbonate, carbonate, etc.). Sodium ions also exchange for intracellular potassium and bind to proteoglycans in the skin [12,13]. Therefore, only a percentage of ions are available for diffusion. The movement of sodium will therefore be determined by differences between the concentrations of non-complexed, electrochemically active ions (sodium activity). The level of sodium ions available for diffusion is further influenced by both temperature and pH. Both the Gibbs–Donnan effect, and the differences in sodium activity allow the movement of sodium and water to become uncoupled during haemodialysis [14]. This makes it possible for patients to sodium load on dialysis, despite dialysate sodium concentration being lower than the pre dialysis serum sodium concentration (commonly termed 'low' dialysate sodium concentration) [15,16]. The situation is made even more complex by the differences that exist in how permissive different dialyzer membranes are to the transport of sodium [17] (based on the charge density of the materials used), and with a new generation of dialyzers (mid cut off membranes) (defined by larger pore size potentially impacting increasing the effective pore area with less electrostatic resistance to sodium movement) [18]. Serum sodium is a poor marker of total body sodium stores, unreliable to assay robustly within standard clinical practice (without resorting to flame photometry) and allows poor appreciation of content within the component of the circulating volume that contains removable sodium (plasma water fraction). All the above factors militate against the implementation of robust reliable theoretically derived sodium modelling approaches.

What might the approach to achieving optimal sodium homeostasis look like? Although this approach is difficult to define, it is reasonable to say approaches using supra physiological dialysate sodium concentrations and sodium profiling should be universally avoided (unless in the rare case of patients with high additional sodium losses, e.g., high output ileostomy).

In contrast to the large degree of observed inter patient variability in pre dialysis serum sodium concentration, the variation observed within individual patients is small. Serum sodium concentration varied from 132 to 144 mmol/L between patients, but by less than 2 mmol/L within individual patients, on a month-to-month basis [19,20]. This large inter-patient and small intra-patient variability suggests that an approach to sodium removal based upon a single default dialysate sodium is likely to be less desirable than one based on individualization of this sodium removal [21]. However, relying on the pre dialysis serum sodium as the direct determinant of dialysate sodium concentration is fraught with problems (as outlined above). Even from the most simplistic considerations of plasma sodium concentrations a serum sodium concentration of 135 mmol/L equates to a plasma sodium concentration of around 144 mmol/L.

Further challenges also exist related to the dialysis machines themselves. Dialysate conductivity monitoring is often inaccurate and prone to drift and lack of appropriate calibration and maintenance [22]. Even small errors can result in large differences in achieved mass transfer of sodium between different machines with apparently similar prescribed dialysate conductivity. When dealing with patients with particularly low plasma water sodium concentrations the lack of ability of most dialysis monitors to deliver sodium concentrations of less than 130–132 mmol/L further hampers the ability to individualize treatment.

Conclusion—what should we do? An individualized approach with an initial dialysate sodium consideration selected as being safe from current clinical and registry-based studies (potentially, being augmented by ongoing large scale RCT), may represent a way forward (136–138 mmol/L). However, this needs to be then further refined (probably lowered) within an individual patient; with iterative consideration of IDWG, hemodynamic stability during HD, BP, quantification of tissue sodium levels (if feasible) and symptomatic tolerability. Unfortunately selecting (and delivering) the correct dialysate sodium concentration for any given patient is currently as difficult as it is crucially important.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The author declares no conflict of interest respective to this article.

