Urea, sodium, and water changes in profiling dialysis

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Introduction

Control of osmolarity, as well as sodium, urea, and water balance in anuric patients under intermittent haemodialysis therapy is fundamentally different from subjects with normal kidney function. Whereas in subjects with normal kidney function excretion of solutes and water is performed continuously, during dialysis, within a short period of time most sodium and only a small amount of urea are removed convectively with the ultrafiltration of water (1 litre of ultrafiltrate = 8.5 g sodium chloride and about 1.5 g urea). On the other hand most urea and a small amount of sodium is removed by diffusion, depending on the dialyser clearance and the difference in concentration between plasma and dialysis fluid.

The relatively short period of treatment induces acute changes in fluid volume, urea, and sodium concentration as well as in plasma osmolarity, which in healthy subjects never happen. The consequence are side-effects of dialysis therapy such as osmotic dysequilibrium syndrome, muscle cramps, symptomatic hypotension, and thirst.

Having no mechanism to excrete sodium during the long period between two dialyses, the anuric patient only has the possibility to dilute a high sodium concentration by drinking or to minimize sodium ingestion. Consequently the amount of fluid ingestion depends on the amount of sodium chloride ingestion by eating and probably on an increase in sodium concentration due to dialysis treatment itself.

Among other methods profiling of ultrafiltration and sodium concentration in dialysis fluid has been proposed to optimize dialysis therapy. To evaluate the benefit of profiling to the patient the basic conditions of water and solute distribution and exchange in dialysis therapy have to be considered.

The physiological properties of the cell membrane

The cell membrane separates the intracellular from the extracellular fluid compartment and maintains a small concentration of sodium inside the cell by active transport, whereas sodium concentration in the extracellular compartment is 30-fold greater (Figure 1). Whereas the cell membrane is nearly impermeable to sodium it is 100-fold more permeable to urea and about 1000-fold more permeable to water. Under steady-state conditions there is no great difference in osmolarity between the intracellular (ICV) and extracellular (ECV) compartments. This means that differences in osmolarity between the intra- and the extracellular compartments induced by dialysis are very rapidly compensated for by a shift of water. Differences in urea concentration are rapidly equilibrated by diffusion of urea. So it is mainly the change in extracellular sodium concentration that has a strong influence on water shift between the compartments. Ten millimoles per litre of sodium chloride = 18 mOsmol/l ≈ 350 mmHg. Because total extracellular osmolarity is more than 90% due to sodium and the cellular membrane is nearly impermeable to sodium, changes in osmolarity due to the elimination of urea do not cause a shift of water. Therefore osmotic dysequilibrium is mainly induced by decrease in sodium concentration and not by changes in urea concentration (Figure 2).

Transport of urea during dialysis therapy

Predialysis urea concentration depends on protein degradation and the distribution volume of urea which is total body water. Predialysis blood urea concentration is usually between 20 and 40 mmol/l. Urea excretion mainly depends on dialyser blood flow. Dialysis-induced changes in osmolarity due to urea are up to 30 mOsmol/l. Because of its rapid diffusion, there is...
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Concentration and Osmolarity Changes

![Diagram showing concentration and osmolarity changes](image)

Corresponding Volume Changes

![Diagram showing volume changes](image)

Transport of sodium during dialysis therapy

Sodium is mainly excreted by convection. Convective sodium transport alone does not alter sodium concentration. But there are additional changes in sodium concentration due to diffusive transport, which depends on the difference in sodium concentration between blood and dialysing fluid. Diffusive transport may be positive or negative. Whereas convective sodium transport can more easily be estimated as indicated in Figure 3, diffusive sodium transport is mostly unknown. It can be calculated if concentrations of sodium in blood and dialysis fluid are known or given. As is shown in Figure 3, at a given difference in sodium concentration of 5 mmol/l, the diffusive sodium transport during 5 h of dialysis treatment is about 10 g NaCl [1]. Since the error of sodium concentration provided by the proportioning unit of the dialysis machine may be 2% (±3 mmol/l sodium) and the variation of sodium concentration of the blood also may be ±2%, the error of sodium gradient between blood and dialysing fluid may be 6 mmol/l. This unknown difference in sodium concentration is great enough to induce side-effects such as osmotic dysequilibrium and the consequent uncertainty of sodium balance is about 10 g NaCl.

