Haemodynamic stability in standard bicarbonate haemodialysis and long-hour slow-flow bicarbonate haemodialysis

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Abstract

Background. The interplay of correct solute mass balances, such as that of sodium (Na⁺) and potassium (K⁺) (respectively, Na⁺MB and K⁺MB) with adequate ultrafiltration volumes (VUF), is crucial in order to achieve haemodynamic stability during haemodialysis (HD). The GENIUS single-pass batch dialysis system (Fresenius Medical Care, Germany) consists of a closed dialysate tank of 90 L; it offers the unique opportunity of effecting mass balances of any solute in a very precise way.

Methods. The present study has a crossover design: 11 stable anuric HD patients underwent two bicarbonate HD sessions, one of 4 h and the other of 8 h in a random sequence, always at the same interdialytic interval, at least 1 week apart. The GENIUS system and high-flux FX80 dialysers (Fresenius Medical Care, Germany) were used. The volume of blood and dialysate processed, VUF and dialysate Na⁺ and K⁺ concentrations were prescribed to be the same. Plasma water Na⁺ and K⁺ trends during dialysis as well as Na⁺MBs and K⁺MBs were determined. At the same time, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate trends during dialysis were analysed. Plasma volume (PV) changes were computed from plasma total protein concentrations and their trends analysed.

Results. Plasma water Na⁺ and K⁺ levels were not significantly different when comparing the start and the end of the 8-h sessions when compared with the 4-h ones (P < 0.048 and P < 0.006, respectively). Dialysis sessions were uneventful. SBP decreased significantly during the 4-h sessions, whereas it remained stable during the 8-h ones (P < 0.0001 and P = NS, respectively). Statistically significantly lower intradialysis decreases of SBP (−4.5 ± 16.2 vs −20.0 ± 15.0 mmHg, P < 0.02) and MAP (−1.4 ± 11.7 vs −8.6 ± 11.0 mmHg, P < 0.04) were achieved in the 8-h sessions with respect to the 4-h sessions, in spite of no significant difference for mean VUF (2.9 ± 0.9 vs 2.9 ± 0.8 L; P = NS) and mean Na⁺MBs (−298.1 ± 142.2 vs −286.2 ± 150.7 mmol; P = NS). The decrease of PV levels in the first 4 h was significantly slower during the 8-h sessions when compared with the 4-h ones (P < 0.04). PV decrease was significantly higher at the end of the 4-h HD sessions than at the end of the 8-h HD sessions (P < 0.043).

Conclusions. The present highly controlled experiments using a crossover design and precise Na⁺MB and K⁺MB controls showed that better haemodynamic stability was achieved in the 8-h sessions with respect to the 4-h sessions, in spite of no difference for mean VUF and Na⁺MBs. Thus, other pathophysiological mechanisms, namely, a better PV preservation, must be advocated in order to explain the better haemodynamic stability peculiar to long-hour slow-flow nocturnal HD treatments.

Keywords: blood pressure; haemodialysis; haemodynamic stability; plasma volume; sodium mass balance
Introduction

The achievement of a normal hydration state is one of the major targets of haemodialysis (HD) therapy [1]. The abnormal hydration state has been related to arterial hypertension, dialysis-associated hypotension and other symptoms and signs including pulmonary and peripheral oedema, heart failure, left ventricular hypertrophy and other adverse cardiovascular sequelae [1]. A correct sodium (Na+) mass balance (Na+MB) during HD is crucial in order to achieve a normal hydration state: it should be negative and of the same order of magnitude of the positive interdialysis Na+MB in order to prevent both intradialysis hypotension and interdialysis hypertension.

Cardiovascular diseases represent the main cause of death in HD patients, and arrhythmias are frequently observed in patients undergoing HD [2]. Dialysis treatment per se can be considered as an arrhythmogenic stimulus; moreover, uraemic patients are characterized by a 'pro-arrhythmic substrate' because of the high prevalence of ischaemic heart disease, left ventricular hypertrophy and autonomic neuropathy [2]. One of the most important pathogenetic elements involved in the onset of intradialysis arrhythmias is the alteration in electrolyte concentration, particularly potassium (K+). A correct K+ mass balance (K+MB) during HD is crucial: it should be negative and of the same order of magnitude of the positive interdialysis K+MB, in order to prevent both dangerous intradialysis hypokalaemia and fatal interdialysis hyperkalaemia.

