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Automatic feedback control of relative blood volume changes during hemodialysis improves blood pressure stability during and after dialysis

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Abstract

Automatic feedback systems have been designed to control relative blood volume changes during hemodialysis (HD) as hypovolemia plays a major role in the development of dialysis hypotension. Of these systems, one is based on the concept of blood volume tracking (BVT). BVT has been shown to improve intra-HD hemodynamic stability. We first questioned whether BVT also improves post-HD blood pressure stability in hypotension-prone patients and second, whether BVT is effective in reducing the post-HD weight as many hypotension-prone patients are overhydrated because of an inability to reach dry weight. After a 3-week period on standard HD, 12 hypotension-prone patients were treated with two consecutive BVT treatment protocols. During the first BVT period of 3 weeks, the post-HD target weight was kept identical compared with the standard HD period (BVT-constant weight; BVT-cw). During the second BVT period of 6 weeks, we gradually tried to lower the post-HD target weight (BVT-reduced weight; BVT-rw). In the last week of each period, we studied intra-HD and 24 hr post-HD blood pressure behavior by ambulatory blood pressure measurement (ABPM). Pre- and post-HD weight did not differ between standard HD and either BVT-cw or BVT-rw. Heart size on a standing pre-dialysis chest X-ray did not change significantly throughout the study. There were less episodes of dialysis hypotension during BVT compared with standard HD (both BVT periods: $p<0.01$). ABPM data were complete in 10 patients. During the first 16 hr post-HD, systolic blood pressure was significantly higher with BVT in comparison with standard HD (both BVT periods: $p<0.05$). The use of BVT in hypotension-prone patients is associated with higher systolic blood pressures for as long as 16 hr post-HD. BVT was not effective in reducing the post-HD target weight in this patient group.

Key words: Hemodialysis, dialysis hypotension, relative blood volume, blood volume monitoring

INTRODUCTION

Dialysis hypotension occurs in up to 20% of hemodialysis (HD) sessions[1], and is a major cause of morbidity ranging from complaints of discomfort, cramps and nausea to serious vascular complications such as cerebral infarction and cardiac and mesenteric ischemia.[2,3] Frequent dialysis hypotension may contribute to chronic overhydration

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because of the inability to reach dry weight. Hypotension may also lead to underdialysis because of interruptions of the HD session[1,2] and/or enhanced solute sequestration in hypoperfused tissues during hypotension.[4] Dialysis hypotension usually resolves with treatment in the dialysis unit but may persist for hours after the patient leaves the unit.[2]

The cause of dialysis hypotension is multifactorial. The basic concept, however, is that hypotension during HD only occurs when the normal cardiovascular compensatory mechanisms cannot compensate for the inevitable blood volume reduction that occurs when a large volume of water is removed over a short period of time.[1] Especially, the combination of a critical decline in blood volume and impaired cardiovascular compensatory mechanisms may lead to cardiac underfilling, activation of the sympaticoinhibitory cardiopressor reflex and sudden hypotension.[5] From the above concept, it follows that blood pressure during HD can be maintained by either avoiding critical blood volume reductions and/or by improving cardiovascular compensatory mechanisms.

As hypovolemia plays an important role in the development of dialysis hypotension, automatic feedback systems have been designed to control intra-HD changes of relative blood volume (RBV), i.e., the changes in blood volume from the value at the start of the HD session. The goal of these systems is to prevent critical RBV reductions during HD. One of these systems is based on the concept of blood volume tracking (BVT):[6] based on target values for weight change and treatment duration, the BVT system guides the actual RBV along a pre-set individual RBV trajectory by continuously adjusting the ultrafiltration rate and dialysate conductivity. Several authors have shown that treatment with BVT is associated with improved intra-HD hemodynamic stability in comparison with standard HD.[4,6–12] We first questioned whether BVT also improves post-HD blood pressure stability in hypotension-prone patients, second, whether BVT is effective in reducing the post-HD weight as many hypotension-prone patients are overhydrated because of an inability to reach dry weight. To address these questions, we studied intra- and post-HD blood pressure behavior and weight change in 12 chronic hypotension-prone HD patients during standard HD and during 2 consecutive BVT treatment protocols. During the first BVT period of 3 weeks, the post-HD target weight was kept identical compared with the standard HD period (BVT-constant weight; BVT-cw). During the second BVT period of 6 weeks, we gradually tried to lower the post-HD target weight (BVT-reduced weight; BVT-rw).