References

- Davenport, A. Audit of the effect of dialysate sodium concentration on inter-dialytic weight gains and blood pressure control in chronic haemodialysis patients. *Nephron Clin. Pract.* **2006**, *104*, c120–c125. [[CrossRef](#)] [[PubMed](#)]
- Burton, J.O.; Jefferies, H.J.; Selby, N.M.; McIntyre, C.W. Hemodialysis-Induced Repetitive Myocardial Injury Results in Global and Segmental Reduction in Systolic Cardiac Function. *Clin. J. Am. Soc. Nephrol.* **2009**, *4*, 1925–1931. [[CrossRef](#)] [[PubMed](#)]
- McIntyre, C.W.; Burton, J.O.; Selby, N.M.; Leccisotti, L.; Korsheed, S.; Baker, C.S.R.; Camici, P.G. Hemodialysis-induced cardiac dysfunction is associated with an acute reduction in global and segmental myocardial blood flow. *Clin. J. Am. Soc. Nephrol.* **2008**, *3*, 19–26. [[CrossRef](#)] [[PubMed](#)]
- Buchanan, C.; Mohammed, A.; Cox, E.; Köhler, K.; Canaud, B.; Taal, M.; Selby, N.; Francis, S.T.; McIntyre, C.W. Intradialytic Cardiac Magnetic Resonance Imaging to Assess Cardiovascular Responses in a Short-Term Trial of Hemodiafiltration and Hemodialysis. *J. Am. Soc. Nephrol.* **2017**, *28*, 1269–1277. [[CrossRef](#)] [[PubMed](#)]
- Qirjazi, E.; Salerno, F.R.; Akbari, A.; Hur, L.; Penny, J.; Scholl, T.; McIntyre, C.W. Tissue sodium concentrations in chronic kidney disease and dialysis patients by lower leg sodium-23 magnetic resonance imaging. *Nephrol. Dial. Transplant.* **2020**, *36*, 1234–1243. [[CrossRef](#)]
- Oberleithner, H.; Peters, W.; Kusche-Vihrog, K.; Korte, S.; Schillers, H.; Kliche, K.; Oberleithner, K. Salt overload damages the glycocalyx sodium barrier of vascular endothelium. *Pflügers Arch.-Eur. J. Physiol.* **2011**, *462*, 519–528.
- Koch, J.; Idzerda, N.M.A.; Ettema, E.M.; Kuipers, J.; Dam, W.; Born, J.V.D.; Franssen, C.F.M. An acute rise of plasma Na⁺ concentration associates with syndecan-1 shedding during hemodialysis. *Am. J. Physiol. Physiol.* **2020**, *319*, F171–F177. [[CrossRef](#)] [[PubMed](#)]
- Marants, R.; Qirjazi, E.; Lai, K.-B.; Szeto, C.-C.; Li, P.K.; Li, F.; Lee, T.-Y.; McIntyre, C.W. Exploring the Link Between Hepatic Perfusion and Endotoxemia in Hemodialysis. *Kidney Int. Rep.* **2021**, *6*, 1336–1345. [[PubMed](#)]
- Marants, R.; Qirjazi, E.; Grant, C.J.; Lee, T.Y.; McIntyre, C.W. Renal Perfusion during Hemodialysis: Intradialytic Blood Flow Decline and Effects of Dialysate Cooling. *J. Am. Soc. Nephrol.* **2019**, *30*, 1086–1095. [[CrossRef](#)]
- Eldehni, M.T.; Odudu, A.; McIntyre, C.W. Brain white matter microstructure in end-stage kidney disease, cognitive impairment, and circulatory stress. *Hemodial. Int.* **2019**, *23*, 356–365. [[CrossRef](#)]
- Lemoine, S.; Salerno, F.R.; Akbari, A.; McIntyre, C.W. Influence of Dialysate Sodium Prescription on Skin and Muscle Sodium Concentration. *Am. J. Kidney Dis.* **2021**, *78*, 156–159. [[CrossRef](#)] [[PubMed](#)]
- Titze, J. Water-Free Na⁺ Retention: Interaction with Hypertension and Tissue Hydration. *Blood Purif.* **2008**, *26*, 95–99. [[CrossRef](#)] [[PubMed](#)]
- Titze, J.; Shakibaei, M.; Schaffhuber, M.; Schulze-Tanzil, G.; Porst, M.; Schwind, K.H.; Dietsch, P.; Hilgers, K.F. Glycosaminoglycan polymerization may enable osmotically inactive Na⁺ storage in the skin. *Am. J. Physiol. Circ. Physiol.* **2004**, *287*, H203–H208. [[CrossRef](#)] [[PubMed](#)]
- Flanigan, M.J. Role of sodium in hemodialysis. *Kidney Int.* **2000**, *58*, S72–S78. [[CrossRef](#)] [[PubMed](#)]
- Locatelli, F.; Salvatore, D.; Celestina, M. Sodium Kinetics during Dialysis. *Semin. Dial.* **1999**, *12*, S41–S44.
- Funck-Brentano, J.-L.; Man, N.K. Optimization of Na Content in Dialysis Fluid. *Nephron Exp. Nephrol.* **1984**, *36*, 197–200. [[CrossRef](#)]
- Lopot, F.; Kotyk, P.; Blaha, J.; Válek, A. Influence of the Dialyzer Membrane Material on Sodium Transport in Hemodialysis. *Artif. Organs* **1995**, *19*, 1172–1175. [[CrossRef](#)]
- Penny, J.D.; Salerno, F.R.; Akbari, A.; McIntyre, C.W. Pruritus: Is there a grain of salty truth? *Hemodial. Int.* **2021**, *25*, E10–E14. [[CrossRef](#)]
- Odudu, A.; Lambie, S.; Taal, M.W.; Fluck, R.J.; McIntyre, C.W. Use of Online Conductivity Monitoring to Study Sodium Mass Balance in Chronic Haemodialysis Patients: Prospects for Treatment Individualisation. *Kidney Blood Press. Res.* **2011**, *34*, 439–446. [[PubMed](#)]
- Gotch, F.A.; Lam, M.A.; Prowitt, M.; Keen, M. Preliminary clinical results with sodium-volume modeling of hemodialysis therapy. *Proc. Clin. Dial. Transpl. Forum* **1980**, *10*, 12–17.
- Keen, M.L.; Gotch, F.A. The association of the sodium “setpoint” to interdialytic weight gain and blood pressure in hemodialysis patients. *Int. J. Artif. Organs* **2007**, *30*, 971–979. [[CrossRef](#)]
- Stragier, A.; Lopot, F.; Švára, F.; Polakovič, V. Fallacies and Pitfalls of Dialysis Sodium Prescription and Control. *Blood Purif.* **2018**, *46*, 27–33. [[CrossRef](#)] [[PubMed](#)]