The main aim of the present crossover study was to evaluate the interplay of solute mass balances (Na+MBs and K+MBs) with ultrafiltration volumes (VUF) and ultrafiltration rates (UFR) in the achievement of intradialysis haemodynamic stability. Eleven stable HD patients underwent two bicarbonate HD sessions (~4 and ~8 h) in a random sequence in which the volume of blood and dialysate processed, VUF and dialysate Na+ and K+ concentrations were prescribed to be the same. The GENIUS single-pass batch dialysis system with a closed dialysate tank of 90 L (Fresenius Medical Care, Bad Homburg, Germany) was chosen because it offers the unique opportunity of effecting mass balances of any solute in a very precise way, at variance with those obtained with the standard single-pass dialysis systems, which are always at risk of systematic errors [3].

Materials and methods

Design of the study

The present crossover study was approved by our institutional review board and was conducted in accordance with good clinical practice guidelines and ethical principles of the Helsinki Declaration. The inclusion criteria were: (i) standard bicarbonate HD treatment for at least 6 months; (ii) uncomplicated HD sessions: no clinical history of haemodynamic instability and/or arrhythmias during the treatment. Twenty-two out of 135 prevalent patients treated in our dialysis unit were considered eligible because of their intradialysis absolute haemodynamic stability. However, 11 of them did not adhere to the protocol of the study, mainly because it prescribed to undergo one experimental dialysis session lasting 8 h. Thus, a group of 11 stable white prevalent anuric uraemic patients (nine males and two females; mean age ± SD, 54.1 ± 17.8 years; dialysis vintage, 78.0 ± 60.2 months) was enrolled; nine of them had a clinical history of arterial hypertension with recent echocardiographic findings of left ventricular hypertrophy (five of them were still treated with antihypertensive drugs, namely, calcium channel blockers, ACE inhibitors and angiotensin receptor blockers). A pre-enrolment EKG showed sinus rhythm in all patients; three of them exhibited left anterior hemiblock; in one of them, the latter was associated with right bundle branch block. After obtaining informed consent, they underwent one standard bicarbonate HD of 4 h and one slow-flow bicarbonate HD session lasting 8 h in a random sequence, always at the same interdialytic interval, at least 1 week apart. The experimental HD sessions utilized the GENIUS single-pass batch dialysis system [3]. GENIUS provided 90 L of bicarbonate dialysate per dialysis session. It uses a double-ended roller pump that generates equal blood and dialysate flows up to 350 mL/min, as in the case of the 4-h HD sessions. As a consequence, dialysis sessions in spite of markedly different duration will still apply an identical blood and dialysate volume, hence offering the opportunity to evaluate the impact of time as the sole variable. The system consists of a closed dialysate tank of 90 L and, although fresh and spent dialysate are stored together, dialysis may last up to 8 h when using a blood and dialysate flow of 187 mL/min, without mixing of fresh and spent dialysate. The excess body water that is ultrafiltered out of the patient plasma is collected in an ultrafiltrate recipient [3]. The sessions were pair-matched as far as the dialysate and blood volume processed (90 L) and VUF are concerned. Thus, the duration treatment was dictated by the achievement of the target dialysate and blood volume processed (i.e. 90 L): for this reason, it was slightly different from 4 and 8 h (Table 1). Notably, the same dialysis machine was utilized in all sessions. The high-flux FX80 dialysers (Fresenius Medical Care, Bad Homburg, Germany) were utilized in all sessions. The characteristics of the dialyser are described elsewhere [3]. Dialysate composition was as follows: calcium (Ca++), 1.5 mmol/L; magnesium, 0.5 mmol/L; K+, 2 mmol/L; Na+, 140 mmol/L; bicarbonate, 35 mmol/L; chloride, 113 mmol/L; glucose, 5.55 mmol/L; citrate, 0.10 mmol/L.

Blood and dialysate sampling

Blood samples were taken from the inlet blood lines immediately before the onset of dialysis and at 60, 120, 180 and 240 min during the 4- and 8-h sessions. Additional samples were taken at 360 and 480 min during the 8-h sessions. Dialysate was collected from the inlet dialysate lines at the same time points of the blood samples. Furthermore, at the end of dialysis, two samples were taken, respectively, from the ultrafiltrate recipient and from the dialysate tank after thorough mixing in order to quantify solute concentration in total spent dialysate.