SUBJECTS AND METHODS

Patients

We included 12 non-hospitalized hypotension-prone chronic HD patients. Selection criteria were as follows: chronic HD for more than 6 months; a thrice-weekly HD schedule; and the presence of symptomatic hypotension that necessitated treatment intervention in $>50\%$ of HD sessions over the past 6 weeks. Treatment interventions were defined as temporary interruption of ultrafiltration and/or administration of i.v. fluid. In case of hemodynamic instability, the following algorithm is used in our center: patients are placed in a supine or Trendelenburg position and ultrafiltration is temporarily halted. Only if these measures do not restore hemodynamic stability i.v. fluids are administered: usually, 150 mL NaCl 0.9% or colloids. Exclusion criteria were hypotension caused by primary cardiac rhythm disturbances and a history of frequent (more than 2 U/month during the past 3 months) transfusion of packed red blood cells as the BVT system cannot function properly during red blood cell transfusions. All patients gave informed consent to the study protocol. The study was performed in accordance with the principles of the Declaration of Helsinki.

STUDY PROTOCOL

This prospective study had an overall duration of 12 weeks. The study included 3 phases: in the first phase of 3 weeks, patients were treated with standard HD with a constant dialysate sodium concentration and a constant ultrafiltration rate. The post-HD target weight was set as close to the presumed dry weight as could clinically be tolerated by the patients. Dry weight was evaluated clinically (peripheral edema, signs of pulmonary congestion, intra- and extra-HD blood pressure pattern) and by (changes of) cardiopulmonary radiological aspect. The settings for the RBV curve during treatment with BVT (vide infra) were evaluated.

Next, the patients were dialyzed with 2 consecutive BVT treatment protocols. During the first BVT period of 3 weeks' duration, the post-HD target weight was kept identical to the weight that had been achieved at the end of the standard HD period. This period was named BVT-constant weight (BVT-cw). During the second BVT period of 6 weeks' duration patients were again dialyzed with the BVT system but, now, we gradually tried to lower the post-HD target weight. This period was named BVT-reduced weight (BVT-rw). The post-HD target weight was, again, set as low as could clinically be tolerated.

In the last week of each of the 3 study periods, measurements were performed before, during and following a midweek HD session that took place in the morning. Variables measured were as follows: pre- and post-HD weight, intra-HD weight loss, RBV course, blood pressure and heart rate during HD, 24 hr ambulatory blood pressure monitoring (ABPM) following the HD session, Kt/V, hemoglobin, albumin and plasma sodium levels. Post-HD blood samples for Kt/V and plasma sodium levels were drawn 15 min after the end of the HD session. Pre- and post-HD blood pressure and heart rate were measured 3 times within 5 min and averaged to obtain pre-HD and post-HD values. Blood pressure and heart rate were measured every 15 min by an automated oscillometric monitor that is incorporated into the HD apparatus. During the course of the study, it became technically possible to monitor ionic mass balance by Diascan (Hospal–Dasco, Medolla, Modena, Italy) during HD.[13] Therefore, in a limited number of patients ionic mass balance was measured during standard HD and at BVT-rw. Ionic mass balance represents the sodium balance because of the predominance of sodium ions in the plasma and dialysate. A positive ionic mass balance means a transfer of sodium from the patient to the dialysate.

The 24 hr ABPM (Spacelab 90207; SpaceLab, Redmond, WA, U.S.A.) started at approximately 14:00 hr, which was 20–40 min after the end of the HD sessions. Recordings were made every 15 min at daytime (07:00–23:00 hr) and every 30 min at night (23:00–07:00 hr). Data are presented separately for 3 post-HD periods: 0–8 hr post-HD (14:00–22:00 hr), 8–16 hr post-HD (22:00–06:00 hr) and 16–24 hr post-HD (06:00–14:00 hr). ABPM data were only analyzed in those patients in whom all three 24 hr ABPM were available for analysis.

As a surrogate marker of hydration state, a pre-dialysis standing chest X-ray was performed before the midweek dialysis session in the last week of the standard HD period and the last week of the BVT-rw period, respectively. The cardiothoracic ratio was assessed by a physician who was blinded to the order in which the chest X-rays had been performed. Only a light bread meal was provided during HD.

BVT system

The HD apparatus was an Integra Physio (Hospal-Dasco), equipped with the BVT system (Hemocontrol, Hospal-Dasco) and an optical device to measure RBV changes.[14] The BVT system is described in detail elsewhere.[4,8,9] In brief, RBV changes during HD are measured every minute based on assessment of hemoglobin concentration variations.[14] The software responds to changes in RBV and continuously adjusts the ultrafiltration rate and dialysate conductivity (lower and upper limits 13.5 and 16.0 mS/cm, respectively) through a feedback mechanism. The main objective of the system is to guide the patient's RBV along a pre-determined individual; the so-called ideal RBV trajectory. Simultaneously, the BVT system aims at achieving the pre-set ultrafiltration volume target and avoids sodium overload by means of a kinetic sodium model that establishes a pre-set so-called equivalent conductivity. The equivalent conductivity represents the dialysate conductivity that produces the same sodium mass balance at the end of a BVT treatment session as HD with constant dialysate conductivity.[8] In this study, the equivalent conductivity was set at 13.8 mS/cm with lower and upper tolerances of 13.6 and 14.0 mS/cm, respectively. We chose this setting as (in a pilot study) we had found that these settings resulted in post-HD sodium levels that were comparable with the levels after HD sessions with a constant dialysate conductivity of 13.9 mS/cm.

