



SODIUM

SODIUM 138, 139, 140 mmol/l

EFFECTS OF LOW CONCENTRATION

- Intradialytic cardiovascular instability
- Disequilibrium symptoms (fatigue, muscle cramps, headache and others)

- Refractory hypertension
- Intradialytic hypertension
- Increased thirst sense possible
- Positive sodium balance
- Weight gain



SODIUM 138, 139, 140 mmol/l

PREDIALYSIS SERUM SODIUM LEVEL, DIALYSATE SODIUM AND ASSOCIATION WITH MORTALITY IN DIALYSIS PATIENTS (DOPPS STUDY)

Possible associations between predialysis serum concentration, dialysate sodium and mortality were analyzed by Hecking et al. using data from the DOPPS study, an international prospective cohort study. Analysis of data from 11,555 patients in 12 countries showed country-dependent differences in mean predialysis sodium levels, with highest serum predialysis sodium level in Japan (139 \pm 2.6 mEq/l) and lowest in Australia/New Zealand (137.4 \pm 2.8 mEq/l). The mean serum sodium level in all participating DOPPS study sites was 138.5 \pm 2.8 mEq/l. Following analysis of the data, higher serum sodium levels were associated with lower adjusted all-cause mortality. The dialysate sodium prescription was not associated with predialysis serum sodium levels, but patients with low serum sodium of 137 mEq/l showed lower mortality risk when treated with dialysate sodium of 140 mEq/l. This may be a consequence of increased cardiovascular stability during dialysis.

DIALYSATE SODIUM: HIGH OR LOW

A recently published review by Basile et al. addressing the question of whether the use of either uniform high-DNa⁺ (DNa⁺ \ge 140 mmol/l or low-DNa⁺ (DNa⁺ 133-140 mmol/l) prescriptions is correlated with better patient outcomes could not give a conclusive answer. In conclusion, use of high uniform DNa⁺ was correlated to higher interdialytic weight gain (IDWG), while a subset of three analyzed studies showed that the use of low uniform DNa⁺ was associated with an increase in intradialytic hypotensive episodes. Considering available clinical data, no recommendation for either use of high or low DNa⁺ can be given, as stated by authors.

THE RELEVANCE OF DIETARY SODIUM

Data from the HEMO Study, a prospective, multicenter, randomized clinical trial, were analyzed post-hoc by Mc Causland et al. addressing the impact of dietary sodium on mortality in a hemodialysis population of 1,770 subjects. Higher reported dietary Na⁺ itself, or set into proportion to caloric or potassium intake, was associated with greater mortality in prevalent hemodialysis patients. No difference for mortality was seen comparing patients either under Na⁺ restriction (≤ 2 g/day) or liberal prescription (> 2 g/day), probably due to noncompliance of the restrictive group. Mean Na⁺ in the restrictive group was only 200 mg/day lower than in the liberal prescription group.

Hecking M et al. Predialysis serum sodium level, dialysate sodium and mortality in maintenance hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis. 2012 Feb;59(2)

Basile C et al. High versus low dialysate sodium concentration in chronic haemodialysis patients: a systematic review of 23 studies. Nephrol Dial Transplant. 2015 Apr 5

SODIUM

POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE





SODIUM

POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE

GLUCOSE

POTASSIUM

0, 1, 2, 3, 4 mmol/l

EFFECTS OF LOW CONCENTRATION

 Arrhythmogenic effect amplified by a rapid correction of metabolic acidosis, low dialysate calcium concentration and may high dialysate to blood potassium gradient

- Risk of insufficient potassium removal with secondary hyperkalemia in the interdialytic period due to may low dialysate to blood potassium-gradient
- Increased mortality



POTASSIUM 0, 1, 2 3, 4 mmol/l

MODIFIABLE PRACTICES ASSOCIATED WITH SUDDEN DEATH (DOPPS STUDY)

Associations between different modifiable dialysis practices such as treatment time, Kt/V, ultrafiltration volume, prescription of Q-wave/T-wave interval-prolonging drugs, dialysate-potassium concentration and occurrence of sudden death were analyzed by Jadoul et al. Data analysis of 37,765 patients in 12 countries participating in the DOPPS study showed that short dialysis treatment time, high ultrafiltration volumes and low Kt/V are associated with higher risk of sudden death. For patients with lower dialysate potassium levels K(D) \leq 1.5 and K(D) = 2-2.5 mEq/I, the risk of sudden death was elevated when compared to K(D) \geq 3 mEq/I.

