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A neglected issue in dialysis practice: haemodialysate

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Abstract

The intended function of dialysate fluid is to correct the composition of uraemic blood to physiologic levels, both by reducing the concentration of uraemic toxins and correcting electrolyte and acid–base abnormalities. This is accomplished principally by formulating a dialysate whose constituent concentrations are set to approximate normal values in the body. Sodium balance is the cornerstone of intradialysis cardiovascular stability and good interdialytic blood pressure control; plasma potassium concentration and its intradialytic kinetics certainly play a role in the genesis of cardiac arrhythmias; calcium is related to haemodynamic stability, mineral bone disease and also cardiac arrhythmias; the role of magnesium is still controversial; lastly, acid buffering by means of base supplementation is one of the major roles of dialysis. In conclusion, learning about the art and the science of fashioning haemodialysates is one of the best ways to further the understanding of the pathophysiologic processes underlying myriad acid–base, fluid, electrolyte as well as blood pressure abnormalities of the uraemic patient on maintenance haemodialysis.

Key words: bicarbonate, calcium, haemodialysate, potassium, sodium

Introduction

Paracelsus, a German–Swiss Renaissance physician, wrote: 'All things are poison and nothing (is) without poison; only the dose makes the poison, not the thing' [1]. This sentence seems to apply perfectly to haemodialysate. The intended function of dialysate fluid is to correct the composition of uraemic blood to physiologic levels, both by reducing the concentration of uraemic toxins and correcting electrolyte and acid–base abnormalities. This is accomplished principally by formulating a dialysate whose constituent concentrations are set to approximate normal values in the body. Moreover, dialysate composition is a factor strongly affecting cardiovascular stability during treatment [2]. Composition is an essential element of dialysis prescription, as well as dialyser membrane, blood and dialysate flow rates and treatment time.

Dialysate sodium

Why deal with sodium? Sodium is the main extracellular ion and defines osmolality and size of the extracellular volume; increased plasma sodium concentration results in a rise of osmolality, thirst and extracellular volume expansion. The latter results in cardiovascular diseases such as arterial hypertension and left ventricular hypertrophy [3].

Sodium mass balance in haemodialysis (HD) patients is primarily dependent on two factors: dietary salt intake and sodium removal during dialysis. Salt intake during the interdialysis period is dependent on the patient's behaviour and is a strong driver of volume overload [4]. Most Western societies consume between 150 and 250 mmol/day [5]. There is evidence that HD patients ingest similar amounts of sodium. A small series of Spanish dialysis patients showed baseline sodium intake of ~173 mmol/day [6]. Likewise, a study of 28 English HD patients showed an average estimated sodium intake of 251 mmol/day [7]. NKF KDOQI guidelines recommend an upper limit of daily salt intake of 5 g (~85 mmol of sodium) [8]. Despite the fact that dietary salt restriction is the most logical measure to prevent accumulation of salt and water in dialysis patients, it is not applied in most dialysis centres [9].

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Therefore, one of the most important goals of the dialysis therapy is to remove exactly the mass of sodium that has been accumulated in the interdialysis period in order to reach a zero sodium mass balance. The latter can be achieved through convection and diffusion. Current prescribing practices for maintenance HD rely primarily on convective and less on diffusive losses [10, 11]. This relative distribution, however, is dependent on the amount of ultrafiltration occurring during any given dialysis session (i.e. convective losses), and the prescribed dialysate sodium concentration (Na^+D) and its relationship with the patient's own plasma sodium (the so-called inlet dialyser diffusion concentration gradient between dialysate and plasma) [10]. Actually, Basile *et al.* had shown that convection is the main determinant of the sodium mass balance, with diffusion counterbalancing convection-driven mass balance by ~17% (the mean Na^+D was 138.7 mmol/L) [10]. Odudu *et al.* reported that the diffusive component of ionic mass balance was 29% of the total sodium removal, when dialysing with a fixed Na^+D of 140 mmol/L [11]. Thus, it can be concluded that the diffusive gradient between plasma and the inlet dialyser sodium concentration is an important factor in the 'fine-tuning' of sodium mass balance in HD.

