Ionic mass balance and blood volume preservation during a high, standard, and individualized dialysate sodium concentration

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Abstract

Background. Although a higher dialysate sodium concentration (DNa) is frequently used to improve haemodynamic stability during haemodialysis, few studies have compared ionic mass balance (IMB) during different DNa. Moreover, DNa is usually a standard prescription, whereas inter-individual pre-dialytic serum sodium levels may differ widely. The aims of the study were to assess IMB and the decline in blood volume (ΔBV) during isovolaemic HD as well as during HD combined with ultrafiltration (UF) during DNa [140], DNa [144], and an individualized DNa [ind], in which DNa is equal to pre-HD plasma conductivity × 10.

Methods. IMB and plasma conductivity were assessed by on-line conductivity measurements (Diascan®; Hospal®) in 13 HD patients. After 1 h of isovolaemic HD, measurements were continued during UF q HD until dry weight. ΔBV was assessed by an optical method (Hemoscan®).

Results. During isovolaemic HD with DNa [140] and [144], Pre-Na was significantly related to IMB (r = 0.83 and r = 0.61; P < 0.05). Diffusive Na flux into the patient occurred when the difference between DNa and pre-dialytic serum sodium was larger than 5 mmol/l. During UF + HD, IMB was 318 ± 166 mmol during DNa [140], 277 ± 116 mmol during DNa [ind], and 239 ± 111 during DNa [144] (mean ± SD; P < 0.05 compared with the other treatment modalities) whereas ΔBV did not differ significantly. In the five patients with a pre-dialytic sodium concentration below 140 mmol/l, ionic removal was significantly higher during DNa [ind] (324 ± 87) compared with DNa [140] (228 ± 127 mmol; P < 0.05) without a significant difference in ΔBV (−9.7 ± 1.6 vs −7.8 ± 2.3%).

Conclusion. A large difference in IMB was observed between DNa 144 and DNa 140, without a significant difference in ΔBV. In patients with low pre-dialytic serum sodium levels, diffusive ionic influx from the dialysate into the patient may occur. In patients with low pre-dialytic sodium levels, DNa [ind] leads to an enhanced ionic removal compared with DNa [140] without large differences in ΔBV.

Keywords: blood volume; dialysate sodium concentration; ionic mass balance; haemodialysis; ultrafiltration

Introduction

The dialysate sodium concentration is a two-edged sword. Whereas a low dialysate sodium concentration may lead to large removal of sodium but also to an impaired preservation of blood volume provoking intra-dialytic hypotension, a high dialysate sodium concentration may improve haemodynamic instability during dialysis, although possibly at the cost of increased inter-dialytic weight gain and hypertension.

In general, an optimal dialysate sodium concentration would find a balance between both an adequate blood volume preservation and sodium removal [1]. In earlier studies, but also more recently [2, 3], several authors recommended higher dialysate sodium concentrations in order to prevent intra-dialytic haemodynamic instability in hypotension-prone dialysis patients [2, 3]. Few data are, however, available on ionic mass balance (IMB) during dialysis with different dialysate sodium concentrations, although such data are of pivotal importance in view of the relation between sodium, hypertension, and left ventricular abnormalities in dialysis patients [4–6].

In most of the literature, the dialysate sodium concentration is seen as a standard prescription, whereas the pre-dialytic plasma sodium concentration

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may differ between dialysis patients. The fact that this phenomenon may lead to large inter-individual differences in diffusive ionic transfer suggests that individualization of dialysate, i.e. based on pre-dialytic plasma conductivity or sodium measurements or effected by biofeedback modules, would seem judicious. Nevertheless, although the use of individualization of the dialysate sodium concentration may be appealing in the sense of a more physiologic and patient-based dialysis prescription, it is not known whether such an approach actually improves the dialysis treatment in terms of the balance between blood volume preservation and ionic removal.

New techniques based on conductivity measurements enable the physician to assess IMB during dialysis, which is likely to be representative of sodium balance, due to the quantitative predominance of sodium ions in both plasma and dialysate. In this aspect, however, it is of great importance to distinguish between convective transport evoked by ultrafiltration and purely diffusive ionic transport. The aims of the present study were to first assess IMB in vivo both during isovoltaemic dialysis as well as during haemodialysis combined with ultrafiltration using different dialysate sodium concentrations, and secondly to compare standard and individualized dialysate sodium concentrations in terms of blood volume preservation and IMB.