For each patient, the ideal RBV trajectory was established after analyzing at least 6 standard HD sessions in which the spontaneous RBV course was related to the cumulative ultrafiltration volume and intra-HD blood pressure behavior. Typically, the form of the ideal RBV curve shows a rapid decline in the beginning of HD and a trend toward isovolemia during the second half of the HD session.[6]

HD schedule

All patients were on bicarbonate dialysis 3 times 4 hr a week with a low-flux polysulfon hollow-fiber dialyzer, F8 (Fresenius Medical Care, Bad Homberg, Germany). The blood flow rate was 250–350 mL/min, and dialysate flow was 500 mL/min. Dialysate temperature was 36.0 °C in all patients and was not changed during the study period. Dialysate composition for standard HD was as follows: sodium 140 mmol/L, potassium 1.0 mmol/L, calcium 1.5 mmol/L, magnesium 0.5 mmol/L, chloride 108 mmol/L, bicarbonate 34 mmol/L, acetate 3.0 mmol/L and glucose 1.0 g/L. Dialysate conductivity in standard HD was 13.9 mS/cm. Dialysate composition during treatment with BVT was identical, except for dialysate sodium, which was variable according to the concept of the BVT system.

Hypotensive episodes

Dialysis hypotension was defined as a drop in systolic blood pressure of more than 40 mmHg from the pre-HD value in combination with a treatment intervention by the dialysis nurse (temporary stop of ultrafiltration and/or infusion of i.v. fluids). For each study period, all HD sessions in which one or more episodes of dialysis hypotension occurred were counted. The results are expressed as the percentage of HD sessions during which 1 or more episodes of dialysis hypotension occurred.

Statistical analysis

Data are presented as mean ± standard deviation (SD) unless otherwise stated. Comparisons of weight, intra-HD weight loss, pre- and -post-HD blood pressure, the frequency of dialysis hypotension episodes, Kt/V, cardio-thoracic ratio (chest X-ray) and sodium levels between standard HD on the one hand and BVT-cw and BVT-rw on the other were made with a paired Student's t-test.

Blood pressure and heart rate during HD were first averaged to hourly means and comparisons between standard HD and both BVT periods were made with a paired Student's t-test. The 24 hr ABPM blood pressure and heart rate data were first interpolated to exact 15 min (07:00–23:00 hr) or 30 min (23:00–07:00 hr) intervals by standard data interpolation. Missing data were also filled in by data interpolation. Then, comparisons between standard HD and both BVT periods were made with a non-parametric ANOVA (Friedman) for repeated measurements. The analysis was carried out separately for 3 intervals: (A) 0–8 hr post-HD (14:00–22:00 hr), (B) 8–16 hr post-HD (22:00–06:00 hr) and (C) 16–24 hr post-HD (06:00–14:00 hr). p-values of <0.05 were considered significant.

RESULTS

Patients

The mean age (± SD) of the patient group was 64.2 ± 9.8 years (range 52–78 years). The average time (± SD) on dialysis was 4.5 ± 3.4 years (range 1.4–26.5 years). The cause of renal failure was diabetes mellitus (n=5), hypertension (n=4) and polycystic kidney disease (n=1), systemic lupus erythematosus (n=1) and acute renal failure after abdominal aortic aneurysm rupture (n=1). Seven patients had diabetes mellitus (type I: n=1; type II: n=6). All but 2 patients had significant cardiovascular comorbidity: myocardial infarction (n=4), angina pectoris New York Heart Association grade 2 or greater (n=5), heart failure (n=2), aortic valve stenosis with pressure gradients ranging from 17 to 59 mmHg (n=4), peripheral vascular disease (n=2). None of the patients were severely overhydrated at any period of the study. However, mild overhydration was suspected in 8 patients because of ankle edema (n=3), pre-HD hypertension (n=6, 2 of whom also had ankle edema) or mild cardiopulmonary congestion on chest X-ray (n=1). Six patients used cardiovascular medication: β-adrenergic blockers (n=4; indication: angina pectoris in all), nitrates (n=3), and calcium antagonists (n=2; indication: angina pectoris in both). As this medication was indicated for angina pectoris, we did not try to reduce the dose throughout the study. The medication dose and timing of administration in relation to the HD session were not changed throughout the study. β-adrenergic blockers and calcium antagonists were taken after the HD session. Three patients had residual renal function with urine volumes of 360, 480 and 800 mL/24 hr, respectively. The mean (± SD) hemoglobin and albumin levels at the start of the study were 7.4 ± 0.6 mmol/L and 37.7 ± 2.2 g/L, respectively, and did not change significantly during the study. HD access was an arteriovenous fistula or PTFE graft in 11 patients and a tunneled central venous catheter in 1 patient.