As reviewed by Flanigan, in the early years of dialysis (1960s) when there was no hydrostatic ultrafiltration, osmotic ultrafiltration was accomplished using large amounts of glucose in the dialysate, where the dialysis time was 6–12 h, and Na^+D was kept low in the order of 125–130 mmol/L [12]. In the 1980s, hydrostatic ultrafiltration was applied, where Na^+D was ~136 mmol/L and the dialysis time 4–5 h. In the past years, there remains widespread acceptance of higher Na^+D (≥140 mmol/L) promulgated by continued trends towards shorter dialysis time that may result in the use of hypertonic saline, high Na^+D and sodium modelling in order to avoid haemodynamic instability during the shortened dialysis treatment [13].

A number of options of Na^+D are currently being used in daily practice including fixed, low or high Na^+D or variable (individualized) Na^+D (e.g. Na^+D tailored to serum concentrations, sodium modelling strategies or online monitoring of plasma conductivity with automatic adjustment of dialysate conductivity) [14].

A recent report from the Dialysis Outcomes and Practice Patterns Study (DOPPS) showed that the majority of HD facilities (57%) adopted uniform rather than variable Na^+D prescriptions in more than 90% of patients [15]. Nevertheless, the issue as to whether low or high fixed Na^+D prescriptions should be advocated in chronic HD patients is still debated. High Na^+D prescriptions can be useful for preventing hypotensive episodes but may lead to a positive sodium mass balance that may elicit, in turn, an increase in blood pressure and weight gain. Conversely, low Na^+D prescription may reduce thirst, blood pressure and weight gain but can be harmful, particularly in hypotension-prone subjects. Very recently, a strong controversy about Na^+D prescription arose in the USA: at one side, the recommendations of a consensus meeting of chief medical officers of 14 large dialysis organizations [16, 17], and at the other side, the recommendations of a panel of DOPPS group [18]. The apparent consensus of the former authors was that the prescription of Na^+D should be lowered to 134–138 mmol/L [16, 17]. In contrast, the DOPPS group claimed that it is premature to make such substantial changes in Na^+D prescription without convincing evidence and appropriate balance of the advantages and disadvantages of such a change [18]. With this background in mind, Basile *et al.* aimed at performing a systematic review of the available literature [15, 19–40] to analyse possible benefits and harms of low or high Na^+D prescription in chronic HD patients [41]. Twenty-three studies (76 635 subjects) were reviewed. There was high heterogeneity in the number of patients analysed, overall study quality, duration of follow-up, Na^+D and even in the definition of 'high' or 'low' Na^+D. The only three studies looking at mortality were observational. The risk of death was related to the plasma–Na^+D gradient but was also shown to be confounded by indication from the dialysate sodium prescription itself. Blood pressure was not markedly affected by high or low Na^+D. Patients treated with higher Na^+D had overall higher interdialytic weight gain when compared with those with low Na^+D. Three studies reported a significant increase in intradialytic hypotensive episodes in patients receiving low Na^+D. Data on hospitalizations and use of anti-hypertensive agents were sparse and inconclusive [41].

In conclusion, the evidence in the current literature on benefits and harms of fixed (either high or low) Na^+D prescriptions is sparse and incongruent. This makes it extremely challenging to draw even preliminary conclusions whether an optimal Na^+D to be recommended indeed exists. Future trials specifically targeting the impact of different Na^+D on mortality or other hard outcomes or comparing fixed with individualized or real-time-modelled Na^+D prescriptions are therefore advocated [41].

Until there is new evidence from randomized, controlled trials, Na^+D should not be lowered. The current range of 138–140 mmol/L should be maintained until well-designed trials will offer new insights.

Dialysate potassium

The control of plasma potassium (K^+) is still one of the most severe problems in the global treatment of HD patients. One of the main goals of HD is the removal of K^+ that has accumulated in the body in the interval between two dialyses. A correct K^+ mass balance during HD is crucial: it should be negative and of the same order of magnitude of the positive interdialytic K^+ mass balance, in order to prevent both dangerous intradialysis hypokalaemia and fatal interdialysis hyperkalaemia [42]. K^+ removal during HD can occur through diffusion and convection. Current prescribing practices for chronic intermittent HD rely primarily on diffusive and less on convective losses [42–44]. Thus, intradialysis K^+ kinetics is quite different from that of sodium, in which convection accounts for ~80% of intradialytic sodium mass balance, while the diffusive gradient between plasma and the inlet dialyser sodium concentration is an important factor in the 'fine-tuning' of sodium mass balance [10]. The magnitude of plasma K^+ concentration is dependent on dietary K^+ intake, dialysate K^+ concentration (K^+D), the efficiency of the dialyser, the duration and frequency of dialysis [13]. Actually, a very recent paper by Basile *et al.* [42] investigated the isolated effect of the factor time *t* on intradialysis K^+ mass balance: 11 stable prevalent Caucasian anuric patients underwent one standard (~4 h) and one long hour (~8 h) bicarbonate HD session. The latter were pair matched as far as the dialysate and blood volume processed (90 L) and volume of ultrafiltration are concerned. A statistically significantly larger K^+ removal was observed in the 8-h sessions (Δ 13.56 mmol, equivalent to an increased removal of 15.34%, $P = 0.02$) compared with 4-h sessions [42].