Measurements

Plasma Na+, K+ and Ca++ concentrations, blood bicarbonate and pH were measured immediately after blood sampling by means of an ion-selective electrode (Radiometer ABL 800, Kopenhagen, Denmark); Na+, K+ and Ca++ concentrations were measured in the fresh and spent dialysate and in the ultrafiltrate recipient (Radiometer ABL 900, Kopenhagen, Denmark). In order to calculate mass balances, Na+, K+ and Ca++ concentrations in the inlet dialysate were considered as that given by the average of the five hourly measurements in the 4-h sessions and of the seven measurements in the 8-h sessions). Furthermore, Na+, K+ and Ca++ concentrations in total spent dialysate and in the ultrafiltrate recipient were considered as that given by the average of five consecutive measurements performed on the same sample. Here, it must be stressed that feasibility studies performed before starting the experimental sessions had shown very small coefficients of variation for the measurement of Na+, K+ and Ca++ in the dialysate fluid; 10 samples of inlet dialysate and 10 samples of total spent dialysate had been collected in these feasibility studies and five consecutive measurements had been performed on the same sample. The ranges of the coefficients of variation of the 20 samples (10 samples of inlet dialysate and 10 samples of total spent dialysate) were: 0–0.004 mmol/L for Na+, 0–0.03 mmol/L for K+ and 0–0.0006 mmol/L for Ca++; then, the mean ± SD of the 20 coefficients of variation had been calculated as 0.001 ± 0.002 for Na+, 0.01 ± 0.01 for K+ and 0.003 ± 0.004 for Ca++.

Blood samples collected at the time points described above were utilized also for the measurement of plasma total protein (TP) concentrations by means of routine automated methods. Systolic blood pressure (SBP)
Table 1. Na+MBs, K+MBs and laboratory data in the 11 HD patients undergoing two experimental (4- and 8-h) dialysis sessions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>4 h</th>
<th>8 h</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment time (min)</td>
<td>257.7 (1.1)</td>
<td>469.1 (2.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body weight, pre (kg)</td>
<td>72.2 (10.8)</td>
<td>71.9 (10.7)</td>
<td>0.205</td>
</tr>
<tr>
<td>Body weight, post (kg)</td>
<td>69.2 (10.3)</td>
<td>69.1 (10.1)</td>
<td>0.458</td>
</tr>
<tr>
<td>UF rate (mL/h/kg)</td>
<td>2.9 (0.8)</td>
<td>2.9 (0.9)</td>
<td>0.851</td>
</tr>
<tr>
<td>Plasma water Na+, pre (mmol/L)</td>
<td>144.7 (3.0)</td>
<td>143.9 (3.6)</td>
<td>0.208</td>
</tr>
<tr>
<td>Plasma water Na+, post (mmol/L)</td>
<td>148.7 (3.6)</td>
<td>148.8 (1.9)</td>
<td>0.180</td>
</tr>
<tr>
<td>Inlet dialysate Na+ (mmol/L)</td>
<td>137.6 (1.4)</td>
<td>138.0 (0.8)</td>
<td>0.420</td>
</tr>
<tr>
<td>Na+MB (mmol)</td>
<td>286.2 (150.7)</td>
<td>298.1 (142.2)</td>
<td>0.403</td>
</tr>
<tr>
<td>Plasma water K+, pre (mmol/L)</td>
<td>5.9 (0.8)</td>
<td>5.8 (1.1)</td>
<td>0.810</td>
</tr>
<tr>
<td>Plasma water K+, post (mmol/L)</td>
<td>4.1 (0.4)</td>
<td>4.1 (0.4)</td>
<td>0.783</td>
</tr>
<tr>
<td>Inlet dialysate K+ (mmol/L)</td>
<td>2.03 (0.3)</td>
<td>2.03 (0.3)</td>
<td>1.000</td>
</tr>
<tr>
<td>K+MB (mmol)</td>
<td>-89.2 (22.3)</td>
<td>-97.1 (28.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>Plasma TP, pre (g/dL)</td>
<td>6.0 (0.8)</td>
<td>6.1 (0.7)</td>
<td>0.471</td>
</tr>
<tr>
<td>Plasma TP, post (g/dL)</td>
<td>7.2 (0.9)</td>
<td>6.9 (0.8)</td>
<td>&lt;0.017</td>
</tr>
<tr>
<td>Plasma volume, pre (L)</td>
<td>3.90 (0.6)</td>
<td>3.88 (0.6)</td>
<td>0.102</td>
</tr>
<tr>
<td>Plasma volume, post (L)</td>
<td>3.17 (0.4)</td>
<td>3.48 (0.7)</td>
<td>&lt;0.043</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD). pre, pre-dialysis; post, post-dialysis.
*Student’s t-test for paired data.

and diastolic blood pressure (DBP) were measured during dialysis every hour or more frequently, if required, by means of an electronic sphygmomanometer; at that time, heart rate (HR) was also recorded.