Weight, weight loss, dialysis hypotension episodes and heart size

As shown in Table 1, pre- and post-HD weight and intra-HD weight loss did not differ significantly between standard HD and either BVT-cw and BVT-rw. Although we had aimed at a lower body weight in the BVT-rw period, only modest and non-significant reductions of the pre-HD (− 0.2 kg) and post-HD weight (− 0.3 kg) were achieved at BVT-rw compared with standard HD. Dialysis hypotension necessitating a treatment intervention occurred in 64 ± 32% of the standard HD sessions and in 37 ± 21% and 28 ± 21% of the BVT treatment sessions during BVT-cw and BVT-rw, respectively (both $p<0.01$ compared with standard HD). Heart size on a standing chest X-ray did not change significantly throughout the study: the cardio-thoracic ratio on a pre-dialysis chest X-ray was 0.542 ± 0.087 and 0.535 ± 0.079 during standard HD and at the end of the BVT-rw period, respectively.

Blood pressure and heart rate during HD

As shown in Figure 1, pre-HD systolic and diastolic blood pressure and heart rate did not differ significantly between standard HD and either BVT-cw or BVT-rw. At BVT-rw, intra-HD systolic blood pressure was significantly higher from the second hour onward in comparison with standard HD. The lowest recorded systolic blood pressure was significantly lower with standard HD (95 ± 17 mmHg) than at BVT-rw (109 ± 19 mmHg; $p<0.05$) but did not differ significantly in comparison with BVT-

Table 1 Weight, weight loss, sodium levels and Kt/V during standard hemodialysis and at BVT-cw and BVT-rw (mean ± SD)

	Standard HD (n=12)	BVT-cw (n=12)	BVT-rw (n=12)
Weight (kg)			
Pre-HD	79.4 ± 15.6	79.8 ± 15.0	79.2 ± 15.5
Post-HD	77.4 ± 15.2	77.7 ± 14.8	77.1 ± 14.9
Weight loss during HD (kg)	2.0 ± 0.7	2.1 ± 0.6	2.1 ± 0.9
Plasma sodium (mmol/L)			
Pre-HD	138.6 ± 3.0	139.3 ± 3.5	138.8 ± 2.0
Post-HD	141.6 ± 1.4	141.4 ± 1.7	140.1 ± 1.6[a]
Kt/V	1.26 ± 0.17	1.28 ± 0.10	1.38 ± 0.19

[a] $p < 0.05$ compared with standard HD.

BVT-cw, blood volume tracking-constant weight; BVT-rw, blood volume tracking-reduced weight; SD, standard deviation; HD, hemodialysis.

cw (100 ± 13 mmHg). Intra-dialytic diastolic blood pressure did not differ significantly between standard HD and either BVT-cw or BVT-rw. Immediate post-HD systolic blood pressure was higher at BVT-cw (130 ± 22) and at BVT-rw (132 ± 27) compared with standard HD (120 ± 29) but the difference was not statistically significant (BVT-cw vs. standard HD: $p=0.07$; BVT-rw vs. standard HD: $p=0.15$). The immediate post-HD diastolic blood pressure at BVT-cw and BVT-rw, however, was significantly (both $p<0.05$) higher compared with standard HD.

During standard HD, the mean increase of heart rate throughout the HD session was only 5 b.p.m. In contrast, increase in heart rate was more pronounced during both BVT periods than during standard HD, although the difference at all time points was not statistically significant. The post-HD heart rate at BVT-cw and BVT-rw tended to be higher in comparison with standard HD but the difference was not significant (BVT-cw vs. standard HD: $p=0.06$; BVT-rw vs. standard HD: $p=0.10$).

Blood volume during HD

Figure 2 shows the mean RBV course during standard HD and at BVT-cw and BVT-rw. These curves should be interpreted with caution because the RBV curves are influenced by the i.v. administration of NaCl 0.9% or colloid solutions. To diminish this effect, we eliminated RBV values at the moment of and during 5 min following the i.v. administration of fluids from the analysis. The overall form of the mean RBV curve appeared to differ between standard HD and BVT. During standard HD, RBV declined rapidly during the first 30 min. Thereafter, the mean RBV curve decreased further in an almost linear manner. Only at the end of the HD session did the mean RBV curve level off because of treatment interventions for symptomatic hypotension. With BVT (both BVT-cw and BVT-rw), the mean RBV curve declined even faster during the first 30 min but was more or less stable during the last 90 min of the HD session.