Intradialysis kinetics of plasma K^+ has been described in some studies [42–44]. Plasma K^+ concentration rapidly decreases during the first 60 min and stabilizes during the last 60 min of dialysis. Plasma K^+ reaches a steady state during the last hour of dialysis, while K+ continues to emerge into the dialysate. Therefore, it can be assumed that K^+ removal rate is equal to theintra- to extracellular mass transfer rate at these time points [42].

Furthermore, Fissell and Hakim underlined that dialysis treatment lowers plasma K^+, both by removal of K^+ with dialysate and by rapid shift of K^+ from the extracellular to the intracellular space as metabolic acidosis is treated [45].

Basile *et al.* [42] were able to identify and rank the factors determining the intradialysis K^+ mass balance in bicarbonate HD: plasma K^+ → dialysate K^+ gradient is the main determinant, and acid–base balance plays a much less important role. The duration of HD session per se is an independent determinant of K^+ mass balance, as described earlier [42]. This study confirmed that the rate of K^+ removal during dialysis is largely a function of the pre-dialysis plasma K^+ concentration. The higher the initial plasma concentration, the greater the gradient between plasma and dialysate and, hence, the greater the K^+ removal [13]. Actually, Zehnder *et al.* showed in a prospective, randomized, cross-over study that a 0-mmol/L K^+D was able to remove more K^+ than 1 or 2 mmol/L K^+D ($P < 0.001$) [44]. Alkalosis causes a shift of K^+ into cells, and acidosis results in K^+ efflux from cells. Introduction of buffer base into blood during dialysis promotes cellular uptake of K^+ and thereby attenuates the dialytic removal of K^+ (this is more evident in an acidotic patient). There are case reports in which dialysis succeeded in reducing plasma K^+ concentrations, even though K^+D was higher than the pre-dialysis plasma K^+ values. The decline in plasma K^+ concentration was associated with a corresponding dialysis-induced rise in blood pH [46, 47]. Finally, a randomized, controlled trial showed an association between higher dialysate bicarbonate concentration and a faster decrease in intradialysis plasma K^+ concentration [48].

Cardiovascular diseases account for 38–40% of all deaths in dialysis patients with a large proportion (~25%) attributed to sudden cardiac death [49–52]. The Q wave-T wave (QT) interval is a recognized electrocardiographic marker of the ventricular repolarization, and its prolongation has been associated with increased risk of sudden death in both pathological and healthy populations [53]. Electrolyte disorders are one of the main HD-related factors that can cause QT interval alterations and cardiac arrhythmias, because of their involvement in the genesis, duration, morphology and propagation of the cellular action potential. The electrolytes that mostly influence the ventricular repolarization are K^+ and calcium (Ca^{2+}) [53]. The Nernst equation indicates that the electrical activity of the heart is related to the ratio between the intracellular and extracellular K^+ levels. With the use of a low K^+D, one removes K^+ mainly from the extracellular space and very little from the intracellular one. Surprisingly, most patients are able to tolerate the intradialytic increase in hyperpolarization of the cardiac muscle membrane potential, induced by a rise in the intracellular/extracellular K^+ ratio brought about by a reduction in the extracellular K^+ value as a result of dialysis. However, it is not infrequent to encounter a patient with heart disease who develops arrhythmias during dialysis [13]. Not surprisingly, it has been noted that the frequency of arrhythmias is greater during the first 2 h of dialysis, because the rate of fall in plasma K^+ level is greater due to the presence of a higher K^+ gradient [42]. K^+ modelling first suggested by Redaelli *et al.* involves decreasing K^+D exponentially to maintain a constant plasma to dialysate K^+ gradient of 1.5 mmol/L [54]. In this way, the extracellular K^+ level will not fall too abruptly and the intracellular/extracellular K^+ ratio will not increase too rapidly, thus trying to minimize cardiac irritability and the occurrence of ventricular ectopic activity in high-risk individuals. The approach succeeded in reducing dialysis-induced premature ventricular contractions, the effect being more prominent during the first hour of dialysis [54]. More recently, Santoro *et al.* showed a greater arrhythmogenic activity with the use of a constant and relatively low K^+D when compared with decreasing K^+ profiling in dialysis-sensitive arrhythmic patients [55].