Subjects and methods

Study protocol

Validation study. During nine treatment sessions, IMB was assessed both by Diascan (vide infra) and by direct dialysis quantification. Using direct dialysis quantification, the total amount of spent dialysate was collected in a box. Conductivity measurements were performed in a sample of spent dialysate taken from the box, as well as in a sample of incoming dialysate. IMB by direct dialysis quantification was assessed according to the formula: \( (C_{\text{din}} \times Q_{\text{d}} \times \text{dialysis time}) - (V_{\text{out}} \times C_{\text{dout}}) \), in which \( Q_{\text{d}} \) is dialysate flow, \( C_{\text{din}} \) is dialysate conductivity of incoming dialysate, \( V_{\text{out}} \) is volume of spent dialysate, and \( C_{\text{dout}} \) is the conductivity of spent dialysate. Conductivity of incoming and spent dialysate was measured with a conductivity meter (IBP HDN-3, Johnson and Johnson).

Clinical study. Patients were studied during three dialysis sessions with dialysate sodium concentrations of, respectively, 140 (DNa [140]), and 144 mmol/l (DNa [144]), and an individualized sodium concentration (DNa [ind]). Dialysate sodium was individualized according to pre-dialytic plasma conductivity (dialysate sodium is equal to pre-dialytic plasma conductivity \( \times 10 \), as measured by Diascan (Hospal) (vide infra). Three different dialysis sessions with, respectively, DNa [140], DNa [144], and DNa [ind] were compared, in randomized order. Sessions were performed at exact intervals of 1 week, in order to prevent large differences in ultrafiltration volume and also to prevent an effect of a previous modification of dialysate sodium on the subsequent study sessions. In the other dialysis treatments, during which no measurements were performed, a DNa of 140 mmol/l was used, as is standard policy in our clinic.

During each session, patients were first studied during 1 h of isovoltaemic dialysis, followed by combined ultrafiltration and haemodialysis until clinical dry weight, using the same dialysate sodium concentration. Parameters assessed were IMB, relative blood volume, serum sodium, and plasma conductivity, which were measured at the start of the study, after 1 h of isovoltaemic dialysis, and at the end of the dialysis session (after combined haemodialysis and ultrafiltration).

Patients

Thirteen patients were included in the study (eight male; five female). Mean \( \pm \) SD age of the patients was 65.5 \( \pm \) 16.0 years (range 26–81). Patients with acute renal insufficiency with severe hypotensive episodes were excluded. Mean dry body weight was 66.8 \( \pm \) 12.2 kg (range 43–92). Seven patients still had residual renal function. Mean urine volume in the patient group was 770 \( \pm \) 91 ml/day (range 0–2.25 l). All patients gave informed consent for participation in the study.

Dialysis schedule

The dialysis schedule of the patients was twice weekly in five patients and three times a week in eight patients. Mean treatment time was 231 \( \pm \) 23 min (range 180–270). Polysulfone (F9HPS; Fresenius) dialysis membranes were used. Composition of the dialysate was: potassium 2.0 mmol/l, calcium 1.5 mmol/l, magnesium 0.5 mmol/l, bicarbonate 32 mmol/l, acetate 3.0 mmol/l, and glucose 1 g/l. Temperature of the dialysate was 36°C. Patients were ultrafiltered until their clinically determined dry weight.

Study parameters

Ionic mass balance. IMB was estimated by Diascan (Hospal) [7,8]. In short, Diascan measures IMB by constant measurement of the conductivity in the dialysis outlet and inlet according to the formula \( \text{IMB} = (Q_{\text{din}} \times C_{\text{din}} - \frac{Q_{\text{d}} \times C_{\text{dout}}}{C_{\text{in}}} \times 10 \times \text{time (min)}. \) \( Q_{\text{d}} \) and \( Q_{\text{din}} \) are dialysate flow at, respectively, outlet and inlet; \( C_{\text{dout}} \) and \( C_{\text{din}} \) are dialysate conductivity at, respectively, outlet and inlet. A positive IMB means sodium removal from the patient, a negative IMB means sodium transport to the patient.