This is also an explanation of why side-effects of dialysis therapy are inconstant and may vary from one treatment to another or from dialysis machine to another because the sodium gradient also varies and remains unknown.

This problem cannot be overcome by measuring sodium concentration in blood and dialysing fluid at the beginning of a dialysis session, because the error of sodium measurement under optimum conditions is ±1%. Under clinical conditions it is about ±5% (±7 mmol/l) and the uncertainty of diffusive sodium transport may amount to 20 g NaCl, when the setting of dialysis fluid sodium concentration is based on inaccurate measurements.

So by clinical experience dialysis is best tolerated in home-dialysis patients using their own proportioning unit with always the same sodium concentration, with a constant error of proportioning and conductivity control, when the patients subconsciously adapt their salt and fluid intake to present always the same blood sodium concentration.

Clinical side-effects of dialysis therapy

There are some important side-effects of dialysis therapy due to change in solutes and osmolarity that happen in more or less every dialysis unit.
Osmotic dysequilibrium syndrome

Osmotic dysequilibrium syndrome is characterized by headache, increasing nausea, high blood pressure, vomiting, and eventually cerebral cramping. After dialysis treatment the symptoms need several hours to disappear. As can be shown by continuous telemetric recording of the electroencephalogram, osmotic dysequilibrium occurs when sodium concentration during dialysis decreases by more than 7 mmol/l (Figure 4). It is caused by increase of intracranial pressure caused by fluid shift into the intracellular compartment. There is no evidence that osmotic dysequilibrium is caused by excretion of urea [2–5].

Symptomatic hypotension

Symptomatic hypotension is mostly induced when ultrafiltration exceeds refilling of the intravascular compartment. It is intensified when simultaneously fluid shifts to the intracellular compartment because of decreasing extracellular sodium concentration. Therefore symptomatic hypotension may also happen when the so-called dry weight of the patient is not attained. But not all episodes of symptomatic hypotension during dialysis are caused by change in fluid and osmolarity. There are also other reasons such as cardiac arrhythmia or insufficiency of the autonomic nervous system.

Muscle cramps

Muscle cramps occur mainly towards the end of a dialysis session. They are more pronounced in patients who require excessive ultrafiltration. They quickly disappear after injection of some grams of hypertonic solutes such as sodium chloride or glucose, although sodium chloride is more effective than glucose or other substances. Cramps also may happen while the patient is still fluid overloaded.

Thirst

Thirst is very severe in some patients. It often has its greatest intensity directly after termination of dialysis treatment. In some cases dialysis patients drink much more than ever in their life before. There is no doubt that thirst is associated with ingestion of salt and rapid increase in sodium concentration by dialysis [6–8]. Sometimes patients drink much more than necessary for dilution of increased sodium concentration. A vicious cycle may develop where the patient overloads his sodium concentration by drinking, and sodium concentration during dialysis increases, or because of muscle cramps is even further increased by injections of hypertonic sodium chloride, which forces him to drink more. The amount of retained sodium chloride after bolus injection to treat muscle cramps is mostly underestimated. In Figures 5 and 6 the absolute and relative retention of sodium chloride is shown, e.g. about 78% of the injected sodium at 1 h before the end of dialysis is retained by the patient.

Profiling as a means of optimizing dialysis therapy

There is no need for profiling of urea, since under normal conditions side-effects of dialysis treatment are not caused by urea or by changes in osmolarity due to urea. To optimize dialysis only ultrafiltration rate and sodium concentration in dialysis fluid may be altered, corresponding to a certain profile.