POTASSIUM AND BICARBONATE

The interaction between three different dialysate bicarbonate concentrations (27 – 35 – 39 mmol/l) and serum potassium levels was investigated by Heguilén et al. in a double-blind randomized crossover study. Use of bicarbonate with the highest concentration (39 mmol/l) was correlated to the fastest decrease in intradialysis K⁺ concentration, but not with an increased K⁺ removal. The decrease in plasma K⁺ using higher concentrations of bicarbonate is theorized to be due to an enhanced shift of K⁺ into the intracellular compartment. Rebound rates for a small patient subgroup did not show statistically significant differences.

POTASSIUM AND CHANGES IN BLOOD PRESSURE

In a randomized single-blind crossover study with 24 dialysis patients, Gabutti et al. assessed the influence of changing the dialysate potassium concentration at steps of +/- 1 mmol/l (based on the routine potassium prescription) on haemodynamics. For measurements, a finger beat-to-beat monitor was used as an indirect, noninvasive measurement method at three defined timepoints of dialysis. They demonstrated that a rapid decrease in potassium causes a decrease in systolic and mean blood pressure and correlated peripheral resistance. Reduction of routinely used potassium concentration by 1 mmol/l was associated with a higher incidence of hypotensive episodes. POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE



CALCIUM



CALCIUM 0, 1.25, 1.5, 1.75 mmol/l

EFFECTS OF LOW CONCENTRATION

- Hypotension and cardiac arrhythmias during hemodialysis and long-term risk of secondary hyperparathyroidism
- Increased risk of sudden cardiac arrest
- Increased circulating parathyroid hormone levels (PTH) in the presence of adynamic bone disease and low serum PTH levels
- Risk of excessive bone-mineral loss in patients with long daily or nocturnal hemodialysis sessions

- Long-term risk of vascular and valve calcifications
- Significantly higher risk of cardiovascular and sudden death in patients who are taking a calcium-based phosphate binder
- Risk of oversuppression of parathyroid hormone and adynamic bone disease, with high plasma [Ca²⁺] and soft-tissue calcifications



CALCIUM

0, 1.25, 1.5, 1.75 mmol/l

DIALYSATE CALCIUM: CORONARY ARTERY CALCIFICATION AND LOW BONE TURNOVER

In a randomized controlled trial including 425 hemodialysis patients with PTH levels \leq 300 pg/ml, Ok et al. looked for the influence of dialysate calcium of either 1.25 mmol/l or 1.75 mmol/l on coronary artery calcification (CAC) and low bone turnover over a time period of 24 months, with morphological correlates. Changes in CAC were analyzed by use of a multislice CT, changes in bone formation by biopsy. The progression rate for CAC was significantly lower for DCa²⁺ of 1.25 mmol/l (CAC score 160 +/- 299) than for DCa²⁺ of 1.75 mmol/l (303 +/- 624). The use of DCa²⁺ 1.25 mmol/l was also associated with an improvement in low bone turnover displayed by higher bone-formation rate, trabecular thickness and bone volume for patients with intact PTH levels.

DIALYSATE CALCIUM AND ARTERIAL STIFFNESS

Charitaki et al. analyzed data from 289 dialysis patients treated for six months under routine conditions to evaluate the influence of different dialysate calcium concentrations of 1.0 mmol/l (18.8% of patients), 1.25 (20.9%), 1.35 (53%) and \geq 1.5 mmol/l (7.3% of patients) on arterial stiffness by tracking pulse wave velocity. After six months, mean pulse wave velocity increased for patients treated with DCa²⁺ of 1.0, 1.25 and 1.35 mmol/l, but not for the group treated with DCa²⁺ \geq 1.5 mmol/l, although the relatively low number of patients in this group has to be taken into consideration for interpretation of these results. Aortic augmentation index and central aortic pressure were unchanged for all groups. The observed similar increase in pulse wave velocities for patients treated with dialysate of 1.0, 1.25 or 1.35 mmol/l calcium let the authors suggest that factors other than DCa²⁺ contribute significantly to arterial stiffening.