Plasma conductivity. Plasma conductivity (\( P_{\text{c}} \)) is measured by Diascan by measuring dialysance (\( D \)) in combination with measurements of \( C_{\text{dout}} \) and \( C_{\text{din}} \) according to the formula. \( P_{\text{c}} = (C_{\text{dout}} - [1 - D \cdot Q_{\text{d}}] \times C_{\text{din}}) / (D \cdot Q_{\text{d}}) \). \( D \) is assessed every 30 min by measuring the increase in \( C_{\text{dout}} \) after a temporary increase in \( C_{\text{din}} \) by 1 ms/cm according to the formula \( D = Q_{\text{d}} / (1 - [C_{\text{dout}} - C_{\text{din}}]/C_{\text{dout}}) \). 1 and 2 indicate, respectively, the measurements before and after the temporary increase in \( C_{\text{din}} \) [7,8].

Relative blood volume. Blood volume was measured continuously by continuous optical assessment of changes in haemoglobin during the dialysis session (Hemoscan) [9].
**Serum sodium.** Serum sodium was assessed by ionometry (Vitros 950®), which assesses sodium activity in the serum. Sodium activity is automatically converted to the molar ionized sodium concentration. Obtained values were corrected by converting the molar concentration to flame photometer values by a standard correction factor (0.93) [10]. The coefficient of variation for this method, as given by the manufacturer, is 0.4%.

**Statistical analysis**

Results obtained at the different treatment sessions were compared using Friedman’s ANOVA and, if significant, further analysed by a Wilcoxon test. Correlations between variables were assessed by Pearson’s $r$. $P$ values $<0.05$ were considered significant. Statistical analysis was performed using a SPSS 10.0 software package.

**Results**

**Validation study**

IMB assessed by Diascan® and direct dialysis quantification were highly significantly related ($r=0.94$; $P<0.05$; Figure 1). Dialysate conductivity of incoming dialysate assessed by the Integra® monitor was highly significantly related to dialysate conductivity assessed by the independent method ($r=0.99$; $P<0.05$). Moreover, dialysate sodium concentration and dialysate conductivity were highly significantly related ($r=0.96$; $P<0.05$).

**Isovolaemic dialysis**

All measurements were successful, except for one initial plasma conductivity measurement during DNA [140]. Pre-dialytic plasma conductivity and serum sodium concentrations are displayed in Tables 1 and 2. Pre-dialytic plasma conductivity was significantly related to pre-dialytic serum sodium ($r=0.80$; $P<0.05$).

Plasma conductivity and serum sodium did not change significantly during isovolaemic dialysis (Tables 1 and 2). In order to test the preciseness of serum sodium and plasma conductivity measurements, serum sodium levels at the start and after the end of isovolaemic dialysis were correlated, as were plasma conductivity measurements. The correlation coefficient was $r=0.92$ for plasma conductivity but only $r=0.70$ for serum sodium levels ($P<0.015$).

Mean dialysate conductivity during DNA [ind] was 143 ± 2.1 mmol/l. IMB differed significantly between the session with DNA [140] on the one hand and DNA [140] and DNA [ind] on the other, whereas DNA [140] and DNA [ind] were not significantly different (Table 1). IMB during isovolaemic dialysis with DNA [144] and DNA [140] was significantly related to the pre-dialytic plasma conductivity ($r=0.97$ and $r=0.81$; $P<0.05$) (Figures 2A and 3A), and to a somewhat lesser degree, to the pre-dialytic serum sodium concentration ($r=0.83$ and $r=0.61$; $P<0.05$) (Figures 2B and 3B).

**Ultrafiltration combined with haemodialysis**

The mean ultrafiltration volume was comparable between the three treatment sessions (Table 2). Serum sodium increased significantly during DNA [144] but not during the other treatment modalities (Table 2). Moreover, IMB was significantly less positive during DNA [144], indicating less ionic removal, compared with DNA [140] and DNA [ind] ($P<0.05$) (Table 2 and Figure 4). IMB was significantly related to ultrafiltration volume during both DNA [140] ($r=0.87$), DNA [144] ($r=0.81$), and DNA [ind] ($r=0.64$; all $P<0.05$). During DNA [140], but not during the other treatment sessions, IMB was significantly related to pre-dialytic plasma conductivity ($r=0.59$; $P<0.05$).

The decline in relative blood volume (Table 2 and Figure 5) did not differ between the three treatment sessions. However, daily inter-dialytic weight gain following the treatment session was significantly higher after DNA [144] (0.66 ± 0.33 kg/day) compared with DNA [140] (0.57 ± 0.33 kg/day; $P<0.05$), whereas the difference with DNA [ind] (0.58 ± 0.30) did not reach significance.

