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Individualising / personalizing hemodialysate composition

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Abstract--The effectiveness of the haemodialysis (HD) treatment directly affects the survival and quality of life of dialysis patients. In this regard, the composition of the dialysate, including the quality of the water, is very important. Normalizing the plasma electrolyte and mineral concentrations before to dialysis while reducing significant changes in the patient's intradialytic plasma concentrations is one of HD's main goals. For the purpose of avoiding intra- and interdialytic hypotension as well as pulmonary edoema, adequate sodium (Na) and water elimination is essential. The cardiovascular system and the bones may be protected by having the right amounts of calcium (Ca) and magnesium (Mg) in the dialysate. This will help to avoid extraskeletal calcifications, severe secondary hyperparathyroidism, and adynamic bone disease. A steady pH in body fluids is required for proper protein and membrane function as well as bone protection, and this is achieved by maintaining an adequate bicarbonate concentration [HCO₃]. A sufficient dialysate glucose concentration prevents life-threatening hypoglycemia and severe hyperglycemia, which can cause serious cardiovascular problems and exacerbate diabetic comorbidities.

Keywords--chronic kidney disease (CKD), sodium, potassium, chronic renal insufficiency, dialysate individualization, haemodiafiltration, haemodialysis, secondary hyperparathyroidism, electrolyte.

Introduction

Dialysate composition affects the electrolyte exchanges between blood and dialysate. This dialysate composition helps to maintain body's acid base balance and has a significant impact on intradialytic cardiovascular stability. The content of the dialysate is an essential aspect of performing haemodialysis (HD) in a safe and effective manner [1]. The ideal dialysate should ensure appropriate toxin and phosphate removal, restore pre-dialysis plasma electrolytes, limit large swings in the concentrations of numerous substances, and decrease such swings. Prolonged or more frequent HD makes this goal easier to achieve by lowering the chemical and electrolyte gradients among blood and dialysate. Due to organisational, financial, and patient-quality issues, it is regrettable that this method is difficult to put into practise [1].

Dialysate Sodium (Dial-Na⁺)

To make patients feel more comfortable the content of Dial-Na⁺ has been adjusted over the years. During the earlier days in dialysis, low level of sodium dialysate was used to decrease chronic volume overload, including blood pressure problems as well as heart related issues. Shortening dialysis treatment periods exacerbated hemodynamic instability by increasing intravascular volume and plasma osmolality (especially early in the dialysis operation). Increasing dialysate sodium to 139–144 mEq/L improved hemodynamic stability and procedure tolerance [2]. Higher sodium concentration in dialysate was anticipated to cause weight gain and hypertension regulation. Studies show that dialysate salt increases interdialytic weight gain. With better ultrafiltration tolerance, this excess weight was simply eliminated [3]. Dialysis fluid sodium concentrations have been tinkered with recently in an effort to reduce the hazards of higher sodium sol. while keeping the hemodynamic properties of the fluid [3]. Dial-Na⁺ concentrations begin high but are gradually decreased to isotonic or hypotonic levels. Numerous investigations [1-3] compared dialysates with steady and declining sodium concentrations.

Patients receiving routine, night time, and conventional hemodialysis participated in a randomized crossover trial done by Thamoson et al., 2017 [4]. With 100 days for each crossover research period, Dial-Na⁺ was tailored to 3 mmol/L above “DIALHighSOD” or below “DIALLowSOD” the pre-dialysis plasma sodium set point (SP). The results show that “interdialytic weight gain (IDWG)” (2.15 vs. 1.90 L, p equals to 0.002), IDWG as a percentage of target weight (IDWG percent) (2.78 vs. 2.39 percent, p equals to 0.002), pre-dialysis systolic (143.3 vs. 138.3 mm Hg, p equals to 0.001), diastolic (78.6 vs. 75.6). Despite hemodialysis frequency (HDF) was related to a higher percentage of IDWG (R equals to 0.507, slope equals to 0.002, p equals to 0.001), HDF was related to lower percentage of IDWG (R equals to -0.295, slope equals to -0.002, p equals to 0.034). Whereas the HDF raised post-dialysis diastolic BP (blood pressure) (R equals to 0.366, slope equals to 3.464, p equals to 0.008), the HDF raised the intradialytic diastolic BP change (R equals to 0.280, slope equals to 1.127, p equals to 0.044). Dialysis duration & frequency correlate in opposite ways in IDWG, according to the study's findings on dialysate sodium's effects on health outcomes in quotidian and nocturnal HD patients.