Body weight was measured to the nearest 0.1 kg.

Calculations

Plasma water concentration of the solutes (Na+, K+ and Ca++) was calculated as follows:

$$C_w = C_p / (1 - \alpha TP)$$

where $C_w$ is the plasma water solute concentration, $C_p$ is the plasma solute concentration and $\alpha$ is a factor to calculate the protocrit from plasma TP ($\alpha = 0.00107 L/g$) [4].

Mean arterial pressure (MAP) was calculated as the sum of DBP plus one-third of the pulse pressure. Pre-dialysis plasma volume (PV0) was assumed to be 5.4% of the pre-dialysis body weight. This figure is derived from previous studies in which PV was measured twice in nine stable HD patients by means of the 125I human serum albumin dilution principle [5].

PV at time $t$ ($PV_t$) was calculated from the formula:

$$PV_t = PV_0 \times TP_0 / TP_t$$

where TP0 and TP were the plasma TP concentrations at time 0 and time $t$. These data allowed the calculation of PV changes during each fraction of time and during the entire session. This equation was derived assuming that there was no loss of protein from the vascular compartment and that the plasma compartment behaves as a well-mixed single pool during the HD treatment [6].

Statistical analyses

Data are reported as means ± SD. The Kolmogorov–Smirnov test was performed in order to assess the normality of the distribution of the data. The values of all the parameters at the start and at the end of each HD session were compared by means of the Student’s $t$-test for paired data. Then, the trend analysis for the parameters studied during the HD sessions was made by using the repeated-measures ANOVA with the Wilks lambda as multivariate test for the significance of each effect studied and with the Mauchly’s test of sphericity of the matrix. All the statistical inferences were made by means of the SPSS 11.0 software (SPSS Inc., Chicago, IL, USA) and a P-value < 0.05 was considered for the statistical significance.

Statistical power of the study

SBP was considered as the main response variable, and its reduction with standard bicarbonate HD was compared with long-hour slow-flow bicarbonate HD. An absolute difference in SBP of 10 mmHg was considered as clinically relevant. The statistical power of the study, calculated by considering its design, the number of patients enrolled, 10 mmHg as significant difference in SBP values and an $\alpha$ value of 5%, was 85%.

Outcome measures

The primary endpoint of the study was the possible beneficial effect of long-hour slow-flow bicarbonate HD compared with standard bicarbonate HD on haemodynamic stability of dialysis patients, estimated by the difference in SBP, DBP, MAP and HR during single pair-matched dialysis sessions.

Results

All the 22 dialysis sessions were uneventful; no session had to be interrupted because of clinical complications; no therapeutic interventions, such as saline infusions, were necessary. All the data collected in this study were normally distributed at the Kolmogorov–Smirnov test.

Plasma water Na+ trends and Na+MBs

The following results were obtained in the 4- and 8-h HD sessions, respectively: mean $f_{\text{UF}}$ were 2.9 ± 0.8 and 2.9 ± 0.9 L (P = 0.851); mean dialysate Na+ concentrations were 137.6 ± 1.4 and 138.0 ± 0.8 mmol/L (P = 0.420); mean Na+MBs were $-286.2 ± 150.7$ vs $-298.1 ± 142.2$ mmol; P = 0.403 (Table 1). Plasma water Na+ levels were not significantly different when comparing the start and the end of the sessions of the two treatments (Table 1). Trends of plasma water Na+ levels are shown in Figure 1a.

Plasma water K+ trends and K+MBs

The following results were obtained in the 4- and 8-h HD sessions, respectively: mean dialysate K+ concentrations were 2.03 ± 0.3 and 2.03 ± 0.3 mmol/L (P = 1.000); mean K+MBs were $-89.2 ± 22.3$ and $-97.1 ± 28.9$ mmol (P = 0.06) (Table 1). Plasma water K+ levels were not significantly different when comparing the start and the end of
the sessions of the two treatments (Table 1). Trends of plasma water K\+
levels are shown in Figure 1b.