At the end of the HD session, RBV did not differ significantly between standard HD (− 7.5 ± 2.1%) and either BVT-cw (− 7.4 ± 2.8%) or BVT-rw (− 7.2 ± 2.3%). In addition, there was no significant difference in the RBV nadir between standard HD (− 8.5 ± 2.2%) and either BVT-cw (− 8.4 ± 2.7%) or BVT-rw (− 9.2 ± 3.5%).

Ambulatory blood pressure measurements

The ABPM data were complete in 10 patients. One patient had atrial fibrillation during the last hour of the standard test HD session and this precluded ABPM. One other patient did not wish to undergo ABPM at BVT-rw. Figure 3 and Table 2 present the ABPM data. Figure 3 also depicts the intra-HD blood pressure and heart rate behavior in these 10 patients. At BVT-cw and BVT-rw, systolic blood pressures during the first 16 hr after the end of the HD session were significantly (both $p<0.05$) higher than following standard HD. The following morning the differences had disappeared. Diastolic blood pressures did not differ significantly between either BVT-cw or BVT-rw and standard HD. At BVT-cw and BVT-rw, heart rate during the first 4 hr after HD was slightly higher in comparison with standard HD but there were no significant differences compared with standard HD.

Sodium levels and Kt/V

As shown in Table 1, pre-HD plasma sodium levels were comparable between standard HD and both BVT-cw and

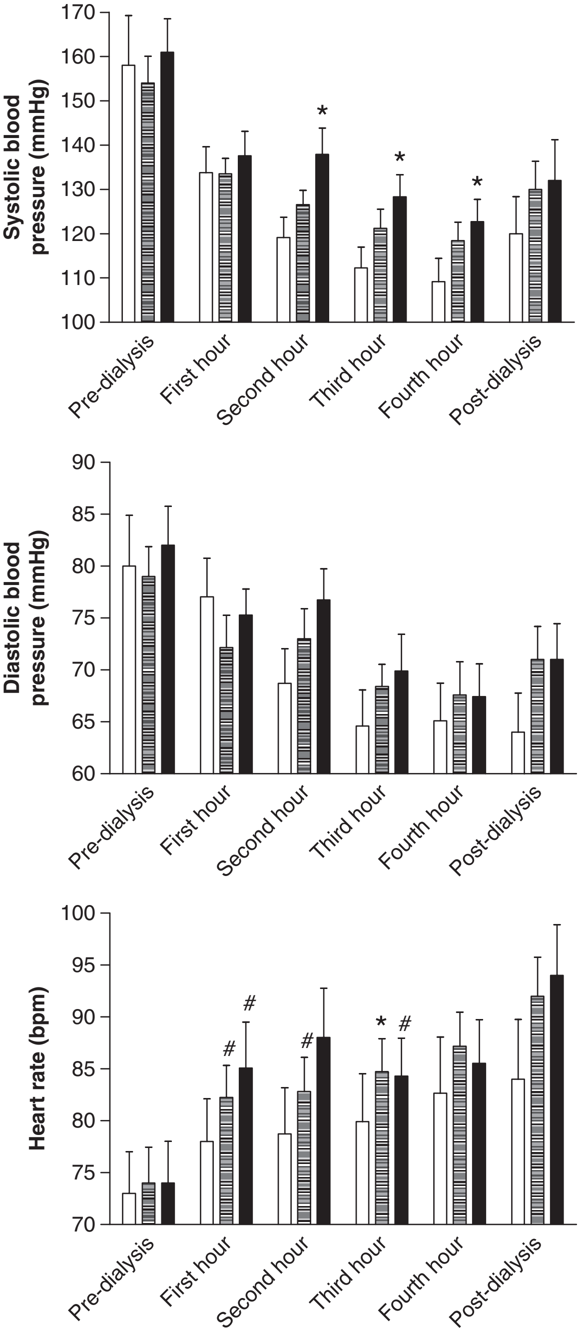

Figure 1 Pre-, intra- and immediate post-hemodialysis (HD) blood pressure and heart rate (n=12). Pre- and post-HD values represent the mean of 3 recordings before and immediately after the HD session, respectively. Intra-HD data are presented as "hourly mean values". Each hourly mean value consists of 4 separate recordings at 15 min intervals (see "Subjects and Methods"). Error bars represent the standard error of the mean. *p < 0.05 and #p = 0.05 compared with standard HD. □ Legend:Standard ▤ HD;BVT-cw; ■ BVT-rw.