Finally, for the sake of completeness, it must be reminded that the colon contributes considerably to K^+ removal in dialysis patients, with colonic disposal being ~30% of the dietary intake, a value that is about three times higher than normal [56].

In conclusion, the true challenge in HD patients is to avoid both life-threatening pre-dialysis hyperkalaemia (plasma K^+ level >6 mmol/L) and post-dialysis relative hypokalaemia (or at least a very rapid decrease in plasma K^+ level, and the related risk of lethal arrhythmias). Resins (calcium or sodium polystyrene sulphonate) may be used; actually, although K^+-binding sodium-based resins have been prescribed for 50 years, there have been no large studies of their effects among HD patients [57]. New resins under development are welcome in order to provide caregivers with additional options in the choice of K^+-binding resins. Finally, alternative strategies, such as longer or more frequent HD sessions and/or dialysate K^+ profiling [55], may be required in such cases.

Dialysate calcium

Which is the ideal dialysate calcium concentration (Ca^{2+}D) is probably an unanswerable question. The relationship between dialysis and global calcium balance is not completely known, due to the complex interplay of dietary calcium content, intestinal absorption and secretion [58]. In addition, the new therapies in the management of chronic kidney disease–mineral and bone disorder (CKD-MBD) render the scenario even more complex. The main sources of calcium in HD patients are the intestinal absorption and the dialysate. The intestinal absorption is highly dependent on vitamin D levels and includes foods and phosphate binders containing calcium. Of note, at the start of maintenance HD incident patients may have a positive calcium balance, especially those on a high-calcium diet [59]. Importantly, there is an exchangeable calcium pool, i.e. a miscible calcium pool that serves as a kind of buffer, which is equilibrated with extracellular compartments, in which 300 mg/day are exchanged for bone resorption and bone formation [60]. Intradialysis calcium mass balance depends on two main factors: convective losses and diffusive movement of Ca^{2+} across the membrane (into or out from the blood of the patients) [61]. By definition, convection leads to removal of Ca^{2+} from the blood; by contrast, diffusion from the blood or to the blood depends on the so-called inlet dialyser diffusion concentration gradient between Ca^{2+}D and plasma water Ca^{2+} [62]. In the past decade, there has been a relevant shift in Ca^{2+}D prescription from 1.75 to 1.25 mmol/L. Both low and high Ca^{2+}D may have either positive or negative effects. On the one hand, a low Ca^{2+}D avoids the risk of vascular calcification and may be effective in adynamic bone disease, but may induce cardiac arrhythmias [53] and parathyroid gland stimulation [63]. On the other hand, a high Ca^{2+}D suppresses parathyroid hormone (PTH) secretion, increases haemodynamic stability, but has been associated with a long-term risk of vascular calcification. Current guidelines recommend different strategies to control CKD-MBD abnormalities; however, little attention has been paid to the choice of the Ca^{2+}D.

The European Best Practice Guidelines (EBPG) on haemodynamic instability (guideline 3.2.3) recommend the use of Ca^{2+}D of 1.50 mmol/L in patients with frequent episodes of intradialytic hypotension, unless contraindications are present (evidence level II) [64]. Furthermore, EBPG advise that any possible adverse haemodynamic effect of a dialysate with a total calcium concentration of 1.25 mmol/L be balanced against its potential benefits

on vascular calcification [64]. The NKF KDOQI clinical practice guidelines for CKD-MBD abnormalities recommend a $Ca^{2+}D$ in HD and peritoneal dialysis of 1.25 mmol/L (opinion) [8]. Furthermore, Kidney Disease Improving Global Outcomes guideline 4.1.3.5 suggests a $Ca^{2+}D$ between 1.25 and 1.50 mmol/L (evidence level 2D) [65]. Against these guidelines, Gotch *et al.* concluded that more than 80% of dialysis patients would have a positive calcium balance even with a $Ca^{2+}D$ of 1.25 mmol/L [66]. Furthermore, the same authors reported the following results in 320 HD patients under treatment with vitamin D analogues: 70% of patients on phosphate calcium-based binders and 20–50% of patients on phosphate non-calcium-based binders would require a $Ca^{2+}D$ of <1.25 mmol/L to prevent long-term calcium accumulation [67].