**Plasma water Ca++**, **blood pH and bicarbonate trends and Ca++MBs**

The data relative to plasma water Ca++, blood pH and bicarbonate trends and Ca++MBs are being submitted for publication in a companion paper (Basile et al., submitted for publication). As far as haemodynamic stability is concerned, Ca++MBs were not statistically significantly differ-
ent when comparing short and long dialyses (Basile et al., submitted for publication).

**Blood pressure and HR trends**

Blood pressure levels (SBP, DBP and MAP) and HR were not significantly different when comparing the start of the two treatments (Table 2). Blood pressure levels (SBP, DBP and MAP) were significantly different when comparing the end of the two treatments, being significantly higher in the 8-h treatments (Table 2). HR was not significantly different between the two treatments at the end of the sessions (Table 2). Trends of SBP, DBP and MAP levels during the dialysis sessions are shown in Figures 2, 3 and 4, respectively. Differences in SBP, DBP and MAP levels between the start and the end of each treatment (ΔSBP, ΔDBP and ΔMAP, respectively) are shown in Figure 5. Trends of HR levels during the dialysis sessions are shown in Figure 6.

**Plasma TP and PV trends**

Table 1 shows pre- and post-dialysis plasma TP concentrations during the 4- and 8-h dialysis sessions. They were not significantly different when comparing the start of the two treatments (Table 1). Plasma TP levels were significantly

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**Table 2.** Blood pressure levels and HR of the 11 HD patients undergoing two experimental (4- and 8-h) dialysis sessions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>4 h</th>
<th>8 h</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, pre (mmHg)</td>
<td>144.5 (26.0)</td>
<td>137.3 (22.4)</td>
<td>0.109</td>
</tr>
<tr>
<td>SBP, post (mmHg)</td>
<td>123.6 (30.0)</td>
<td>132.7 (28.0)</td>
<td>&lt;0.029</td>
</tr>
<tr>
<td>DBP, pre (mmHg)</td>
<td>73.3 (17.4)</td>
<td>77.0 (14.8)</td>
<td>0.091</td>
</tr>
<tr>
<td>DBP, post (mmHg)</td>
<td>70.5 (18.5)</td>
<td>77.3 (15.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP, pre (mmHg)</td>
<td>97.0 (19.4)</td>
<td>97.2 (16.8)</td>
<td>0.478</td>
</tr>
<tr>
<td>MAP, post (mmHg)</td>
<td>88.3 (21.5)</td>
<td>95.8 (19.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HR, pre (bpm)</td>
<td>78.5 (7.7)</td>
<td>76.7 (4.9)</td>
<td>0.251</td>
</tr>
<tr>
<td>HR, post (bpm)</td>
<td>79.0 (8.0)</td>
<td>76.2 (9.2)</td>
<td>0.218</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD). SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure. Pre, pre-dialysis; Post, post-dialysis.

*Student’s t-test for paired data.
higher at the end of the 4-h sessions than the corresponding ones at the end of the 8-h sessions (P < 0.017) (Table 1). Table 1 shows also pre- and post-dialysis PV levels during the 4- and 8-h dialysis sessions. They were not significantly different when comparing the start of the two treatments (Table 1). PV levels were significantly higher at the end of the 8-h sessions than the corresponding ones at the end of the 4-h sessions (P < 0.043) (Table 1). Trends of plasma TP and of PV levels during the dialysis sessions are shown in Figure 7a and b, respectively.