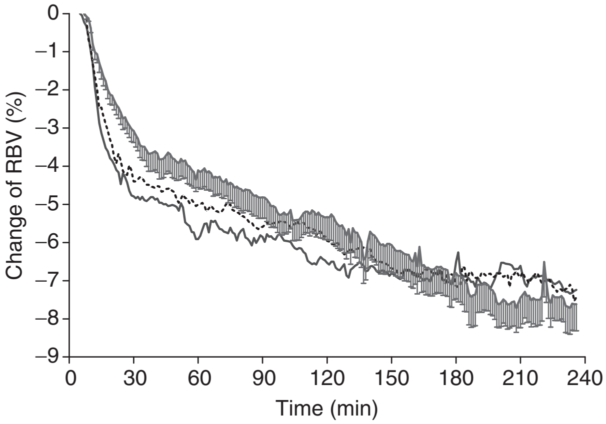

Figure 2 Mean relative blood volume (RBV) curve during standard hemodialysis (HD) and at blood volume tracking-constant weight (BVT-cw) and BVT-reduced weight (rw) (n=12). Each curve represents the mean RBV curve of 12 patients. Error bars represent the standard error of the mean. For the sake of surveyability, error bars are only shown for standard HD. Error bars were of the same magnitude for BVT-cw and BVT-rw. Legend: — Standard HD (with error bars); ---- BVT-cw; — BVT-rw.

BVT-rw. Post-HD plasma sodium levels were significantly lower at BVT-rw in comparison with standard HD. Ionic mass balance was measured in 4 patients. The mean (± SD) ionic mass balance during standard HD and at BVT-rw was 293 ± 66 and 447 ± 83 mEq, respectively (not significant). Kt/V did not differ significantly between standard HD and either BVT-cw or BVT-rw.

DISCUSSION

The present study shows that (in hypotension-prone patients) treatment with the BVT system is not only associated with better intra-HD hemodynamic stability but also with higher systolic blood pressures after the HD session in comparison with standard HD. The finding of an improved intra-HD hemodynamic stability is in line with previous studies that have shown a reduction of dialysis hypotension episodes in hypotension-prone patients during HD with BVT.[4,6,8,9,11]

The finding that HD with BVT is also associated with higher post-HD systolic blood pressures for as long as 16 hr after the end of the HD session has not been reported before. Other groups, however, have reported a reduction of post- or inter-HD symptoms with BVT. Basile *et al.*[9] were the first to show that treatment with BVT reduced post-HD asthenia in comparison with standard HD. Two other groups have reported that HD with BVT