The reduction in $Ca^{2+}D$ has been associated with hypotension and an increase in QT interval with consequent arrhythmias [53, 68]. In addition, it is well known that a low $Ca^{2+}D$ may increase serum PTH levels and induce secondary hyperparathyroidism [63]. A recent highly controlled experiment has shown that a dialysate total calcium concentration of 1.375 mmol/L should be preferred because it is able to keep the patient in a mild positive total calcium mass balance, to maintain normal plasma water Ca^{2+} and not to stimulate PTH secretion [63]. Finally, a very recent study in haemodiafiltration demonstrated that calcium profiling might be a way to reduce the calcium overload risk without compromising cardiovascular stability [69].

In conclusion, the prescription of an individualized $Ca^{2+}D$ in HD patients requires an integrated quantitative assessment of mineral bone metabolism and of vascular status as well. When making the choice of a $Ca^{2+}D$, one needs to consider its impact on calcium balance and the change in serum calcium levels, with the awareness that these two aims might not necessarily be achieved at the same time [58]. $Ca^{2+}D$ should be designed so as not to lower serum Ca^{2+}, especially in sessions at risk for end-dialysis hypokalaemia.

Dialysate magnesium

Magnesium (Mg) is the fourth most abundant cation in the body, which plays an important role in several physiological processes. Mg is located mainly within bone and skeletal muscle, and normal total plasma concentration varies in a narrow range, with ~60% present as free Mg^{2+}, the biologically active form [70]. Plasma Mg concentrations are between 0.8 and 1.2 mmol/L, as Mg^{2+} is prevalently an intracellular ion; changes in plasma levels only partially reflect changes in the total Mg body pool. In a healthy adult, the average dietary Mg intake is ~12 mmol/day, out of which 6 mmol are adsorbed, giving a net absorption (total absorption minus the amount secreted in the gastrointestinal tract) of 4 mmol. This equals the amount excreted by the kidneys. In fact, the amount excreted daily by the kidney is 4 mmol (84 mmol are filtered and 80 mmol resorbed), so the net balance is zero [71]. Until severe reductions in glomerular filtration rate (<30 mL/min) occur, serum Mg levels are usually normal. With lower rates of renal function, serum Mg increases because of impaired urinary elimination [72]. In this context, the role of HD in Mg balance is primarily that of removal. Its negative mass balance in dialysis patients mainly depends on diffusive and convective transport (amount of ultrafiltration). A post-dialysis rebound to pre-dialysis Mg plasma levels is common. Lower Mg^{2+} dialysate concentration ($Mg^{2+}D$, 0.25 mmol/L) may induce a reduction in Mg plasma levels, while to maintain plasma Mg levels, an $Mg^{2+}D$ of 0.75 mmol/L may be advisable. Mg removal during dialysis is significantly dependent on pre-dialysis Mg plasma levels [73]. In other words, Mg diffusion concentration gradient (plasma Mg to $Mg^{2+}D$) is the main driving force in Mg kinetics during dialysis. Both high (≥0.75 mmol/L) and low (≤0.25 mmol/L) $Mg^{2+}D$ may have potential beneficial and harmful effects. A high $Mg^{2+}D$ may suppress PTH secretion and delay the development of arterial calcification. But potential harmful effects are the altered nerve conduction velocity, pruritus and increased risk of osteomalacic renal osteodystrophy. A low $Mg^{2+}D$ may improve bone mineralization and avoid Mg accumulation in the case of the oral Mg prescription as phosphate binder. Potential harmful effects are muscle cramps and increase in serum PTH levels [74]. The commercially available $Mg^{2+}D$ solutions have Mg concentrations ranging between 0.25 and 0.75 mmol/L, but even Mg-free or 1.0 mmol/L solutions are on sale.

In conclusion, when making the choice of $Mg^{2+}D$, one needs to consider CKD-MBD and phosphate binders containing Mg, with the awareness that the normalization of plasma Mg level could be the only desirable goal.