The decline in systolic blood pressure during the entire dialysis session—which was 12.7 ± 21.0 mmHg during DNA [140], 0.0 ± 15.3 mmHg during DNA [144], and −5.9 ± 17.4 mmHg during DNA [ind]—did not differ significantly between the different dialysis...
sessions, although it tended to be higher during DNa [140] compared with DNa [ind] (*P = 0.08").

Also, the decline in diastolic blood pressure—which was \(-5.6 \pm 12.6 \text{ mmHg}\) during DNa [140], \(-7.5 \pm 14 \text{ mmHg}\) during DNa [144], and \(-2.4 \pm 9.4 \text{ mmHg}\) during DNa [ind]—did not differ significantly between the different dialysis sessions.

When patients with a pre-dialytic serum sodium concentration below 140 mmol/l or higher or equal to 140 mmol/l were analysed separately (n = 5), IMB was significantly higher during DNa [ind] compared with DNa [140] in patients with a pre-dialytic serum sodium concentration below 140 mmol/l (Figure 6) \((324 \pm 87 \text{ vs } 228 \pm 127 \text{ mmol}; P < 0.05)\) whereas the decline in relative blood volume did not differ significantly \((-9.8 \pm 1.6 \text{ vs } -7.8 \pm 2.3\% ; P = \text{NS})\). In contrast, in patients with a pre-dialytic serum sodium concentration higher or equal to 140 mmol/l (n = 8), IMB was significantly lower during DNa [ind] compared with DNa [140] \((254 \pm 123 \text{ vs } 350 \pm 178 \text{ mmol}; P < 0.05)\) (Figure 5) whereas also in these patients, the decline in relative blood volume did not differ significantly \((-7.1 \pm 1.8 \text{ vs } -8.1 \pm 3.1\%\)).

**Discussion**

The main findings of the present study are first, the large difference in ionic mass balance between haemodialysis with DNa [140] and DNa [ind] on the one hand and DNa [144] on the other, in combination with the small and non-significant difference in blood volume preservation between these modalities; secondly, the strong relation between pre-dialytic serum sodium and plasma conductivity with ionic mass balance, which explains the diffusive ionic influx during isovolaemic dialysis in patients with low pre-dialytic serum sodium levels; thirdly, the increased ionic removal during DNa [ind] in patients with low pre-dialytic serum sodium levels and reduced ionic removal in patients with high pre-dialytic serum sodium levels despite the absence of differences in blood volume preservation compared with DNa [140].

Ionic mass balance measurements by Diascan® appears to be suitable in detecting ionic changes during dialysis, as shown by the good agreement between Diascan® measurements and conductivity measurements in spent dialysate obtained during an entire dialysis session. As a result of the abundance of sodium ions in both dialysate and plasma, it is likely that IMB reflects predominately sodium balance during dialysis. It should, however, be mentioned that due to rapid changes in pH, chloride, and bicarbonate, the relation of conductivity measurements to sodium balance may deviate slightly during dialysis. Moreover, in the present study, the relation between both serum sodium and plasma conductivity levels was not completely linear. We think, however, that this phenomenon is probably predominantly due to a lack of preciseness of sodium measurements, as shown by the greater reproducibility of plasma conductivity measurements compared with serum sodium levels, presented in the results section on isovolaemic dialysis. Moreover, the relation between
pre-dialytic plasma conductivity measurements and IMB in the present study was far stronger than that obtained using serum sodium measurements. The possible lack of preciseness of serum sodium determination raises some doubt on the usefulness of monitoring serum sodium levels in order to detect differences in ionic removal between various treatment modalities [11].

In general, hypertonic fluid was removed during the studied treatments, even during most treatment sessions with DNa [144]. Nevertheless, during DNa [144], plasma conductivity and serum sodium increased. Although we did not directly measure changes in body fluid compartments during the present study, a likely explanation for this phenomenon is that intracellular volume slightly increases during haemodialysis, as has been shown in earlier studies [12]. Indeed, as can be shown from simple calculations [13], even a small decline in sodium distribution volume resulting from a fluid shift between extracellular and intracellular compartments might result in an increase in plasma conductivity and sodium despite hypertonic fluid removal. Perhaps this phenomenon could also explain the small decrease in relative blood volume during isovolaemic dialysis sessions, although this phenomenon might also theoretically be explained by peripheral vasodilation leading to pooling of haemodynamically inactive blood volume [14].