Discussion

The present controlled crossover study shows a statistically significant difference in blood pressure trends (above all of SBP) during uncomplicated HD sessions of different duration in which, however, the V UF and the dialysate Na+ concentration were prescribed to be the same; Na+MBs were shown not to be different, whereas PV decrease was significantly higher at the end of the 4-h HD sessions than at the end of the 8-h HD sessions. Someone could argue that comparing patients on 4-h dialysis with those on 8-h dialysis and saying that the latter are more stable on the haemodynamic level is stating the plainly obvious. This may be true for the unstable hypotension-prone dialysis patients: the prescription of longer and/or more frequent dialysis sessions allows in this subset of patients the decrease in UFR and reduces the risk of intradialysis complications [7]. However, this is probably not true for the stable dialysis patients. Intuitively, it is more difficult to detect statistically significant differences in a biological parameter in a group of patients undergoing two different intervention studies, when the biological parameter is deemed difficult to modify and overlapping at the baseline time point. Furthermore, to the best of our knowledge, no controlled study has so far been conducted in order to show the benefits of longer dialyses on the haemodynamic stability of the peculiar subset of patients with no clinical history of haemodynamic instability. The novelty of our study is that we could show that, after a comparable UF rate and Na+MBs, the decrease in PV is significantly higher in the 4-h HD sessions than in the 8-h HD sessions, even though the plasma TP levels increase significantly along the time points in both 4- and 8-h sessions (repeated-measures ANOVA: P < 0.0001 in both cases), evincing a more stable haemodynamic level in the 8-h HD sessions. However, the rise of plasma TP levels started after the first hour of treatment in the 4-h sessions, while the same parameter remained stable in the first 4 h in the 8-h sessions.

Fig. 4. Trends of MAP levels during the 4- and 8-h HD sessions. MAP decreased significantly during the first 3 h of HD in both 4- and 8-h sessions (repeated-measures ANOVA: P < 0.001 and P < 0.003, respectively), rising towards the baseline values at the end of the sessions. The trends of MAP in the first 4 h were not significantly different between the two treatments (repeated-measures ANOVA stratified for treatments: P = 0.273).

Fig. 5. Comparison of Δ blood pressure values (differences between the post- and the pre-dialysis blood pressure values) between the 4- and 8-h sessions (means ± SD). The decrease of SBP and MAP was significantly larger during the 4-h sessions (Student's t-test for paired data: P < 0.02 and P < 0.04, respectively). Δ values of DBP were not statistically significantly different.

Fig. 6. Trends of HR during the 4- and 8-h HD sessions. No differences of HR trends were found during and between the two treatments (repeated-measures ANOVA: P = 0.557 for 4-h and P = 0.415 for 8-h sessions; repeated-measures ANOVA stratified for treatments: P = 0.178).

Fig. 7. Trends of plasma TP and of PV levels during the 4- and 8-h HD sessions. (a) Plasma TP levels increased significantly along the time points in both 4- and 8-h sessions (repeated-measures ANOVA: P < 0.0001 in both cases), even though to a lesser extent in the 8-h ones. However, the rise of plasma TP levels started after the first hour of treatment in the 4-h sessions, while the same parameter remained stable in the first 4 h during the 8-h sessions. (b) Opposite trends were shown by PV levels: they decreased significantly along the time points in both 4- and 8-h sessions (repeated-measures ANOVA: P < 0.0001 in both cases). However, the trends of PV in the first 4 h were significantly different between the two treatments (repeated-measures ANOVA stratified for treatments: P < 0.0001); the fall of PV started after the first hour of treatment in the 4-h sessions, while the same parameter remained stable in the first 4 h in the 8-h sessions.
Haemodynamic stability in HD

study is that also in this subset of patients we could show a clear-cut difference in haemodynamic stability when comparing standard bicarbonate HD with long-hour slow-flow bicarbonate HD. Finally, it must be said that other authors felt the necessity of testing the haemodynamic tolerability in stable HD patients [8]: McIntyre et al. compared standard bicarbonate HD with biofeedback controlled HD in 15 non-hypotension-prone stable patients. They reported a reduction in the number of intradialysis symptomatic episodes and of SBP decreases >40%, when this subset of patients was treated with the latter technique [8].