It was discovered by Dahlmann and colleagues (2005) [5] that "Na magnetic resonance imaging" (Na-MRI) can determine the amount of sodium that is stored in the muscle & skin, in addition to the sodium that is eliminated during HD. Contrary to age-matched controls, older HD patients had higher levels of Na & water in their muscles & skin. Low concentrations of epidermal growth factor-C accompanied this "VEGF-C". The greater the content of Na of the skin after HD, the lesser the VEGF-C levels. Despite the fact that these reserves are not reliant on Na osmotic linkages, the revolutionary idea of muscle & skin Na retention is noteworthy and may eventually have substantial therapeutic implications.

According to Locatelli et al., 2015 [6,] the ultrafiltration rate which should be utilised is the same as the rise in weights during interdialytic period. For a Na-zero balance in terms of fluid & Na accumulation at that time, the dialysate [Na] must be tailored. Only a conductance kinetic model can be used to execute this to its best ability. The Donnan factor as well as the gradients among plasma water & dialysate [Na] of a patient must be taken into account while selecting the right dialysate [Na]. They also found out that the dialysis' capacity to maintain fluid balance has dramatically improved [6]. To maintain sodium balance with the same degree of accuracy, the dialysate sodium concentration must be customised. If dialysis weight and plasma sodium level are maintained, the patient is likely in sodium balance. Sodium balance isn't the key issue when choosing constant or variable dialysis fluid sodium concentrations. This approach could cause a pathological excess in total sodium mass, leading to hypotension or heart failure.

Dialysate Potassium

Zehnder et al., (2001) [7] stated in their finding that most enduring patient dialysis centres rarely customise dialysate potassium. Most patients receive a centrally generated one or two mEq/L potassium bath. Using a predetermined dialysate potassium, the quantity of potassium uninvolved through a dialysis session cannot be predicted. With a potassium-free dialysate, potassium elimination shouldn't exceed 80–100 mEq. Despite comparable pre-dialysis potassium levels and dialysis treatments, patient-to-patient potassium elimination varies greatly. Several patient-specific factors affect how potassium travels from intracellular to extracellular to dialysate. Excessive potassium can be eliminated from the body throughout dialysis by using a dialysate with a lesser potassium content than plasma. This gradient affects the frequency of elimination [7].

Locatelli et al. (2015), [6] discovered that after HD, plasma K concentrations increase again, re-establishing the proportion between the 2 compartments. This alteration may exacerbate cellular membrane polarization throughout intradialytic procedures, resulting in arrhythmias. Standard HD primarily eliminates K by diffusion (85%) and sporadically by convection (15%) has been studied [6]. Dialysate [K] analysis is necessary to preserve "K homeostasis" because K exclusion is entirely reliant on gradients among pre-dialysis plasma as well as dialysate [K] (along with HD time & K dialysance). Bleyer et al. (2006) [8] discussed the impact of K in HD and found that the massive proportion of unexpected deaths on the 1st day of the week (at the completion of long

interdialysis time), when plasma [K] is usually higher, shows how important it is to know that high pre-dialysis plasma [K] raises the chances of life-threatening occurrences. Kovcsdy and colleagues (2007) [9] presented that patients with greater pre plasma [K] were more likely to die when they used a relatively high dialysate [K]. There was a significant decline in unexpected death and all-cause patient's mortality rates with plasma [K] >5 mEq/L. Also, there was no clear link between untimely death (and death from all causes) as well as relatively low dialysate [K] in patients whose plasma [K] was 5 mEq/L before dialysis.

Bicarbonate Dialysate

Transferring enough bases to the patient during dialysis neutralises metabolic acid generation, corrects metabolic acidosis, and prevents buffer loss and the dialysate buffer is bicarbonate. Calcium, magnesium, and lactic or acetic acid are in the acid concentration. Carbonic acid (H_2CO_3) and carbon dioxide are created when acid and bicarbonate are mixed (CO_2). CO_2 generation lowers the solution's pH to 7.0–7.4 Lower calcium and magnesium concentrations and a higher acidic pH allow these ions to stay in solution. Final dialysis solution bicarbonate content is 33–38 mmol/L [10]. Ahmad et al., (2000) [10] stated that the citric acid instead of acetic acid in acid concentration may reduce acidosis in long-term dialysis patients. Citric acid reduced from 14 to 7 the number of predialysis patients with bicarbonate levels below 23 mEq/L [10]. Citrate's local anticoagulant action may have increased membrane permeability, leading to a higher dialysis dosage. Palmer (2001) [11] found in his study that the most dialysis centres use a 35 mmol/L bicarbonate concentration. Paid the evidence that correcting chronic acidosis is therapeutically advantageous, more effort should be given to altering bicarbonate concentration to preserve predialysis total CO_2 levels above 23 mmol/L. Some people may need oral bicarbonate therapy to achieve this and consider replacing the acid's formic anhydride with citric acid [11].