LOW DIALYSATE CALCIUM AND SUDDEN CARDIAC ARREST

A case control study comparing data from 510 patients who experienced a witnessed and verified sudden cardiac arrest in dialysis clinics with 1,560 matched control patients was reported by Pun et al. Parameters such as serum Ca²⁺, dialysate Ca²⁺, serum-to-dialysate Ca²⁺ gradient and QT-interval-prolonging medications were analyzed for association with the event of sudden cardiac arrest. Low dialysate calcium < 2.5 mEq/L, increasing serum-to-dialysate Ca²⁺ gradient and higher corrected serum Ca²⁺ (10.1 mg/ dl corresponding to 2.52 mmol/l) were associated with an increased risk of sudden cardiac arrest. In addition, patients treated with low dialysate Ca²⁺ < 2.5 mEq/L were at higher risk of being exposed to higher serum-to-dialysate gradient and presented a greater drop in blood pressure during treatment. QT-prolonging medications were not significantly risk associated. Ok E et al. Reduction of Dialysate Calcium Level Reduces Progression of Coronary Artery Calcification and Improves Low Bone Turnover in Patients on Hemodialysis. J Am Soc Nephrol. 2015 Dec 23 SODIUM

POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE



MAGNESIUM



MAGNESIUM

0.5, 0.75 mmol/l

EFFECTS OF LOW CONCENTRATION

- Improved bone mineralization
- Increased PTH level

- Suppressed PTH secretion
- Delayed arterial calcification

MAGNESIUM 0.5, 0.75 mmol/l

SERUM MAGNESIUM AS A PREDICTOR FOR MORTALITY

In a registry-based cohort study, Sakaguchi et al. analyzed data from 142,555 Japanese dialysis patients for a possible association between magnesium serum level and one-year all-cause and cardiovascular mortality. Patients were stratified following serum magnesium levels. Groups were organized within the range from < 2.3 mg/dl for group 1 up to \geq 3.1 mg/dl for group 6, and groups 2–5 in between using steps of 0.2 mg/dl. Using different adjusted models, Sakaguchi et al. proposed a J-shaped association between serum magnesium levels and odds ratios for all-cause and cardiovascular mortality. Patients with hypomagnesemia characterized by a serum magnesium level < 2.7 mg/dl had a significantly increased risk of mortality, while patients with serum magnesium level in a range from \geq 2.8 up to < 3.1 mg/dl showed the lowest risk.

Results of the Sakaguchi study have been deemed very controversial. Courivaud et al. addressed the question of whether magnesium is an adequate marker for the observed outcomes or one added to other factors associated with the increased mortality rates.

SERUM MAGNESIUM AND PROTON PUMP INHIBITORS

A chart review of 62 hemodialysis patients in a single dialysis unit analyzed the influence of proton pump inhibitors such as Omeprazole or Pantoprazole on magnesium levels in hypomagnesemic c[Mg²⁺] < 1.5 mEq/L and nonhypomagnesemic patients c[Mg²⁺] \geq 1.5 mEq/L. The use of proton pump inhibitors was associated with hypomagnesemia, and therefore, in addition to the concentration of Mg²⁺ in the dialysate, proton pump inhibitors have to be considered as aggravating low serum Mg²⁺ levels. Sakaguchi Y. et al. Hypomagnesemia is a significant predictor of cardiovascular and noncardiovascular mortality in patients undergoing hemodialysis. Kidney Int. 2014 Jan;85(1)

Courivaud C et al. Magnesium and the risk of all-cause and cardiac mortality in hemodialysis patients: agent provocateur or innocent bystander? Kidney Int. 2014 Jan;85(1)



ODIUM

POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE



BICARBONATE



BICARBONATE

32, 33, 36 mmol/l

EFFECTS OF LOW CONCENTRATION

- Insulin resistance
- Acidosis with secondary abnormal protein metabolism and malnutrition
- Osteodystrophy/bone loss

- Post-dialysis alkalosis
- Impact on potassium-calcium balance
- Increased calcium binding to proteins, reduction of ionized calcium and impaired cardiac muscle contraction and arterial pressure preservation
- Hypoxemia, with further impaired cardiac function
- Increased potassium removal
- Accelerated tissue calcium phosphate precipitation



BICARBONATE

32, 33, 36 mmol/l

ASSOCIATION OF DIALYSATE BICARBONATE CONCENTRATION WITH MORTALITY (DOPPS STUDY)

Data from 17,031 patients in 11 countries participating in the DOPPS study were analyzed by Tentori et al. looking for possible association between dialysate bicarbonate concentration and mortality. Mean country dialysate prescription was heterogeneous, with lowest dialysate bicarbonate concentration used in Germany ($32.2 \pm 2.3 \text{ mEq/I}$) and highest in the United States ($37.0 \pm 2.6 \text{ mEq/I}$). Mean dialysate bicarbonate concentration in all participating DOPPS study sites was $35.5 \pm 2.7 \text{ mEq/I}$. Around 50% of the participating sites used individualized prescription for dialysate bicarbonate, while the other half of study sites used the same bicarbonate concentration for all patients. Higher dialysate bicarbonate concentrations $\geq 38 \text{ mEq/I}$ were associated with higher mortality rates, an effect which was more pronounced in patients treated for longer dialysis vintage, suggesting that exposure to high levels of dialysate bicarbonate over time may be harmful.