Concerning ultrafiltration, there is much practical experience that higher rates of ultrafiltration at the beginning of treatment are better tolerated by patients than constant ultrafiltration rates throughout the whole period of treatment. At the end of dialysis there is less danger of symptomatic hypotension when the ultrafiltration rate is low. In any case the whole amount of fluid to be removed should be known at the beginning of the treatment to calculate the profile. Since even with ultrafiltration-profiled dialysis the ultrafiltration may exceed vascular refilling, it is better to control ultrafiltration rate by continuous measurement of circulating blood volume. There are at present several methods of continuous recording of blood volume [9–11] and it is also possible to establish a control system in which ultrafiltration rate is adapted to a given profile of circulating blood volume. Figure 7 shows the difference between controlled and uncontrolled ultrafiltration: in both cases there is the same amount of total ultrafiltration. In the case of constant ultrafiltration rate there is variable blood volume, and in the case of blood-volume-controlled ultrafiltration (lower part of the figure) there is variable ultrafiltration. It can be shown that side-effects are lower in controlled ultrafiltration than in uncontrolled ultrafiltration [12].

Profiling of sodium concentration might be suitable to shift water from the intracellular to the extracellular compartment to make it a viable for ultrafiltration, but it has to be kept in mind that sodium profiling should not be the cause of sodium ingestion and subsequent thirst of the patient. So temporary increase of sodium concentration must be compensated for by subsequent adequate reduction in sodium concentration.

In Figure 8 there is hourly variation of dialysis fluid sodium concentration between 160 and 140 mmol/l. The resulting sodium concentration in blood increases from 140 to 152 mmol/l. In the case of zero ultrafiltration this is equivalent to ingestion of about 25 g of sodium chloride to the patient.

Figure 9 shows a balanced sodium profile where the patient’s blood sodium concentration is not changed by profiling.

Conclusions

Most acute unwanted side-effects of haemodialysis therapy are induced by ultrafiltration and changes in osmolarity.

Changes in osmolarity due to elimination of urea
Fig. 4. Telemetric recording of the EEG in three patients in high- and low-sodium dialysis. In the lower part of the figure sodium and urea concentration during dialysis is shown. Sodium is alternately decreasing (left) and increasing (right). Urea concentration in any case is decreasing. Also the resulting calculated relative changes in the intracellular compartment (ICV) are shown. In the upper part of the Figure there are frequency analyses of the EEG. Main frequency is alpha rhythm at 8–10 cycles/s Only in the left parts, where sodium concentration in blood is decreasing, is there increasing delta and theta activity in the EEG.
Bolus of NaCl During Dialysis

Fig. 5. Retention of sodium chloride injected by bolus (20%) for treatment of muscle cramps. Increase in sodium concentration by injection of 2 g NaCl 20% at 2 and 3 h after dialysis start. Retained amount of sodium chloride is 2.1 g.

Relative Blood Volume Versus Time

Fig. 6. Percentage of retained amount of sodium chloride injected by bolus depending on the time of dialysis. All data are calculated for a patient of 65 kg, blood and dialysate sodium concentration of 140 mmol/l, and standard dialysis data.

have no influence on fluid shift between the extracellular (ECV) and intracellular (ICV) fluid compartments.

Only changes in osmolarity from alterations of sodium concentration strongly influence fluid distribution between ECV and ICV.

Side-effects such as osmotic dysequilibrium, cramps, symptomatic hypotension, and thirst are mainly induced by exchange of sodium.

Profiling dialysis consists in deliberately changing ultrafiltration and dialysis fluid sodium concentration in order to avoid side-effects.

Continuous measurement and control of blood volume seems to be the best method of avoiding symptomatic hypotension.

Temporary increase of plasma sodium concentration by profiling induces fluid shift from the ICV to the ECV. This may facilitate ultrafiltration.

Profiling of sodium should not be the cause of positive sodium balance. It only can be recommended when diffusive sodium balance is comparable to constant sodium concentration in dialysis fluid.

The error in diffusive sodium balance in conventional haemodialysis varies up to 10 g sodium chloride per session.

Any intentional change in dialysis fluid sodium concentration based on sodium measurements under
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Influence of a Balanced Sodium Profile on Plasma Sodium Conc.

Fig. 9. Influence of a balanced sodium profile on patient plasma sodium concentration.

clinical conditions depends largely on the accuracy of the measuring device, and may be uncontrollable.

Sodium profiling needs more precise sodium delivery in dialysis fluid.
The benefits of sodium profiling to the patients have still to be proved.

References


2. Gürich W, Mann H, Stiller S. Sodium elimination and changes in the EEG during dialysis. Artif Organs 1980; 3 [Suppl]: 94