The underlying mechanisms behind individual blood pressure responses to ultrafiltration and HD remain unknown [9]. Reductions in blood pressure with HD may be due to higher fluid or Na+ removal. Other potential aetiologies for differential individual blood pressure responses to HD include timing of blood pressure medications, decreased removal of blood pressure medications with HD, different dialysate prescription, different doses of erythropoietin stimulating agents or some other unknown factors [9]. Alternatively, greater reductions in blood pressure during HD have been postulated to be mediated by decreases in the renin–angiotensin system and/or decreased sympathetic nervous system activity in response to decreases in blood volume [10]. The design of the study (each patient in control of herself/himself) allowed to exclude most of the potential aetiologies for differential individual blood pressure responses to HD; the only factor which in our study seems to play a key role is the statistically significant difference in PV trends during HD. Intradialysis hypotension occurs when compensatory mechanisms for hypovolaemia are overwhelmed by excessive fluid removal [11]. More precisely, intradialysis hypotension is due to an imbalance between the amount of fluid removed and the refilling capacity of the intravascular compartment together with other compensatory mechanisms such as venous capacity, cardiac responses and vascular resistance [12]. Lins et al. suggested that the intradialysis PV decrease might be a better predictor of intradialysis decrease in SBP than the intradialysis decrease in body weight [13]. This is exactly what has been shown in our study: a better preservation of SBP was observed in the 8-h treatments together with a better preservation of PV, whereas the $V_{\text{UF}}$ and the decrease in body weight were similar in the two treatments. An intervention of the renin–angiotensin system and/or the sympathetic nervous system activity in response to decreases in blood volume can be hypothesized in our patients; however, the protocol of the study did not include any test able to prove the intervention of these systems. Furthermore, it must be underlined that the difference in ΔDBP (the difference between the post- and the pre-dialysis DBP values) between the 4- and 8-h treatments was not statistically significant. Actually, other studies have shown that the effects of intradialysis decreases in body weight and PV were greater on SBP than on DBP (Basile et al., submitted for publication) [13].

The importance of HD-induced cardiac injury has recently been stressed by Burton et al.: myocardial hypoperfusion and stunning during HD were clearly associated with intradialysis SBP decrease [14]. Furthermore, the importance that a high UFR during HD may have on the outcomes is well known [15,16]. A 5-year prospective observational multicentre study showed that high UFR were independently associated with increased mortality risk in HD patients [15]. Furthermore, DOPPS data showed that UFR > 10 mL/h/kg body weight was independently associated with higher risk of both intradialysis hypotension and mortality [16]. On the other hand, the relationship between blood pressure and survival in HD has remained quite controversial [17]. One potential confounding factor could be HD-associated hypotension [18]. Actually, intradialysis hypotension has been shown to be a significant and independent factor affecting mortality in HD patients [18].

Finally, some limitations of the study must be acknowledged: the first one is that only a single session was studied; the second one is that we could enrol only a small number of patients. The latter led to differences between the haemodynamic parameters of the two treatments whose statistical significance was not so high, despite a large absolute difference, above all in SBP values. The third limitation is the absence of thermal balance studies: actually, it is well known that thermal balance is an important factor of interference with the cardiovascular response [19].

In conclusion, the present highly controlled experiments using a crossover design and precise Na+MB and K+MB controls showed that better haemodynamic stability was achieved in the 8-h sessions with respect to the 4-h sessions, in spite of no significant difference in the mean $V_{\text{UF}}$ and Na+ MBs. Thus, other pathophysiological mechanisms, namely, a better PV preservation, must be advocated in order to explain the better haemodynamic stability peculiar to long-hour slow-flow nocturnal HD treatments.

Conflict of interest statement. None declared.

References

Effects of acetate-free haemodiafiltration (HDF) with endogenous reinfusion (HFR) on cardiac troponin levels

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Abstract

Background. Haemofiltrate reinfusion (HFR) is a form of haemodiafiltration (HDF) in which replacement fluid is constituted by ultrafiltrate from the patient ‘regenerated’ through a cartridge containing hydrophobic styrene resin. Bicarbonate-based dialysis solutions (DS) used in routine haemodialysis and HDF contain small quantities of acetate (3–5 mMol/L) as stabilizing agent, one of the major causes of intradialytic hypotension. Acetate-free (AF) DS have recently been made available, substituting acetate with hydrochloric acid. Cardiac troponin (cTnT) constitutes an appreciable marker of myocardial damage and cardiac hypertrophy, and correlates with left ventricular mass.

Methods. The aim of this study was to assess the impact of the presence or lack of acetate in DS on cTnT levels in patients treated with HFR and to evaluate outcome of intra-session cardiovascular stability. Twenty-five patients devoid of major cardiovascular comorbidity were randomized and treated with AF HFR for 3 months. The same patients were subsequently treated by means of HFR with DS containing 3 mMol/L acetate for 3 months and finally with AF HFR for a further 3 months. Prior and subsequent to each treatment period, samples were collected for cTnT measurement.

Results. A significant decrease was observed in cTnT levels throughout the first session of AF HFR (1.32±0.35–1.12±0.31 ng/mL, P<0.05) with a subsequent rise being registered during HFR with acetate-containing DS (1.12±0.31–1.28±0.37 ng/mL, P<0.05) and a further drop from 1.28±0.37 to 1.21±0.35 ng/mL in the last