Dialysate bicarbonates

As the kidney is a key organ of hydrogen ion (H^+) handling, metabolic acidosis is one of the main complications of uraemia. Consequently, metabolic acidosis is common in patients receiving maintenance HD and plays an important role in the development of bone and protein–energy wasting through increased protein degradation [75]. H^+ accumulation in the blood of uraemic patients is buffered by plasma bicarbonate, which is used as a surrogate marker of acidaemia. Contribution of dialysis to correct metabolic acidosis occurs through buffer supply, mainly bicarbonate, rather than through H^+ clearance. Diffusive influx of buffer into the patient has been used since the beginning of the dialysis era. Currently, most HD patients are treated with bicarbonate dialysis. The bicarbonate flux from the dialysate to the patient is determined both by the transmembrane concentration gradient and by the bicarbonate dialysance. The usual average dialysate concentration is 35 mmol/L, obtained by proportioning pumps in the dialysis machine that mix purified water with separate 'acid' and bicarbonate concentrate. The acid concentrate contains electrolytes, glucose and 2–8 mmol/L of acetate (which is metabolized into bicarbonate in the liver) to prevent calcium precipitation. The optimal dialysate bicarbonate concentration is one that prevents acidosis at the beginning of the next HD session while avoiding post-dialysis alkalosis [76]. Unfortunately, the correction of metabolic acidosis during the dialysis run temporarily exposes the patient to haemodynamic instability [77] and, especially at the end of the session, to the risks and the potential symptoms induced by metabolic alkalosis such as cramps, reduced cerebral perfusion as well as electrolytic and enzymatic unbalances due to sudden pH changes. Few studies have assessed so far outcomes of patients treated with different dialysate bicarbonate levels. No data for hospitalization and mortality have been published, and a recent report concluded that there were insufficient data for a meta-analysis [78]. Serum bicarbonates <22 mmol/L have been linked to higher all-cause mortality [79]. The prescribed concentration of buffers in HD progressively increased over time. On 4 November 2011, Fresenius Medical Care (FMC) North America sent an internal memo to FMC dialysis units in the USA, including four statements: (i) the total buffer that patients receive could be underestimated; (ii) the pre-dialysis serum bicarbonates increased over time (22.9 versus 24.1 mmol/L comparing 2004 with 2011 with 25% ≥26.0, 15% ≥28.0 and 3% ≥30.0 mmol/L); (iii) an internal case–control study evaluated risk factors in HD patients who suffered from

cardiopulmonary arrest (941 patients from 667 facilities) compared with other HD patients (80 516) within the same facilities between 1 January and 31 December 2010. Logistic regression analysis indicated an unadjusted odds ratio for cardiopulmonary arrest of 6.3 with pre-dialysis serum bicarbonates ≥28.0 mmol/L; (iv) reducing dialysate bicarbonate concentration in patients with pre-dialysis serum values >24 mmol/L was recommended [80].

Recently, Tentori *et al.* (DOPPS group) postulated that high dialysate bicarbonate concentration may contribute to rapid electrolyte shifts during the HD session and to the development of post-dialysis metabolic alkalosis and thus contribute to adverse clinical outcomes. This is the first study to report higher mortality in patients treated with higher dialysate bicarbonate concentrations [81].

In conclusion, the correction of metabolic acidosis and the modulation of dialysate bicarbonate concentration are crucial steps. Pre-dialysis alkalosis and post-dialysis hypokalaemia are modifiable risk factors associated with cardiopulmonary arrest. The adoption of a patient-tailored strategy is mandatory in order, on the one hand, to correct acidosis and, on the other hand, to avoid both symptoms of transient secondary metabolic alkalosis and potential harm.

Conclusions

The three issues that are most relevant for optimizing dialysate composition are as follows: (i) the choice of Na^+D: future trials adequately powered to evaluate the impact of different Na^+D on mortality or other patient-centred outcomes are needed; (ii) the burden of sudden cardiac death: it is extremely high, and every effort should be made to individualize at the same time K^+D and $Ca^{2+}D$ in each HD patient in order to prevent the occurrence of fatal arrhythmias; and (iii) the long-term risk of vascular calcification: current guidelines recommend different strategies to control CKD-MBD abnormalities; however, little attention has been paid to the choice of the $Ca^{2+}D$. Dialysate composition is one of the most fascinating topics in nephrology, where the possibilities for improvements are plentiful [13]. Learning about the art and the science of fashioning haemodialysates is one of the best ways to further the understanding of the pathophysiologic processes underlying a myriad of acid–base, fluid, electrolyte as well as blood pressure abnormalities [13]. Dialysate composition should be treated like other interventional drugs or devices, and therefore studied in well-conducted trials to determine efficacy and safety.

Conflict of interest statement

None declared.

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