Magnesium Dialysate

In a large observation - based research, Jefferies & McIntyre (2010) said that the baseline magnesium in the recommended dialysate [Mg] had only a weak connection with the magnesium in the plasma [Mg]. This shows that other elements, like magnesium from diet, nutritional supplements including antacids & phosphate binders, and possibly even laxatives, may be significant as well. Kyriazis et al. (2004) [13] looked at how different dialysate [Mg] & [Ca] affected BP throughout HD. The dialysate usage with [Ca] of 1.25 mmol/L & [Mg] of 0.25 mmol/L caused a large decline in "mean arterial pressure". This was because the reduction in cardiac index wasn't balanced by a rise in overall "peripheral resistance". On the other hand, Barbagallo & Dominguez (2007) [14] said that a decline in BP could be avoided by mixing the similar dialysate (Ca) with a greater dialysate (Mg) (0.75 mmol/L). When the content of dialysis solution (Mg) was about right, the results were about average. Despite these findings, the intradialytic cardiovascular stabilization or cardiac performances are unaffected by a high dialysate [Mg]. HD patients frequently have plasma [Mg] concentrations up to 2 mmol/L, typically asymptomatic. The active Mg state, however, may be better represented by ionized and intracellular [Mg] [14].

Calcium Dialysate

Dialysate calcium impacts hemodynamics and metabolic bone disease. Patients prone to haemodynamic hypotension should avoid low dialysate calcium concentration. Lower calcium in the dialysate allows for higher dosages of phosphate binders and reduces the demand for aluminium-containing binders. Ca intake from stomach, excretion through any residual renal function (fn.), as well as its balance throughout HD all add to the patient's overall balance. Patients with HD have their own internal balance. Sustaining normal bone turnover as well as mineralization, avoiding cardiovascular & soft tissue calcifications, favouring cardiovascular consistency during HD, preventing cardiac arrhythmias, & stopping "severe secondary hyperparathyroidism (SHPT)", bone pain, as well as broken bones [6] are competing requirements that the ideal dialysate [Ca] must take into account.

A single-pool "kinetic model" with a "nominal" label dialysate [Ca] content of 1.5 mmol/L was reported by Di Filippo and colleagues (2004) [15]. This model was used in the study. A "ionised" dialysate [Ca] concentration of 1.26 mmol/L ("nominal" total [Ca] concentration of 1.50 mmol/L). Patients having predialysis [Ca] that was within the normal range didn't see an increase in plasma water [Ca] as a consequence of the conductivity being altered to create a tailored dialysate [Na] for each patient. It stopped the extracellular buffering (EB) of the high plasma water [Ca] caused by the diffusive gradients since the final plasma water [Ca] that was expected and assessed was the same. Despite utilising an ionised dialysate [Ca] of 1.50 mmol/L ("Nominal" total [Ca] of 1.75 mmol/L), increased plasma [Ca] with EB were the norm. Due to the low amount of calcium that is removed from the soft tissues by 1.75 mmol/L dialysate Ca, this concentration isn't recommended.

Glucose

Takahashi et al., (2004) [16] explained in their study that the dialysate concentration of glucose was significantly decreased in later time period when ultrafiltration was achieved using transmembrane related pressure. To prevent hypertriglyceridemia and the chance of increased bacterial development in the dialysate, several HD centers employed a dialysate free of glucose. However, this method puts patients at risk for hypoglycemia, particularly diabetics taking oral antidiabetic medications [16]. Insulin acts in a manner that is analogous to metabolic alkalosis in that it promotes the migration of potassium from the extracellular area into the intracellular region. As a consequence of this, hypoglycemia causes the transfer of potassium from plasma to cells to be less effective and raises the amount of AA (amino acids) that are lost in the dialysate [16]. According to Locatelli, Filippo, & Manzoni (2004) [17], the most recent generation of high-definition (HD) sols. are either free from glucose, isoglycaemic (100 mg/dL), or just weakly hyperglycaemic (200 mg/dL). Kaysen et al. (2003) [18], Stenvinkel et al., (2002) [19], & Kaysen, (2001) [20] indicated that sugar levels between 100 & 200 mg/dL in dialysate may or may not have a deleterious effect on triglyceride metabolism. Hyperglycemia may operate as a pro-inflammatory trigger if dialysate glucose values of 200 mg/dL are used [18,19,20]. For the first time, the FDA has accepted a dialysate containing 100 mg/dL

glucose. The Food and Drug Administration (FDA) has given its permission to a dialysate that contains a glucose concentration of 100 mg/dL.

Future Development

Various substances can be administered using the dialysate as a vehicle. Some patients have received short-term phosphate supplementation using dialysate that has been phosphate-enriched [21]. The FDA has given its blessing to a new iron supplement known as "ferric pyrophosphate citrate" for use as an iron-free alternative to be added to the dialysate in order to maintain haemoglobin levels in long-term HD patients. Each HD treatment can include the administration of ferric pyrophosphate citrate, which keeps haemoglobin levels steady without raising iron reserves [21].

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