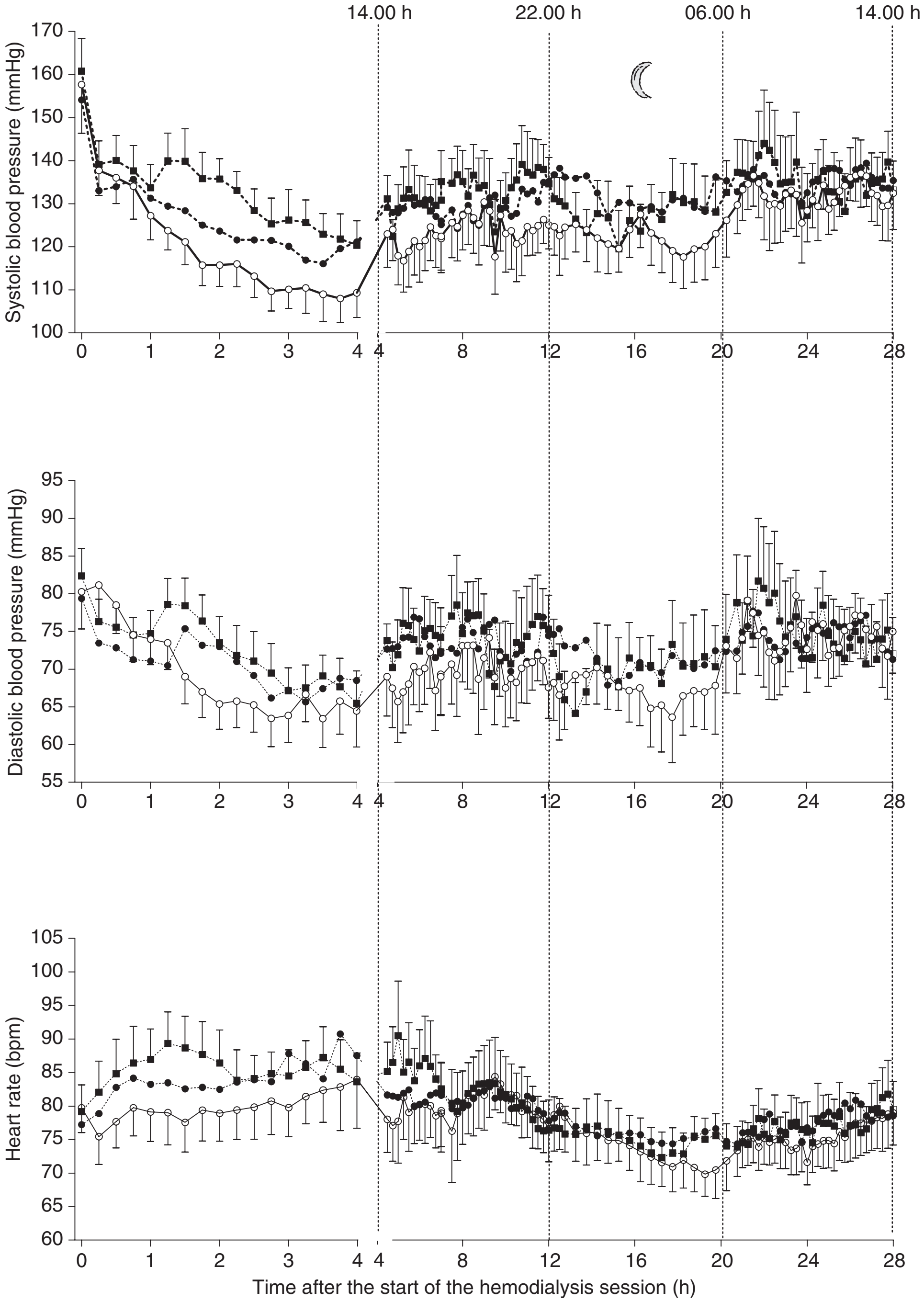

Figure 3 Intra-hemodialysis (HD) and 24 hr post-HD ambulatory blood pressure measurement (ABPM) blood pressure and heart rate data in the 10 patients in whom all three 24 hr ABPM were available for analysis. The left panel depicts the intra-HD data in these patients, and the right panel shows the post-HD data obtained with 24 hr ABPM. Error bars represent the error of the mean. For the sake of surveyability, error bars are shown only for standard HD and blood volume tracking-reduced weight. See Table 2 for statistical comparison between standard HD and BVT. Legend: –○– Standard hemodialysis; ··●·· HC-cw; --■-- HC-rw.

Table 2 Twenty-four hour ABPM following a standard hemodialysis session or following an automatic feedback dialysis session at BVT-cw and BVT-rw (mean ± SD)

	Standard HD (n = 10)	BVT-cw (n = 10)	BVT-rw (n = 10)
Systolic blood pressure			
0–8 hr post-HD (14:00–22:00 hr)	124 ± 21	130 ± 23[a]	133 ± 18[a]
8–16 hr post-HD (22:00–6:00 hr)	123 ± 22	132 ± 31[a]	128 ± 20[a]
16-24 hr post-HD (06:00–14:00 hr)	132 ± 21	135 ± 33	135 ± 25
Diastolic blood pressure			
0–8 hr post-HD (14:00–22:00 hr)	70 ± 14	74 ± 14	74 ± 13
8–16 hr post-HD (22:00–06:00 hr)	68 ± 15	71 ± 19	70 ± 13
16–24 hr post-HD (06.00–14.00 hr)	75 ± 15	74 ± 19	75 ± 17
Heart rate			
0–8 hr post-HD (14:00–22:00 hr)	80 ± 16	81 ± 13	82 ± 15
8–16 hr post-HD (22:00-06:00 hr)	73 ± 12	76 ± 12	75 ± 12
16-24 hr post-HD (06:00–14:00 hr)	76 ± 13	78 ± 11	77 ± 12

[a] $p < 0.05$ compared with standard HD.

BVT-cw, blood volume tracking-constant weight; BVT-rw, blood volume tracking-reduced weight; SD, standard deviation; HD, hemodialysis; ABPM, ambulatory blood pressure measurement.

was associated with a reduction of the combined endpoint of miscellaneous inter-dialytic symptoms (cramps, nausea, headaches and the need to lie down), some of which may well be related to post-HD hypotension.[10,12] We think that the higher post-HD systolic blood pressures with BVT treatment may well explain the improvement of these post- or inter-HD symptoms.

Despite the improved hemodynamic stability and the reduction of dialysis hypotension episodes during BVT treatment, it was not possible to lower post-dialysis weight substantially during the second BVT treatment phase. Weight may not have been the best marker for hydration status. Unfortunately, we did not perform detailed studies on the hydration status, e.g., by bioimpedance studies. However, the combination of clinical assessment and the unchanged cardiothoracic ratio (chest X-ray) throughout the study makes us confident that hydration status in any case did not increase throughout the study. The failure to reduce post-HD weight in this study implies that for adequate control of the hydration status in such severely hypotension-prone patients, a different dialysis regimen is needed, e.g., more frequent and/or longer HD sessions.