Both during isovolaemic dialysis, as well as during haemodialysis combined with ultrafiltration, a significant difference in ionic mass balance was observed between DNa [144] compared with DNa [140] and
DNA [ind], indicating less ionic removal during DNA [144]. Moreover, serum sodium levels increased significantly during DNA [144], but not during the other treatment modalities. The mean difference in measured ionic mass balance between high and standard sodium dialysate was approximately 90 mmol during an entire dialysis session, in theory corresponding to 2000 mg of sodium, thus the entire recommended daily sodium intake of a dialysis patient. The long-term clinical significance of this phenomenon cannot be elucidated from the present study but may not be negligible in view of the strong arguments for a relation between sodium, hypertension, and cardiac abnormalities in dialysis patients [4,5]. Indeed, even inter-dialytic weight gain was higher after treatment with DNA [144]. Remarkable was the small and non-significant difference in blood volume preservation between the three treatment modalities. Nevertheless, in this stable group of dialysis patients, the decline in systolic blood pressure tended to be somewhat higher during DNA [140] compared with DNA [144].

The net diffusive ionic influx during DNA [140] and DNA [144] in patients with low pre-dialytic serum sodium levels is a phenomenon not often described in the literature, but is in line with earlier experimental data [15] and theoretical considerations [16,17]. In the present study, diffusive ionic influx was observed when the dialysate sodium concentration was approximately 5 mmol/l higher than the serum sodium concentration. Factors influencing diffusion between dialysate and serum are complex and include the sodium concentration in serum water, the Donnan effect, and the formation of complexes of sodium ions with anions in serum water and dialysate [17]. Nevertheless, assuming the fact that the sodium concentration of serum water is approximately 9 mmol higher than that in whole serum and assuming a Donnan factor of 0.967 [17], the neutral IMB obtained with a difference of 5 mmol between blood and dialysate can largely be explained by the combination of the Donnan effect and the sodium concentration in serum water.

Individualization of the dialysate in the present study was achieved by adjusting dialysate conductivity (which corresponds to DNA [7]) to the pre-dialytic serum conductivity of the patient. This approach was performed because (effective) serum conductivity measured by Diascan is only related to the concentration of sodium ions which are free to diffuse and not trapped by the Donnan effect [7]. In order to perform individualization of dialysate sodium, on-line measurements of serum conductivity or sodium should be available, which may be difficult in a clinical setting. The best way to achieve a desired serum sodium concentration after dialysis is probably the use of a biofeedback system, which is, however, at present only available on dialysis modules of a single manufacturer. Still, individualization of DNA appeared predominantly relevant in patients with low pre-dialytic sodium levels, because in these patients, an increased ionic removal was achieved compared with DNA [140] whereas the decline in blood volume did not differ significantly. Nevertheless, the mean observed difference of approximately 2% might again be relevant in some patients. Therefore, it would certainly seem judicious to apply blood volume measurements if individualization of DNA is to be applied in hypotensive-prone dialysis patients with low pre-dialytic serum sodium levels.

In the patients with higher pre-dialytic sodium levels, ionic removal was actually less during DNA [140] compared with DNA [ind] whereas again, the decline in blood volume was not apparently different from DNA [140].

Drawbacks of the study are, first the relatively small number of included patients, although this does not
appear to have influenced the primary goal of the study, i.e. to assess IMB during different dialysate [Na] concentrations. Moreover, because the main objection was to study IMB and blood volume preservation during different dialysate sodium concentrations, stable haemodialysis patients were included. Further studies should also address the feasibility of individualized sodium concentrations of the dialysate in hypotension-prone dialysis patients.

Moreover, several patients still have residual renal function, which might have interfered with the influence of dialysate sodium prescription on inter-dialytic weight gain.

In conclusion, a large difference in IMB, which may amount to the entire recommended daily sodium intake of a dialysis patient, was observed between DNa [144] on the one hand and DNa [140] and DNa [ind] on the other despite a nearly comparable blood volume preservation. In patients with a low predialytic serum sodium concentration, net diffusive ionic influx from the dialysate to the patient may occur during a fixed DNa. In patients with a low predialytic serum sodium concentration, individualization of dialysate sodium led to an improved ionic removal in patients, apparently without large implications for blood volume preservation during dialysis.

References


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