No difference in mortality was seen in study sites treating patients with only a single concentration of dialysate bicarbonate (mean dialysate bicarbonate prescription $35.7 \pm 2.2 \text{ mEq/I}$) and sites which prescribed dialysate bicarbonate patient-individually (mean dialysate bicarbonate prescription $35.3 \pm 3.1 \text{ mEq/I}$).

The association between bicarbonate prescription and higher mortality was challenged by Chen et al. The authors argue that confounding factors such as better nutritional status and higher dietary protein intake, hypercatabolism and severe protein-energy wasting have to be taken into consideration in detail for analysis of these data.

DIALYSATE BICARBONATE, DIALYSATE CALCIUM AND HEMODYNAMICS

A randomized crossover study including 21 patients was conducted by Gabutti el al. to analyze the effects of different concentrations of dialysate bicarbonate (26-35 mmol/L) and dialysate calcium (1.25 or 1.5 mmol/L). The authors propose that use of higher concentrations of bicarbonate requires the use of higher calcium to improve the hemodynamic pattern during dialysis. While bicarbonate is associated with a reduction of peripheral resistance, mediating decrease in blood pressure, higher calcium concentration stabilizes or increases blood pressure and stroke volume. SODIUM

POTASSIUM

CALCIUM

MAGNESIUM

BICARBONATE



GLUCOSE



GLUCOSE 100 mg/dl (1g/l)

EFFECTS OF GLUCOSE 0 mg/dl

- Loss of glucose
- Risk of hypoglycemia
- Greater loss of amino acids in the dialysate
- Higher potassium removal secondary to alkalosis

EFFECTS OF

- GLUCOSE 100 mg/dl
- Safe and effective

EFFECTS OF GLUCOSE 200 mg/dl

- Impaired triglyceride metabolism
- Risk of pro-inflammatory stimulus secondary to hyperglycemia

GLUCOSE 100 mg/dl (1g/l)

METABOLIC EFFECTS OF DIALYSATE GLUCOSE IN CHRONIC HEMODIALYSIS PATIENTS

In a prospective, randomized trial, Raimann et al. analyzed the influence of two different dialysate glucose concentrations (100 mg/dl and 200 mg/dl) on metabolic changes in diabetes and non-diabetes patients. The concentration of glucose in the dialysate did not influence the number of hypoglycemic episodes or the interdialytic weight gain. Use of 200 mg/dl glucose in the dialysate was associated with significantly increased serum glucose for both diabetes and non-diabetes patients, while serum insulin was elevated in non-diabetes patients only. Diffusive transport of glucose from the dialysate to the patient is discussed as the key factor for these metabolic changes.

DIALYSATE GLUCOSE AND RISK OF ASYMPTOMATIC HYPOGLYCEMIA

An earlier randomized study conducted by Burmeister et al. analyzed the transport of glucose from dialysate to the patient's blood for two different concentrates, either containing glucose in a concentration of 90 mg/dl or of 0 mg/dl. The use of 0 mg/dl glucose was correlated with a significant number of asymptomatic events of hypoglycemia, while the use of the concentrate with 90 mg/dl was linked to a reduction of severity and number of hypoglycemic episodes. The use of 0 mg/dl glucose in the concentrate led to a mean loss of glucose of 16.7 \pm 10.9 g.

DIALYSATE GLUCOSE AND HYPOGLYCEMIA IN DIABETIC PATIENTS

The use of three different concentrations of dialysate glucose (0 - 55 - 90 mg/dL) and the consequences on intradialytic glycemia levels and hypoglycemia (glucose < 70 mg/dl) in 20 diabetes patients undergoing chronic hemodialysis was evaluated by Burmeister et al. in a randomized study. The use of glucose in concentrations of 0 and 55 mg/dl was associated with hypoglycemia, while the use of 90 mg/dl prevented hypoglycemia in this patient population. An increase in glucose levels was not observed using concentrates of 55 or 90 mg/dl.

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BICARBONATE DIALYSIS CONCEPT BIBLIOGRAPHY

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POTASSIUM 0, 1, 2, 3, 4 mmol/l

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CALCIUM 0, 1.25, 1.5, 1.75 mmol/l

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BICARBONATE DIALYSIS CONCEPT BIBLIOGRAPHY

MAGNESIUM 0.5, 0.75 mmol/l

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BICARBONATE 32, 33, 36 mmol/l

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GLUCOSE 100 mg/dl (1 g/l)

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