The mechanism of the improved intra- and post-HD hemodynamic stability with BVT is not completely understood. The higher blood pressure cannot be explained by better RBV preservation as RBV reductions did not differ significantly between standard HD and BVT. Other studies with BVT have reported divergent results with regard to the relationship between hemodynamic stability and the course of RBV. Some groups[6–8] have reported a slightly (but not significantly) better RBV preservation with BVT, whereas we and others found that the better hemodynamic stability with BVT was not paralleled by better RBV preservation in comparison with standard HD.[9,12] However, not only the mere level but also the rate of decrease of RBV determines the risk of intra-HD hypotension.[15] Therefore, although in most studies the mean RBV reductions did not differ between BVT and standard HD, it is possible that treatment with BVT exerted its favorable hemodynamic effect by preventing rapid RBV fluctuations, as has been suggested by other authors.[6,7]

In addition, the form of the RBV curve during HD with BVT may be an important determinant of hemodynamic stability. Santoro *et al.*[6] have shown that HD with BVT is associated with a more rapid initial decline of RBV and with a more stable RBV during the second part of the HD session in comparison with standard HD, which was confirmed in our study. The rapid initial RBV reduction is caused by a relatively high ultrafiltration rate in the first half of the HD session, and this—together with a relatively high dialysate conductivity during the first part of the HD session—favors plasma refill and may, thus, contribute to the more stable RBV curve in the second part of the HD session.[8] The relatively stable RBV curve during this hemodynamically most critical phase of the HD session probably favors intra-HD hemodynamic stability.[6,8]

The fact that there is no constant relationship between RBV reductions and the development of hypotension in BVT[9] as well as in non-BVT[16,17] HD sessions emphasizes the importance of other factors that render certain patients susceptible to this complication.[18] These include inappropriate activation of cardiovascular reflexes, left ventricular hypertrophy and diastolic dysfunction and abnormal vascular compliance.[18] In the present study, heart rate during standard HD sessions rose only slightly (mean increase 5 b.p.m.), which can be considered an inappropriate heart rate response in the light of the pronounced intra-HD systolic hypotension. Interestingly, increase in intra-HD heart rate was more pronounced during treatment with BVT. The mechanism of this increased heart rate response is not clear but may have contributed to the improved intra-HD and post-HD hemodynamic stability with BVT. The higher heart rate may reflect an overall increase of sympaticoexcitation and may, thus, coincide with improved venous and arteriolar vasoconstriction, each of these factors contributing to a higher intra-dialytic blood pressure.

One of the major differences between BVT and standard HD is the relatively high dialysate conductivity, especially during the first part of the HD session. Apart from plasma volume preservation, the use of high sodium dialysate seems to have a beneficial effect on blood pressure behavior.[6] Straver *et al*.[19] found that HD with a decreasing sodium profile was associated with improved blood pressure preservation, remarkably without a significant difference in RBV preservation compared with standard HD, because of a higher cardiac stroke volume in the first hour of the HD session. It can be hypothesized that modification of the intra-vascular sodium concentration may increase sympathetic activity with a consequently better hemodynamic response as has been suggested by Santoro *et al*.[8] Other groups, however, did not find a favorable effect of increased dialysate conductivity on intra-HD blood pressure or vascular reactivity.[20]

In finding that HD with BVT is associated with higher post-HD systolic blood pressures for as long as 16 hr after the end of the HD session cannot be readily explained. Two possible explanations are as follows: (1) treatment with BVT is associated with a better intra-HD and, consequently, probably also a better post-HD equilibrium between the intra-vascular and the interstitial space and (2) stress of a dialysis hypotension episode necessitates a recovery period during which the autonomic nervous system is less excitable to counteract low blood pressure by adequately increasing heart rate and/or vasoconstriction. According to this hypothesis, the marked reduction of dialysis hypotension episodes during treatment with BVT might favor autonomic regulation during and after the HD session.

One may argue that the higher systolic blood pressure persisting for hours after the HD session may have a deleterious effect on the cardiovascular system. However, the patients in this study suffered from frequent episodes of dialysis hypotension, which probably carries a greater risk for cardiac, cerebral or mesenteric ischemic events[2,3] than the 5–10 mmHg higher systolic blood pressure during the first 16 hr post-dialysis. Moreover, pre-HD blood pressures were not higher during the BVT-cw and BVT-rw periods than during standard HD.

In any HD technique with variable dialysate sodium concentrations, there is a theoretical risk of "sodium loading" of the patient. We did not find evidence of sodium loading in our study. With BVT (both periods), pre-dialysis sodium levels did not differ with levels at standard HD and at BVT-rw post-HD sodium levels were even lower than with standard HD. Thus, improved intra- and post-HD hemodynamic stability with BVT cannot be explained by higher sodium levels.

In conclusion, HD with BVT attenuates not only intra-HD but also post-HD hypotension in hypotension-prone dialysis patients. BVT was not effective in reducing the post-HD target weight in this patient group.

Conflict of interest

None of the authors has had involvement that might raise the question of bias in the work reported or in the conclusions, implications or opinions stated.

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